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Factors associated with potentially problematic opioid prescriptions among individuals with private insurance and medicaid

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HIGHLIGHTS

- Private insurance enrollees with problematic opioid prescription were eight times more likely to develop OUD.
- Medicaid enrollees with problematic opioid prescription were three times more likely to develop OUD.
- Health plan, ED visits, mental health diagnosis associated with problematic opioid prescription: private insurance enrollees.
- Non-Hispanic White, ED visits, mental health diagnosis associated with problematic opioid prescription: Medicaid enrollees.

ABSTRACT

If opioid analgesics are prescribed and used inappropriately, they can lead to addiction and other adverse effects. In this study, we (1) examine factors associated with potentially problematic opioid prescriptions and (2) quantify the link between potentially problematic prescriptions and the development of opioid use disorder. We found that older age; female sex; having back pain, arthritis, or migraine; hydrocodone prescription; previous pharmacotherapy for opioid use disorder; and frequent emergency department use were associated with problematic prescriptions among individuals with Medicaid and private insurance. Patients with commercial insurance and Medicaid who had potentially problematic opioid prescriptions were eight and three times more likely, respectively, to develop an opioid use disorder than patients without potentially problematic opioid prescriptions. Our findings help identify factors associated with problematic prescriptions and underscore the importance of targeted public health interventions.

1. Introduction

Recent estimates indicate that health care providers wrote 259 million prescriptions for opioid analgesics (Paulozzi, Mack, & Hockenberry, 2014), nearly enough prescriptions for every adult in the United States (U.S. Census Bureau, 2012). These prescriptions, intended for therapeutic use, are sometimes misused for their euphoric effects and can lead to addiction and overdose (SAMHSA, 2009). Studies have documented a correlation between opioid prescriptions per capita and opioid-related deaths (Modarai et al., 2013). This suggests that opioid prescriptions might have contributed to the opioid crisis (Centers for Disease Control and Prevention, 2016; Frenk, Porter, & Paulozzi, 2015; Paulozzi, Jones, Mack, & Rudd, 2011; Rudd, Seth, David, & Scholl, 2016). Recent guidelines recommend that providers exercise caution when prescribing opioids, such as providing minimum adequate dose and duration, and avoid extended-release forms that are easier to abuse (Dowell, Haegerich, & Chou, 2016).

Patients who are exposed to potentially problematic opioid prescriptions are at higher risk for opioid misuse and overdose (Bohnert et al., 2011; Dunn et al., 2010; Jann, Kennedy, & Lopez, 2014; Park, Saitz, Ganoczy, Ilgen, & Bohnert, 2015; Peirce, Smith, Abate, & Halverson, 2012; White, Birnbaum, Schiller, Tang, & Katz, 2009). Markers of potentially problematic opioid prescriptions include (1) high-dose opioids, (2) opioids from multiple prescribers, (3)

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overlapping opioid prescriptions, (4) overlapping opioid and benzodiazepine prescriptions, and (5) long-acting/extended-release forms for acute pain.

There has been little empirical work examining factors associated with potentially problematic opioid prescriptions. Understanding these factors may help providers and policy makers identify patients at high risk for opioid misuse for additional screening or targeted interventions. Previous studies focusing on factors associated with opioid overdose have found that males, younger adults, patients with concurrent mental health diagnoses, a history of prior illicit opioid use, and higher levels of psychological distress are at greater risk of opioid misuse (Adams et al., 2004; Arteta, Cobos, Hu, Jordan, & Howard, 2016; Cochran et al., 2014; Dilokthornsakul et al., 2016; Edlund, Steffick, Hudson, Harris, & Sullivan, 2007; Hah, Sturgeon, Zocca, Sharifzadeh, & Mackey, 2017; Ives et al., 2006; Manchikanti et al., 2007; Rice et al., 2012; Zedler et al., 2014).

In this study, we examine patient-level factors associated with five types of potentially problematic opioid prescriptions: high-dose opioids (i.e., greater than or equal to 120 morphine milligram equivalents [MMEs]) for 90 or more consecutive days, overlapping opioid prescriptions, overlapping opioid and benzodiazepine prescriptions, opioids from multiple prescribers, and long-acting/extended-release opioids for acute pain. These patient-level factors include demographic, clinical, and utilization characteristics that previous research indicates may be related to opioid misuse. In addition, we estimate the percentage of individuals with potentially problematic opioid prescriptions who subsequently develop an opioid use disorder.

Previous studies have examined the impact of different factors on opioid use, opioid use disorder, or high-dose opioids (Cochran et al., 2014; Morasco, Duckart, Carr, Deyo, & Dobscha, 2010) without much attention to potentially problematic opioid prescriptions. This study identifies patient factors associated with problematic opioid prescriptions, which may be more actionable for the development of interventions. Also, this study estimates the percentage of people with potentially problematic opioid prescriptions who subsequently develop an opioid use disorder in the following 12 months.

2. Conceptual framework

Health care consumption can be considered a function of predisposing factors, enabling factors, and need (Andersen, 1995). Individuals who misuse opioids may be more likely or predisposed to seek opioid prescriptions from multiple doctors, higher doses, extended release forms, and co-prescriptions of benzodiazepine to enhance the euphoric effects of opioids. Previous studies have found that older age, male sex, white race, and history of opioid misuse are positively associated with a higher rate of having an opioid prescription and opioid misuse (Cochran et al., 2014; Morasco et al., 2010). Also, some individuals who are frequent emergency department (ED) users may be seeking opioid analgesics for nonmedical use (Wilsey, Fishman, & Ogden, 2005). The type of opioid prescribed may predispose individuals to become addicted, misuse, or seek potentially problematic opioid prescriptions (Alpert, Powel, & Pacula, 2017).

Individuals with an insurance plan that has lower out-of-pocket costs may be better able to visit more providers and receive multiple prescriptions for opioids. Individuals living in certain parts of the country also may have access to pain clinics and prescribers who tend to prescribe larger quantities of opioids. Therefore, health plan type and state of enrollees' residence may be associated with potentially problematic opioid prescriptions.

Finally, individuals who have severe or complex health issues may have the most need for pain relief and thus be at risk for potentially problematic opioid prescriptions. Specifically, type of pain (i.e., diagnosis), chronicity of pain (i.e., acute or chronic), and number of chronic conditions may reflect individual need and may be linked to potentially problematic opioid prescriptions.

3. Methods

3.1. Data sources

We used the IBM MarketScan® Commercial Claims and Encounters Database and the IBM MarketScan® Multi-State Medicaid Database for the years 2005 through 2015. The MarketScan Commercial Database includes insurance claims from employees and dependents covered by large, self-insured employers and by regional health plans. This database captures all billed services, including prescription drugs, outpatient services, and inpatient services. It consists of data from about 100 payers and health plans covering approximately 50 million enrollees. The MarketScan Medicaid Database contains claims of approximately 6 million Medicaid enrollees from multiple states.

3.2. Sample population and setting

The study population was comprised of private insurance and Medicaid enrollees aged 18–64 years with at least one valid opioid prescription in 2005 through 2015. We defined a valid opioid prescription as any Schedule II–IV opioid pain medication with a valid days' supply (1–365 days) and number of pills (>0). We excluded opioid pharmacy claims that appeared invalid (days' supply ≤ 0 or >365 or pill quantity ≤ 0) or were outliers (pill quantity $\geq$ 99th percentile). Enrollees with any invalid opioid prescription were excluded from the study.

We required individuals to have continuous enrollment at least 6 months before and 12 months after the date of their first opioid prescription (index date). Individuals with hospice claims or cancer diagnoses prior to their index date were excluded. We also excluded individuals who were dually eligible for Medicare and Medicaid because we did not have their complete pharmacy claims. After applying these exclusion criteria, we identified 4,535,623 and 1,604,143 unique enrollees with a valid opioid prescription for commercial insurance and Medicaid analysis, respectively.

4. Measures

4.1. Demographics

The enrollees' age (18–64 years), sex, state of residence, and health plan type were obtained from enrollment information at the index date. Health plans were categorized into three groups: health maintenance organization (HMO), preferred provider organization (PPO), and a high-deductible health plan (HDHP) or consumer driven health plan (CDHP). We also obtained race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other) from the Medicaid enrollment data; we did not have complete race/ethnicity measures for individuals with commercial insurance.

4.2. Opioid type

Table 1 lists all included opioids and the associated morphine milligram equivalent (MME) conversion factor for each drug. We included combination drugs, which we identified according to the opioid ingredient. For example, the codeine group included codeine, codeine/acetaminophen, and codeine/aspirin. We grouped opioid types into three categories for the models: oxycodone, hydrocodone, and other. We chose this categorization because oxycodone and hydrocodone are the most prescribed and abused opioid pain medications (National Institute on Drug Abuse, 2014).

4.3. Pain characteristics and comorbid conditions

MarketScan pharmacy claims do not include information on the prescriber or the reason (diagnosis) for the prescription. Therefore, to

Table 1
Opioid pain medications and morphine equivalent conversion factors per milligram.

Opioid drug type	Morphine equivalent conversion factor
Butorphanol	7.00
Codeine	0.15
Dihydrocodeine	0.25
Fentanyl	
Fentanyl buccal or sublingual tablets or lozenge/troche	0.13
Fentanyl film or oral spray	0.18
Fentanyl nasal spray	0.16
Fentanyl (transdermal) patch, extended-released	7.20
Hydrocodone	1.00
Hydromorphone	4.00
Levorphanol	11.00
Meperidine	0.10
Methadone	3.00
Morphine	1.00
Oxycodone	1.50
Oxymorphone	3.00
Pentazocine	0.37
Propoxyphene	0.23
Tapentadol	0.40
Tramadol	0.10

Note: Conversion factors are from the Centers for Medicare and Medicaid Services (2015).

determine the likely prescriber and the diagnosis associated with the opioid prescription, we looked back 7 days from the date of each opioid prescription to identify the inpatient, outpatient, or ED claim that occurred closest to the fill date. We assigned the provider ID on that claim to the opioid prescription. We used the diagnoses on this most recent claim to identify the pain type (i.e., back pain, arthritis, joint disorders, fractures, migraine, other) associated with the opioid prescription. To distinguish between acute and chronic pain, we used the Chronic Condition Indicator, a diagnosis classification tool developed as part of the Healthcare Cost and Utilization Project (Healthcare Cost and Utilization Project, 2016) to categorize pain as acute or chronic on the basis of patient diagnosis. If there were no outpatient, inpatient, or ED claims 7 days prior to the prescription fill date, we recorded the diagnosis and acute/chronic indicator as missing. If there was an inpatient and an outpatient service within the prior 7 days, we used the outpatient claim to identify the diagnosis that led to the prescription. For refills, we assigned the prescriber and diagnosis from the initial fill. If a person had multiple outpatient or ED visits 7 days prior to an opioid prescription fill, we attributed the prescription fill to the most recent visit that occurred on the day closest to the drug dispensing date.

We used all inpatient, outpatient, and pharmacy claims from the 6-month period prior to the first opioid prescription fill to identify comorbidities and mental illness. Mental illness included anxiety, mood, cognitive, adjustment, personality or disruptive behavior disorders, dementia, and schizophrenia or psychotic disorders. Comorbidities, as defined by the Clinical Classification Software, included HIV, diabetes, hypertension, hypercholesterolemia, asthma/chronic obstructive pulmonary disease, and heart problems. These are the most commonly reported conditions among opioid users (Wadland & Ferenchick, 2004). We created an index by counting the number of aforementioned comorbidities identified (i.e., 0, 1, 2, and 3 or more).

4.4. Health care utilization

We defined pharmacotherapy for opioid use disorder as receipt of buprenorphine, methadone, naltrexone, or buprenorphine/naloxone. We only included methadone claims that were specifically for treating substance use disorders by using Healthcare Common Procedure Coding System service codes. For individuals without any indicators of problematic opioid prescriptions, we looked for pharmacotherapy in the 12 months after their first opioid fill. For individuals who had problematic opioid prescriptions, we looked at the timeframe between the first opioid fill and the first indicator of potentially problematic opioid prescription. We defined frequent ED use as the presence of 3 or more ED visits at any point in the calendar year.

5. Outcomes

5.1. Potentially problematic opioid prescriptions

Outcomes consisted of five indicators of potentially problematic opioid prescriptions: (1) 90-day prescriptions of greater than or equal to 120 MME, (2) prescriptions from 3 or more providers, (3) opioid overlap with other opioids, or (4) opioid overlap with benzodiazepines, and (5) prescriptions of long-acting/extended-release opioids for acute pain. We also created a dichotomous variable to indicate whether the individual had any of these five indicators in the 12 months following the index date.

We defined high-dose opioids as opioid fills of $>$ 120 MME for 90 or more consecutive days. We calculated the daily dose of each opioid prescription by dividing the quantity of each prescription by its days' supply. We multiplied that number by the drug strength to calculate daily total dose. We converted this number to MME (Table 1) using the Centers for Medicare and Medicaid Services (2015) conversion factors. If there were overlapping opioid prescriptions, we summed the daily MME for each prescription.

To identify long-acting opioid prescriptions written for acute pain, we used the National Drug Code to distinguish long-acting/extended-release opioids from immediate-release opioids. To identify opioid-opioid overlap, we calculated the number of overlap days using reported days' supply. Consistent with the literature (Liu, Logan, Paulozzi, Zhang, & Jones, 2013; Mack, Zhang, Paulozzi, & Jones, 2015), we identified cases in which patients filled or refilled an opioid drug while they still had 7 or more days' supply. We applied the same rule to identify opioid-benzodiazepine overlap. To identify multiple providers, we counted the number of unique prescriber IDs associated with the opioid fill for each person in each year. We categorized individuals with three or more opioid prescribers as having multiple prescribers. All these indicators were created using the first opioid date as the index date. For example, if a patient had three or more opioid prescribers within 12 months after the index date, we categorized the person as having multiple prescribers. These five indicators were adopted from Ali, Henke et al., 2019, Ali, Mutter et al., 2019, who include a more detailed analysis of these indicators.

5.2. Opioid use disorder

To identify opioid use disorder in the 12 months following the first date of potentially problematic opioid prescriptions, we examined all inpatient and outpatient claims and flagged individuals who had a diagnosis for opioid abuse, dependence, poisoning, or adverse effects. We identified these conditions using diagnosis codes from the International Classification of Diseases, Ninth Revision, Clinical Modification (304.0×, 304.7×, 305.5×, 965.00, 965.02, 965.09, E850.01, E850.2, E935.1, or E935.2) and the International Classification of Diseases, Tenth Revision, Clinical Modification (F11.xx, T40.2Xx, T40.3Xx, R78.1).

6. Analysis

We estimated multivariable logistic regression models to measure the association between patient factors and any potentially problematic opioid prescriptions. We also estimated models for each type of potentially problematic opioid prescription separately. All models

included age, sex, chronicity of pain, specific type of pain diagnosis, number of comorbidities, frequency of ED use, diagnosis of mental illness, health plan type, receipt of pharmacotherapy for substance use disorders, opioid type, state, and year as covariates. However, we did not include chronicity of pain in the model that measured long-acting opioid for acute pain because the sample was limited to patients without chronic pain. The Medicaid analysis also included race/ethnicity.

The equation below represents the basic structure of the regression model:

$$Yi = \beta_0 + \beta_1 SEXi + \beta_2 AGEi + \beta_3 CHRONIC + \beta_4 DIAGNOSIS + B_5 COMORBID + \beta_6 DRUG + \beta_7 MH + \beta_8 MAT + \beta_9 ED + \beta_{10} PLAN + \beta_{11} RACE + \gamma c + \varepsilon i$$

In this model, *i* denotes an individual, and *Y* refers to the indicators of potentially problematic opioid prescriptions. *SEX* is a binary measure for sex (1 for male). *AGE* is a categorical variable defined as 18–24 (reference), 25–34, 35–44, 45–54, or 55–64 years. *CHRONIC* is a binary variable for chronicity of pain (1 if chronic). *DIAGNOSIS* is a categorical variable representing pain diagnosis defined as back pain, migraine, joint disorders, arthritis, neck pain, or other (reference). *COMORBID* is a categorical variable representing a count of comorbid conditions defined as 0 (reference), 1, 2, or 3 or more conditions. *DRUG* is a categorical variable representing the type of the first opioid pain medication. It is defined as oxycodone, hydrocodone, or other (reference). *MH* is a binary vector for the diagnosis of mental illness (1 if the individual has any diagnosis for mental illness). *MAT* is a binary variable measuring receipt of pharmacotherapy foropioid use disorders (1 if the individual received pharmacotherapy after their initial prescription). *ED* is a binary indicator of frequent ED visits (1 if the individual had 3 or more visits in a year). *PLAN* is a categorical variable representing the type of health plan coverage. It is defined as an HMO (reference), a PPO, or a HDHP/CDHP. *RACE* is a categorical variable representing race and ethnicity defined as non-Hispanic white (reference), non-Hispanic black, Hispanic, and other. This variable is included only in the Medicaid analysis. State and year fixed-effects are represented by γc.

As a second step, we calculated the number and percentage of enrollees with any potentially problematic opioid prescription who had a diagnosis of opioid use disorder in the 12 months after the first date of any potentially problematic opioid prescription. We repeated this calculation for each type of potentially problematic prescription. We also calculated the same information for enrollees who had an opioid prescription but did not have any instances of a potentially problematic prescription for comparison.

To test the sensitivity of findings to the data, we repeated all analyses limiting the Medicaid sample to states that continuously contributed data to the MarketScan Medicaid database. For the commercial insurance analysis, we limited the sample to continuously contributing commercial clients in states continuously contributing to the MarketScan Medicaid database. The results of the sensitivity analyses are similar to what are reported here and are available from the authors upon request.. All analyses were conducted using SAS® Analytics Software, version 9.4 (Cary, NC).

7. Results

7.1. Sample description

Among the commercially insured population who received at least one opioid prescription, 41.7% were male and the average age was 43.3 years (Table 2). On average, 64.6% received two or more opioid prescriptions within the 12 months following their first opioid prescription, with the average number of prescriptions being 4.8. During a 12-month period following their first opioid prescription, 20.3% had at least one indicator for a potentially problematic opioid prescription. Prescription overlaps were the most common indicators, with 10.1% having opioid-opioid overlap and 9.2% having opioid-benzodiazepine overlap. In this sample, 7.5% received opioid prescriptions from three or more prescribers, 1.7% received high-dose opioids for 90 or more consecutive days, and 1.4% received long-acting/extended-release opioids for acute pain conditions.

Table 2
Patient demographics and opioid drug use among medicaid and commercially insured enrollees with an opioid prescription, 2005–2015.

Characteristic	Commercial population		Medicaid population	
	N	%	N	%
Total	4,535,623	100.0	1,604,143	100.0
Age				
18–24	383,050	8.5	450,655	28.1
25–34	789,783	17.4	451,005	28.1
35–44	1,055,653	23.3	300,031	18.7
45–54	1,329,946	29.3	247,300	15.4
55–64	977,191	21.5	155,152	9.7
Mean	43.3		34.6	
Sex				
Female	2,645,317	58.3	1,192,934	74.4
Male	1,890,306	41.7	411,209	25.6
Race/ethnicity				
White, non-Hispanic	NA	NA	943,763	58.8
Black, non-Hispanic	NA	NA	520,203	32.4
Hispanics	NA	NA	29,274	1.8
Other	NA	NA	110,903	6.9
Opioid fills 12 months after first prescription				
1	1,609,162	35.5	463,120	28.9
2	882,734	19.5	279,055	17.4
3 or more	2,043,738	45.1	861,968	53.7
Mean	4.8		6.1	
Potentially problematic opioid prescriptions[a]				
Any type	918,956	20.3	409,801	25.6
High-dose opioids	77,181	1.7	22,366	1.4
Multiple providers	339,635	7.5	113,542	7.1
Opioid-opioid overlap	456,282	10.1	231,581	14.4
Opioid-BZD overlap	416,129	9.2	209,040	13.0
Long-acting opioid for acute pain	64,529	1.4	33,845	2.1

Abbreviations: BZD, benzodiazepine; NA, not available.
Note: Percentages may not sum to 100% because of rounding issues.
[a] Patients with potentially problematic opioid prescriptions can have more than one type, so the numbers sum to more than the total number of potentially problematic opioid prescriptions.

Among the Medicaid sample who received at least one opioid prescription, 25.6% were male and the average age was 34.6 years (Table 2). Most were non-Hispanic white (58.8%), with 32.4% being non-Hispanic black and 1.8% being Hispanic. On average, 71.1% received two or more opioid prescriptions in the 12 months following their first prescription, with the average number of prescriptions being 6.1. During a 12-month period following their first opioid prescription, 25.6% had at least one indicator for a potentially problematic opioid prescription. The most common type of potentially problematic prescription was opioid-opioid overlap, which was present for 14.4% of the sample, followed by 13.0% who had an opioid-benzodiazepine overlap. Among the remaining indicators, 7.1% received opioid prescriptions from three or more prescribers, 2.1% received long-acting/extended-release opioids for acute pain conditions, and 1.4% received high-dose opioids for 90 or more consecutive days.

Table 3
Adjusted odds ratios associated with potentially problematic opioid prescriptions among individuals with commercial insurance, 2005–2015.

Variables (reference value)	Any potentially problematic opioid prescription (*N* = 918,956)		Specific potentially problematic opioid prescriptions									
			High-dose opioid (*N* = 77,181)		Multiple providers (*N* = 339,635)		Opioid-opioid overlap (*N* = 456,282)		Opioid-BZD overlap (*N* = 416,129)		Long-acting opioids for acute pain (*N* = 64,529)	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Sex (Female)												
Male	0.86 (0.83–0.88)	< 0.0001	1.31 (1.24–1.37)	< 0.0001	0.84 (0.82–0.86)	< 0.0001	0.99 (0.95–1.02)	0.398	0.65 (0.63–0.67)	< 0.0001	1.08 (1.06–1.10)	< 0.0001
Age group (18–24)												
25–34	1.80 (1.72–1.88)	< 0.0001	2.76 (2.50–3.05)	< 0.0001	1.50 (1.43–1.57)	< 0.0001	2.23 (2.15–2.31)	< 0.0001	2.34 (2.24–2.44)	< 0.0001	1.04 (1.00–1.09)	0.047
35–44	2.78 (2.65–2.90)	< 0.0001	5.05 (4.49–5.67)	< 0.0001	1.99 (1.90–2.08)	< 0.0001	3.62 (3.51–3.73)	< 0.0001	3.99 (3.86–4.13)	< 0.0001	1.22 (1.17–1.27)	< 0.0001
45–54	3.77 (3.56–4.00)	< 0.0001	6.88 (6.04–7.85)	< 0.0001	2.40 (2.28–2.53)	< 0.0001	4.85 (4.67–5.03)	< 0.0001	5.59 (5.35–5.83)	< 0.0001	1.37 (1.31–1.43)	< 0.0001
54–64	4.16 (3.91–4.43)	< 0.0001	5.77 (5.02–6.63)	< 0.0001	2.51 (2.31–2.73)	< 0.0001	5.14 (4.92–5.37)	< 0.0001	5.91 (5.62–6.21)	< 0.0001	1.56 (1.49–1.64)	< 0.0001
Specific pain diagnosis (Other)												
Back pain	1.99 (1.78–2.22)	< 0.0001	2.05 (1.88–2.23)	< 0.0001	2.49 (1.82–3.41)	< 0.0001	1.67 (1.58–1.76)	< 0.0001	1.60 (1.52–1.69)	< 0.0001	1.69 (1.59–1.79)	< 0.0001
Arthritis	2.59 (2.22–3.01)	< 0.0001	2.29 (1.97–2.67)	< 0.0001	2.85 (2.04–3.98)	< 0.0001	2.41 (2.23–2.62)	< 0.0001	1.62 (1.47–1.79)	< 0.0001	1.45 (1.23–1.69)	< 0.0001
Joint disorders	0.89 (0.79–1.00)	0.061	0.52 (0.47–0.58)	< 0.0001	1.45 (1.07–1.96)	0.015	0.60 (0.57–0.63)	< 0.0001	0.74 (0.71–0.77)	< 0.0001	1.73 (1.65–1.81)	< 0.0001
Fractures	1.09 (0.94–1.27)	0.26	0.19 (0.16–0.23)	< 0.0001	1.76 (1.27–2.45)	0.001	0.48 (0.45–0.52)	< 0.0001	0.45 (0.42–0.48)	< 0.0001	7.00 (6.49–7.55)	< 0.0001
Migraine	1.36 (1.20–1.53)	< 0.0001	0.81 (0.70–0.93)	0.004	1.88 (1.36–2.60)	< 0.0001	0.93 (0.86–0.99)	0.032	1.39 (1.30–1.49)	< 0.0001	1.23 (1.13–1.34)	< 0.0001
Chronicity of pain (Acute)												
Chronic	0.80 (0.75–0.86)	< 0.0001	0.66 (0.60–0.72)	< 0.0001	0.91 (0.66–1.24)	0.537	0.81 (0.77–0.84)	< 0.0001	0.78 (0.75–0.81)	< 0.0001	—[a]	—[a]
Comorbidity (0)												
1	1.67 (1.60–1.74)	< 0.0001	1.77 (1.58–1.98)	< 0.0001	1.75 (1.65–1.84)	< 0.0001	1.72 (1.62–1.84)	< 0.0001	1.75 (1.62–1.88)	< 0.0001	1.07 (0.99–1.15)	0.052
2	1.93 (1.82–2.04)	< 0.0001	2.19 (1.92–2.51)	< 0.0001	2.09 (1.92–2.27)	< 0.0001	2.06 (1.88–2.26)	< 0.0001	2.09 (1.88–2.31)	< 0.0001	0.83 (0.77–0.89)	< 0.0001
3 or more	2.19 (2.02–2.37)	< 0.0001	2.71 (2.27–3.24)	< 0.0001	2.46 (2.18–2.77)	< 0.0001	2.43 (2.16–2.73)	< 0.0001	2.43 (2.12–2.78)	< 0.0001	0.68 (0.64–0.72)	< 0.0001
Type of first opioid drug (Other)												
Oxycodone	1.04 (0.99–1.08)	0.09	1.97 (1.78–2.17)	< 0.0001	1.01 (0.97–1.05)	0.612	1.09 (1.04–1.13)	< 0.0001	1.16 (1.11–1.21)	< 0.0001	1.48 (1.42–1.55)	< 0.0001
Hydrocodone	0.71 (0.68–0.73)	< 0.0001	0.21 (0.19–0.23)	< 0.0001	0.88 (0.85–0.90)	< 0.0001	0.56 (0.54–0.58)	< 0.0001	0.82 (0.80–0.84)	< 0.0001	1.01 (0.98–1.04)	0.622
Health plan (HMO)												
PPO	1.09 (1.02–1.17)	0.014	1.10 (0.96–1.27)	0.172	1.01 (0.81–1.27)	0.91	1.13 (1.08–1.18)	< 0.0001	1.15 (1.11–1.20)	< 0.0001	1.05 (0.99–1.11)	0.068
HDHP or CDHP	0.89 (0.77–1.02)	0.107	0.73 (0.65–0.81)	< 0.0001	0.85 (0.50–1.45)	0.554	0.91 (0.85–0.97)	0.007	0.92 (0.87–0.96)	0.001	1.04 (0.98–1.11)	0.229
Mental illness (No)												
Yes	1.13 (0.97–1.33)	0.12	1.08 (0.75–1.54)	0.687	0.96 (0.81–1.12)	0.584	1.13 (0.88–1.44)	0.336	1.04 (0.81–1.33)	0.769	2.57 (2.23–2.95)	< 0.0001

(*continued on next page*)

Table 3 (*continued*)

Variables (reference value)	Any potentially problematic opioid prescription (*N* = 918,956)		Specific potentially problematic opioid prescriptions							
			High-dose opioid (*N* = 77,181)		Multiple providers (*N* = 339,635)		Opioid-opioid overlap (*N* = 456,282)		Opioid-BZD overlap (*N* = 416,129)		Long-acting opioids for acute pain (*N* = 64,529)	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Frequent ED use (No)												
Yes	1.92 (1.78–2.06)	< 0.0001	1.32 (1.28–1.37)	< 0.0001	2.66 (2.52–2.80)	< 0.0001	1.62 (1.57–1.67)	< 0.0001	1.68 (1.63–1.73)	< 0.0001	2.43 (2.32–2.54)	< 0.0001
Pharmacotherapy for OUD (No)												
Yes	6.21 (5.83–6.61)	< 0.0001	4.66 (4.28–5.08)	< 0.0001	3.06 (2.82–3.32)	< 0.0001	6.81 (6.41–7.22)	< 0.0001	5.41 (5.04–5.79)	< 0.0001	2.03 (1.90–2.16)	< 0.0001

Abbreviations: BZD, benzodiazepine; CDHP, consumer driven health plan; ED, emergency department; HDHP, high-deductible health plan; HMO, health maintenance organization; OR, odds ratio; PPO, preferred provider organization; SUD, substance use disorder.

[a] We excluded patients with chronic pain from this model.

7.2. Factors associated with potentially problematic opioid prescriptions

Among the privately insured sample, we found that sex, age, type of pain diagnosis, chronicity of pain, number of comorbidities, type of opioid drug, type of health plan, frequency of ED use, and pharmacotherapy for opioid use disorders were significantly associated with any potentially problematic prescriptions (Table 3). Specifically, the odds of any potentially problematic opioid prescription increased with age and number of comorbidities. Odds were higher for patients with back pain (OR = 1.99, CI = 1.78–2.22), arthritis (OR = 2.59, CI = 2.22–3.01), and migraine (OR = 1.36, CI = 1.20–1.53) compared with other types of pain; patients who had a PPO (OR = 1.09, CI = 1.02–1.17) compared with those who had an HMO; patients with frequent ED use (OR = 1.92, CI = 1.78–2.06) compared with those without such use; and patients receiving pharmacotherapy for opioid use disorders after their initial opioid prescription (OR = 6.21, CI = 5.83–6.61) compared with those who did not receive such treatment. Odds were lower for males (OR = 0.86, CI = 0.83–0.88) than females and for patients with hydrocodone prescriptions (OR = 0.71, CI = 0.68–0.73) compared with those taking an opioid drug type other than oxycodone or hydrocodone.

When we examined each indicator of potentially problematic opioid prescription separately among individuals with commercial insurance, males had significantly higher odds of having high-dose opioids (OR = 1.31, CI = 1.24–1.37) and receiving a long-acting opioid for acute pain (OR = 1.08, CI = 1.06–1.10) than females, but sex did not predict opioid-opioid overlap. Compared with acute pain, chronic pain was associated with lower odds for three types of problematic opioid prescription types, the most substantial one being a high-dose opioid (OR: 0.66, CI = 0.60–0.72). Compared with other types of pain diagnoses, the strongest significant association was found between having a fracture and receipt of long-acting/extended-release opioids for acute pain (OR = 7.0, CI = 6.49–7.55). Compared with opioid drugs other than oxycodone and hydrocodone, receiving oxycodone was associated with significantly higher odds of having the high-dose opioids (OR = 1.97, CI = 1.78–2.17), opioid-opioid overlap (OR = 1.09, CI = 1.04–1.13), opioid-benzodiazepine overlap (OR = 1.16, CI = 1.11–1.21), and long-acting/extended-release opioids for acute pain (OR = 1.48, CI = 1.42–1.55). Compared with HMO plans, individuals with PPO health plans had significantly higher odds of having opioid-opioid overlap (OR = 1.13, CI = 1.08–1.18) and opioid-benzodiazepine overlap (OR = 1.15, CI = 1.11–1.20). Patients with a mental illness diagnosis had significantly higher odds of receiving a long-acting/extended-release opioid for acute pain (OR = 2.57, CI = 2.23–2.95) than those without such a diagnosis. Patients with frequent ED use had significantly higher odds of having all five specific outcomes, with their largest likelihood being multiple providers (OR = 2.66, CI = 2.52–2.80), compared with those without such use. Patients who received pharmacotherapy for opioid use disorders also had significantly higher odds of having all five specific outcomes, with their largest likelihood being opioid-opioid overlap (OR = 6.81, CI = 6.41–7.22), compared with those who did not receive such pharmacotherapy.

In the Medicaid sample, age, race, type of pain diagnosis, chronicity of pain, number of comorbidities, opioid drug type, type of health plan, frequency of ED use, and pharmacotherapy for opioid use disorders were significantly associated with potentially problematic opioid prescriptions (Table 4). Specifically, the odds of any potentially problematic opioid prescription increased with age and number of comorbidities. Compared with non-Hispanic whites, odds were significantly lower for non-Hispanic blacks (OR = 0.40, CI = 0.30–0.52) and Hispanics (OR = 0.50, CI = 0.41–0.62). Odds were significantly higher for patients who had back pain (OR = 1.77, OR = 1.56–1.99), arthritis (OR = 2.12, CI = 1.76–2.56), and migraine (OR = 1.16, CI = 1.02–1.33) compared with those who had other types of pain; for patients who received oxycodone prescriptions (OR = 1.18,

Table 4
Adjusted odds ratios associated with potentially problematic opioid prescriptions among individuals with medicaid, 2005–2015.

Variables (reference value)	Any potentially problematic opioid prescription (*N* = 409,801)		Specific potentially problematic opioid prescriptions									
			High-dose opioid (*N* = 22,366)		Multiple providers (*N* = 113,542)		Opioid-opioid overlap (*N* = 231,581)		Opioid-BZD overlap (*N* = 209,040)		Long-acting opioids for acute pain (N = 33,845)	
	OR (95%CI)	*p* value	OR (95%CI)	*p* value	OR (95%CI)	*p* value	OR (95%CI)	*p* value	OR (95%CI)	*p* value	OR (95%CI)	*p* value
Sex (Female)												
Male	1.06 (0.97–1.15)	0.208	1.68 (1.55–1.81)	< 0.0001	1.08 (0.98–1.17)	0.103	1.23 (1.10–1.38)	< 0.0001	0.78 (0.69–0.88)	< 0.0001	1.29 (1.21–1.37)	< 0.0001
Age group (18–24)												
25–34	2.17 (1.94–2.44)	< 0.0001	5.26 (4.45–6.20)	< 0.0001	1.75 (1.64–1.85)	< 0.0001	2.76 (2.29–3.31)	< 0.0001	3.22 (3.01–3.44)	< 0.0001	1.04 (0.97–1.11)	0.317
35–44	4.01 (3.46–4.64)	< 0.0001	11.71 (9.77–14.0)	< 0.0001	2.55 (2.24–2.91)	< 0.0001	5.19 (4.16–6.47)	< 0.0001	6.27 (5.68–6.91)	< 0.0001	1.12 (0.99–1.26)	0.068
45–54	5.83 (4.85–7.02)	< 0.0001	15.25 (12.9–18.0)	< 0.0001	2.99 (2.46–3.63)	< 0.0001	7.30 (6.40–8.33)	< 0.0001	8.55 (7.46–9.78)	< 0.0001	1.22 (1.11–1.34)	< 0.0001
54–64	5.08 (3.90–6.62)	< 0.0001	11.68 (8.67–15.7)	< 0.0001	2.43 (2.07–2.85)	< 0.0001	6.28 (5.33–7.37)	< 0.0001	7.30 (5.77–9.21)	< 0.0001	1.12 (1.03–1.22)	0.007
Race/ethnicity (Non-Hispanic white)												
Non-Hispanic black	0.40 (0.30–0.52)	< 0.0001	0.32 (0.24–0.43)	< 0.0001	0.46 (0.42–0.52)	< 0.0001	0.50 (0.37–0.66)	< 0.0001	0.22 (0.16–0.30)	< 0.0001	0.97 (0.91–1.04)	0.437
Hispanic	0.50 (0.41–0.62)	< 0.0001	0.40 (0.30–0.55)	< 0.0001	0.54 (0.48–0.61)	< 0.0001	0.56 (0.45–0.69)	< 0.0001	0.40 (0.31–0.52)	< 0.0001	0.95 (0.85–1.06)	0.33
Other	0.73 (0.55–0.98)	0.038	0.76 (0.66–0.87)	< 0.0001	0.72 (0.62–0.82)	< 0.0001	0.84 (0.61–1.17)	0.312	0.65 (0.52–0.82)	< 0.0001	1.07 (0.99–1.14)	0.056
Specific pain diagnosis (Other)												
Back pain	1.77 (1.56–1.99)	< 0.0001	1.32 (1.01–1.71)	0.039	1.60 (1.22–2.09)	0.001	1.52 (1.32–1.75)	< 0.0001	1.44 (1.33–1.54)	< 0.0001	0.72 (0.62–0.84)	< 0.0001
Arthritis	2.12 (1.76–2.56)	< 0.0001	1.57 (1.15–2.14)	0.004	1.86 (1.33–2.60)	< 0.0001	1.92 (1.62–2.26)	< 0.0001	1.29 (1.15–1.44)	< 0.0001	0.66 (0.43–1.01)	0.057
Joint disorders	0.71 (0.64–0.79)	< 0.0001	0.43 (0.32–0.57)	< 0.0001	1.01 (0.87–1.17)	0.923	0.57 (0.49–0.67)	< 0.0001	0.65 (0.58–0.72)	< 0.0001	0.84 (0.76–0.93)	0.001
Fractures	0.87 (0.72–1.05)	0.158	0.33 (0.23–0.49)	< 0.0001	1.12 (0.88–1.41)	0.364	0.61 (0.45–0.81)	0.001	0.52 (0.44–0.60)	< 0.0001	2.94 (2.62–3.30)	< 0.0001
Migraine	1.16 (1.02–1.33)	0.026	0.48 (0.32–0.73)	< 0.0001	1.28 (1.07–1.54)	0.007	0.88 (0.71–1.08)	0.216	1.22 (1.10–1.35)	< 0.0001	0.71 (0.60–0.84)	< 0.0001
Chronicity of pain (Acute)												
Chronic	0.72 (0.65–0.79)	< 0.0001	0.85 (0.72–1.01)	0.067	0.93 (0.84–1.03)	0.145	0.75 (0.68–0.82)	< 0.0001	0.74 (0.69–0.80)	< 0.0001	–[a]	–[a]
Comorbidity (0)												
1	1.27 (1.18–1.37)	< 0.0001	0.92 (0.82–1.02)	0.134	1.29 (1.23–1.35)	< 0.0001	1.18 (1.10–1.26)	< 0.0001	1.30 (1.20–1.39)	< 0.0001	1.29 (1.23–1.35)	< 0.0001
2	1.37 (1.25–1.51)	< 0.0001	0.83 (0.70–0.99)	0.035	1.43 (1.29–1.58)	< 0.0001	1.22 (1.12–1.32)	< 0.0001	1.37 (1.24–1.52)	< 0.0001	1.60 (1.55–1.64)	< 0.0001
3 or more	1.30 (1.12–1.49)	< 0.0001	0.70 (0.54–0.92)	0.01	1.54 (1.41–1.68)	< 0.0001	1.12 (0.96–1.30)	0.135	1.26 (1.10–1.44)	0.001	1.84 (1.77–1.91)	< 0.0001
Type of first opioid drug (Other)												
Oxycodone	1.18 (1.02–1.36)	0.022	2.13 (1.73–2.62)	< 0.0001	0.93 (0.80–1.07)	0.32	1.23 (1.11–1.36)	< 0.0001	1.37 (1.24–1.50)	< 0.0001	1.68 (1.44–1.96)	< 0.0001
Hydrocodone	0.90 (0.78–1.04)	0.151	0.31 (0.24–0.39)	< 0.0001	0.99 (0.92–1.06)	0.792	0.78 (0.69–0.88)	< 0.0001	1.11 (0.99–1.23)	0.056	0.98 (0.90–1.05)	0.509
Health plan (HMO)[b]												

(*continued on next page*)

Table 4 (*continued*)

Variables (reference value)	Any potentially problematic opioid prescription (*N* = 409,801)		Specific potentially problematic opioid prescriptions									
			High-dose opioid (*N* = 22,366)		Multiple providers (*N* = 113,542)		Opioid-opioid overlap (*N* = 231,581)		Opioid-BZD overlap (*N* = 209,040)		Long-acting opioids for acute pain (N = 33,845)	
	OR (95%CI)	*p* value	OR (95%CI)	*p* value	OR (95%CI)	*p* value	OR (95%CI)	*p* value	OR (95%CI)	*p* value	OR (95%CI)	*p* value
PPO	1.92 (1.64–2.23)	< 0.0001	1.79 (1.46–2.20)	< 0.0001	2.47 (1.65–3.67)	< 0.0001	1.71 (1.53–1.91)	< 0.0001	1.88 (1.68–2.10)	< 0.0001	1.55 (1.34–1.79)	< 0.0001
Mental illness (No)												
Yes	0.49 (0.33–0.71)	< 0.0001	0.55 (0.52–0.59)	< 0.0001	1.09 (1.00–1.18)	0.044	0.52 (0.38–0.70)	< 0.0001	0.60 (0.50–0.70)	< 0.0001	1.25 (1.09–1.43)	0.002
Frequent ED use (No)												
Yes	1.99 (1.54–2.58)	< 0.0001	1.14 (0.97–1.33)	0.108	3.27 (2.58–4.15)	< 0.0001	1.63 (1.33–1.98)	< 0.0001	1.73 (1.51–1.98)	< 0.0001	2.44 (2.23–2.66)	< 0.0001
Pharmacotherapy for OUD (No)												
Yes	1.60 (1.15–2.23)	0.005	1.33 (0.97–1.80)	0.061	1.66 (1.54–1.79)	< 0.0001	1.53 (1.07–2.19)	0.019	1.77 (1.44–2.17)	< 0.0001	1.46 (1.36–1.57)	< 0.0001

Abbreviations: BZD, benzodiazepine; CDHP, consumer driven health plan; ED, emergency department; HDHP, high-deductible health plan; HMO, health maintenance organization; OR, odds ratio; PPO, preferred provider organization; SUD, substance use disorder.

[a] We excluded patients with chronic pain from this model.

[b] Unlike commercial insurance, Medicaid has no high-deductible health plan or consumer driven health plan.

CI = 1.02–1.36) compared with those who received opioid drugs other than oxycodone and hydrocodone; patients who had a PPO (OR = 1.92, CI = 1.64–2.23) compared with those who had an HMO; for patients who used EDs > 3 times in 12 months (OR = 1.99, CI = 1.54–2.58) compared with those who did not; and for patients who received pharmacotherapy for opioid use disorders (OR = 1.60, CI = 1.15–2.23) compared with those who did not.

We also found numerous significant associations between demographic, clinical, and utilization factors and the separate indicators of potentially problematic opioid prescription in individuals with Medicaid (Table 4). Among the more important findings, males had significantly higher odds than females of having high-dose opioids (OR = 1.68, CI = 1.55–1.81), receiving a long-acting/extended-release opioid for acute pain (OR = 1.29, CI = 1.21–1.37), and opioid-opioid overlap (OR = 1.23, CI = 1.10–1.38). Patients with chronic pain had significantly lower odds of having opioid-opioid overlap (OR = 0.75, CI = 0.68–0.82) and opioid-benzodiazepine overlap (OR = 0.74, CI = 0.69–0.80) compared with those who had acute pain. Having a fracture was a strong predictor of receipt of long-acting/extended-release opioids for acute pain (OR = 2.94, CI = 2.62–3.30) compared with having an "other" type of pain diagnosis. Receiving oxycodone was associated with higher odds of having high-dose opioids (OR = 2.13, CI = 1.73–2.62), opioid-opioid overlap (OR = 1.23, CI = 1.11–1.36), opioid-benzodiazepine overlap (OR = 1.37, CI = 1.24–1.50), and long-acting/extended-release opioids for acute pain (OR = 1.68, CI = 1.44–1.96). Compared with HMO coverage, PPO coverage was associated with higher odds of having have high-dose opioids (OR = 1.79, CI = 1.46–2.20), multiple providers (OR = 2.47, CI = 1.65–3.67), opioid-opioid overlap (OR = 1.71, CI = 1.53–1.91), opioid-benzodiazepine overlap (OR = 1.88, CI = 1.68–2.10), and receiving long-acting/extended-release opioids for acute pain (OR = 1.55, CI = 1.34–1.79). Individuals diagnosed with a mental illness had significantly higher odds of having multiple providers (OR = 1.09, CI = 1.00–1.18) and long-acting/extended-release opioids for acute pain (OR = 1.25, CI = 1.09–1.43) than those without such a diagnosis, and had significantly lower odds of having opioid-opioid overlap (OR = 0.52, CI = 0.38–0.70), high-dose opioids (OR = 0.55, CI = 0.52–0.59), and opioid-benzodiazepine overlap (OR = 0.60, CI = 0.50–0.70).

7.3. Percent of enrollees with potentially problematic opioid prescriptions that developed opioid use disorder

When examining the entire sample of individuals with an opioid prescription fill, we found that 2.8% and 0.7% of individuals with Medicaid and commercial insurance, respectively, developed an opioid use disorder within the 12 months after their first opioid prescription fill (Table 5). When these opioid use disorder rates were stratified by the presence or absence of problematic opioid prescription fills, the rates were considerably greater for individuals who had such problematic prescriptions (5.9% for Medicaid and 2.4% for commercial insurance) than for individuals who did not (1.8% for Medicaid and 0.3% for commercial insurance). These results indicate that, in the private insurance group, individuals who had any potentially problematic prescription were eight times more likely to develop an opioid use disorder compared with those without any potentially problematic opioid prescription. In the Medicaid group, individuals who had any potentially problematic prescription were approximately three times more likely to develop an opioid use disorder compared with those without any potentially problematic opioid prescription. When stratified by the type of potentially problematic opioid prescription, the rate of development of an opioid use disorder was highest among individuals who were prescribed high-dose opioids over 90 days (6.9% for privately insurance and 11.3% for Medicaid).

8. Discussion

Older age, female sex, arthritis, back pain, migraines, fractures, number of comorbid conditions, type of health plan, frequent ED use, and pharmacotherapy for opioid use disorders were associated with problematic opioid prescriptions for patients with private insurance. For patients with Medicaid, older age, white race, acute pain, arthritis, back pain, migraines, fractures, number of comorbid conditions, frequent ED use, and pharmacotherapy for opioid use disorders were associated with problematic opioid prescriptions. Individuals with a potentially problematic opioid prescription were much more likely to develop an opioid use disorder within 12 months following their initial prescription than individuals that did not have any potentially problematic opioid prescriptions. This was most pronounced among individuals who received a high-dose opioid for 90 or more days.

Many of the characteristics associated with potentially problematic prescriptions have been previously found to be associated with opioid misuse (Cochran et al., 2014; Rice et al., 2012; White et al., 2009). This was not surprising as individuals who misuse opioids may seek opioids in higher doses, quantities, and in easier-to-abuse forms. The patients' sex was one of a few characteristics that had a different direction of association depending on the type of problematic prescription. Females had higher odds of receiving opioids from multiple providers (private insurance only) and having an opioid-benzodiazepine overlap, but females had lower odds of high-dose opioids and receipt of long-acting/extended-release opioids for acute pain. Females may be more likely to have disorders related to anxiety and stress that are more likely to be treated with a benzodiazepine prescription (Bruce et al., 2011). A recent study found that, among individuals with a substance use disorder,

Table 5
Prevalence of opioid use disorder among individuals with commercial insurance and medicaid, 2005–2015.

Categories	Individuals with an opioid prescription fill		Individuals who developed an opioid use disorder			
	Commercial	Medicaid	Commercial		Medicaid	
			N	%	N	%
Total	4,535,623	1,604,143	31,163	0.7	44,994	2.8
Individuals *without* any potentially problematic opioid prescription	3,616,667	1,194,342	9552	0.3	20,958	1.8
Individuals *with* any potentially problematic opioid prescription[a]	918,956	409,801	21,611	2.4	24,036	5.9
Individuals with specific types of potentially problematic opioid prescriptions[a]						
High-dose opioids	77,181	22,366	5329	6.9	2534	11.3
Multiple providers	339,635	113,542	7481	2.2	5375	4.7
Opioid-opioid overlap	456,282	231,581	15,838	3.5	16,642	7.2
Opioid-benzodiazepine overlap	416,129	209,040	12,861	3.1	14,871	7.1
Long-acting opioids for acute pain	64,529	33,845	1503	2.3	2596	7.7

[a] In this study, potentially problematic opioid prescriptions represent those that occurred within 12 months of individuals' first opioid prescription fill.

females were more likely to receive multiple benzodiazepine fills (O'Brien et al., 2017). Males may be more likely to have a higher dose if they have multiple pain problems, as this was found to be a risk factor in for high-dose prescriptions in previous work (Morasco et al., 2010).

Previous work found an association between non-medical use of prescription pain relievers and mental health (Ali et al., 2015; Becker, Sullivan, Tetrault, Desai, & Fiellin, 2008). The current study examines the association between mental health and different types of problematic prescriptions by insurance type. Among privately insured individuals, having a mental health diagnosis was associated with higher odds of receiving a long-acting/extended-release opioid for acute pain, but this diagnosis was not associated with any of the other types of problematic prescriptions. Among Medicaid enrollees, having a diagnosis of a mental illness was associated with higher odds of receiving a long-acting/extended-release opioid for acute pain and receiving opioids from multiple providers. However, having a diagnosis of a mental illness was associated with lower odds of having high-dose opioids, opioid-opioid overlap, and opioid-benzodiazepine overlap among Medicaid enrollees. It is possible that Medicaid enrollees with a mental illness receive more intense care management or are more likely to receive comprehensive medication review to ensure appropriateness of prescribed medications.

Our finding that individuals who had received pharmacotherapy for opioid use disorders after their initial opioid prescription were much more likely to have a potentially problematic prescription was consistent with previous work that has found substance abuse to be a consistent predictor of opioid misuse (Becker et al., 2008; Ives et al., 2006). The short timeframe between the initial opioid prescription and receipt of pharmacotherapy for opioid use disorders ($<$ 1 year per study specifications) suggests that these individuals may have obtained opioids from other sources, such as friends or family members (Ali, Henke, et al., 2019, Ali, Mutter, et al., 2019).

Older age was associated with potentially problematic prescriptions for individuals with commercial insurance and with Medicaid. Previous work has found younger age adults are at greater risk for misuse and dose escalation (Buntin-Mushock, Phillip, Moriyama, & Palmer, 2005; Ives et al., 2006). A study that focused on a small sample of patients who were hospitalized found that older patients received significantly lower doses of opioids than younger and middle-aged patients and required significantly lower amounts of opioids than younger patients to achieve analgesia (Gnjidic, Murnion, & Hilmer, 2008). Further, providers may be more likely to conduct more intense monitoring for opioid use among older patients because of the possibility of adverse effects specific to this age group (Chau, Walker, Pai, & Cho, 2008).

Our study found that patients with certain types of pain, including arthritis and back pain, were more likely to receive a potentially problematic prescription. Back pain has been shown in previous research to be associated with opioid misuse and aberrant medication-taking behaviors (Martell et al., 2007; Sullivan et al., 2010). The benefits of opioids for management of back pain and arthritis were the topics of articles approximately 15 years ago when untreated pain was considered a major public health issue (Jamison, Raymond, Slawsby, Nedeljkovic, & Katz, 1998; Roth, 2002). For Medicaid patients, we found that having arthritis was not correlated with receiving a long-acting/extended-release opioid for acute pain. This merits further investigation, given that the result was different for individuals with private insurance. Patients with acute pain had higher odds of receiving a potentially problematic prescription; this result was surprising, because most of the focus on changing prescribing behavior addresses prescriptions for chronic conditions. Greater attention may need to be paid to opioid prescribing for acute pain, for example, following surgical procedures (Brummett et al., 2017).

Receiving oxycodone was associated with higher odds of having high-dose opioids, opioid-opioid overlap, opioid-benzodiazepine overlap, and long-acting/extended-release opioids for acute pain. Oxycodone is one of the most abused opioid pain medications, and previous studies have found that people with current opioid prescriptions or a history of opioid mediation were more likely to misuse opioids or have a problematic opioid prescription (Hah et al., 2017; Rice et al., 2012; Wightman, Perrone, Portelli, & Nelson, 2012). Previous literature of the commercially insured population has shown a strong association between opioid use disorders with extended-release oxycodone but not with immediate-release oxycodone (Rice et al., 2012). Consistent with previous literature (Rice et al., 2012), our results indicated that patients taking hydrocodone are less likely to have a problematic opioid prescription.

We also found that individuals with commercial insurance who were in a PPO health plan had higher odds of having a potentially problematic opioid prescription. Previous literature has found that individuals who were prescribed opioid analgesics were more likely to have PPO health plans than those who were not prescribed opioid analgesics (Xie et al., 2014). This can happen because PPO health plans cover services outside the plans' network and no referral is required to see specialists, which gives individuals in PPO plans more flexibility than those in HMO plans to see whichever doctors they choose. Our study also found that individuals with frequent ED visits were more likely to receive a problematic opioid prescription. Previous studies have shown that substance use disorder is a predictor of frequent ED use because emergency medicine doctors can be seen as a potential source of prescriptions by patients seeking opioid pain medications for nonmedical use (Doran, Raven, & Rosenheck, 2013; Millard, 2007). Our findings align with previous results that demonstrate how EDs may be used to get opioid analgesics for nonmedical use (Millard, 2007; Shaffer & Moss, 2010).

Our analysis linking potentially problematic prescriptions to the subsequent development of an opioid use disorder highlights the risks associated with each type of potentially problematic opioid prescription. Of these five types of potentially problematic prescriptions, we found that patients with high-dose opioids were the most likely to develop opioid use disorder among both the privately insured and Medicaid beneficiaries, followed by opioid-benzodiazepine overlap (Medicaid) and long-acting/extended-release opioids for acute pain (commercial insurance). Policymakers and providers may consider focusing attention on reducing specific factors linked to subsequent development of opioid use disorder among people with potentially problematic prescriptions and engaging patients who are receiving high-dose of opioids, long-acting/extended-release opioids for acute pain, and overlapping prescriptions for efforts to reduce and/or avoid these practices.

Our results should be interpreted in the light of a few limitations. Because pharmacy claims do not include prescriber ID, we attributed opioid prescription fills to the provider of the most current visit prior to the prescription fill. Some patients may have multiple office visits for clinical issues prior to an opioid prescription being filled, and others may delay filling their prescription. Patients also may not have an encounter associated with each opioid prescription. These nuances may lead to incorrect attribution of prescriber ID to an opioid prescription. Therefore, it is not possible to say with certainty that individuals seeing multiple providers in our data actually were receiving opioids from multiple prescribers. A related limitation is that our data did not include office visit and pharmacy claims paid for using cash payments. However, these limitations are not unique to MarketScan, rather they are applicable to all insurance claims databases. Finally, given the nature of our data set, this analysis is unable to establish causality, but rather offers evidence of association.

Prescription Drug Monitoring Programs (PDMPs) have evolved over time to give prescribers information about other opioid and benzodiazepine prescriptions an individual patient has received (Ali, Dowd, Classen, et al., 2017; National Alliance for Model State Drug Laws, 2017). Although we did control for year, there were state differences in the use of PDMPs and subsequent changes in knowledge and awareness of appropriate prescribing that we were not able to capture. Another

limitation is that we were only able to identify opioid use disorder if this diagnosis was present on a claim. Individuals with opioid use disorder may not receive treatment or may receive treatment that does not appear on a claim (e.g., they may pay with cash). Finally, we only looked forward 12 months for an indicator of opioid use disorder. An important area for future studies would be to investigate the development of subsequent opioid use disorder over a longer period of time.

We identified several factors linked with potentially problematic prescriptions that suggest either potential patient misuse or injudicious prescription practice by providers. We also estimated the percentage of individuals with a problematic opioid prescription who subsequently developed an opioid use disorder within 12 months. The findings of the study could inform policy efforts at both the state and the federal level to mitigate these risk factors and reduce the prevalence of problematic opioid prescriptions. For example, increasing mandates to check a state's PDMP before prescribing opioids, limiting the days' supply of opioids, and making referrals to pain specialists are some areas where opportunities for further engagement potentially exist. In addition, the 21st Century Cures Act authorized funding to enable a comprehensive approach to expanding opioid use disorder prevention, treatment, and recovery support services, and these activities might play a critical role in addressing the opioid crisis (Library of Congress, 2015; Mutter, Patton, & Ali, 2017). The patient factors we identified as being associated with various potentially problematic opioid prescriptions and the association of those prescriptions with the subsequent development of opioid use disorder can be used to inform the continued prevention and treatment outreach efforts to patients, providers, and payers necessary to address the opioid crisis.

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