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National Variation in Opioid Prescribing and Risk of Prolonged Use for Opioid-Naïve Patients Treated in the Emergency Department for Ankle Sprains

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Abstract

Objective: To inform opioid stewardship efforts, we describe the variation in emergency department (ED) opioid prescribing for a common minor injury, ankle sprains, and determine the association between initial opioid prescription intensity and transition to prolonged opioid use.

Methods: We analyzed 2011–2015 U.S. private insurance claims (Optum Clinformatics DataMart) for ED treated ankle sprains among opioid-naïve patients aged ≥ 18 years. We determined: 1) the patient- and state-level variation in the opioid prescription rate and characteristics; and 2) the risk-adjusted association between total morphine milligram equivalents (MME) of the prescription and transition to prolonged use (filling 4 or more opioid prescriptions 30–180 days after the index visit).

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Contributions

MKD, JM, ZM, and DP conceived the study and obtained research funding. MKD and DP acquired the data. MKD and YH conducted the analysis. DP and SH provided statistical guidance and supervised the analysis. All authors interpreted the results. MKD and MY drafted the manuscript. All authors contributed to the critical revision of the manuscript. MKD takes responsibility for the manuscript as a whole.

Conflict of Interest Summary

Dr. Delgado reports receiving an honorarium for participating in an Expert Roundtable on Innovative Solutions for Pain Management convened by United Health Group. All other authors declare no conflicts of interest.

Results: 30,832 patients met inclusion criteria. Of these, 25.1% received an opioid prescription with a median total MME of 100 (IQR 75–113), tablet quantity of 15 (IQR 12–20), and days supplied of 3 (IQR 2–4). State-level prescribing rates ranged from 2.6% in North Dakota to 40.0% in Arkansas. Among patients who received a total MME of > 225 (equivalent to > 30 tabs of oxycodone 5 mg), the adjusted rate of prolonged opioid use was 4.9% (95% CI: 1.8–8.1%) compared with 1.1% (95% CI: 0.7–1.5%) among those who received at total MME of 75 or and 0.5% (95% CI: 0.4–0.6%) among those who did not fill an opioid.

Conclusion: Opioid prescribing for ED patients treated for ankle sprains is common and highly variable. Although infrequent in this population, prescriptions greater than 225 MME were associated with higher rates of prolonged opioid use. This is concerning since these prescriptions could still fall within 5- or 7-day supply limit policies aimed at promoting safer opioid prescribing.

INTRODUCTION

Background

The U.S. opioid epidemic claimed 42,249 lives in 2016.¹ In response, many states in the country and some health insurers and pharmacy chains have enacted policies limiting the duration of new opioid prescriptions for acute pain conditions.^{2–4} In the early part of 2018, Congress introduced the Comprehensive Addiction and Recovery Act (CARA) 2.0, a bipartisan bill that includes a three-day supply limit on all new opioid prescriptions. The goal of opioid stewardship and prescription limit policies is to reduce the potential for transition to prolonged use, potential misuse, as well as the diversion of unused tablets. Despite recent policy action, the scientific evidence base on the threshold prescription intensity associated increased risk of transition to prolonged use and misuse is limited.

Importance

Prior studies have found an association between increasing opioid prescription duration or intensity and transition to prolonged use, but were not designed to account for differences in the indication for the initial prescription.^{5–7} This is problematic because the onset of some pain conditions, such as acute lumbar radiculopathy, often leads to chronic pain. Therefore, it cannot be determined whether prolonged use is due to the development of opioid dependence following the initial prescription or to the independent development of increased pain sensitivity (hyperalgesia), a chronic pain syndrome, or other factors. A second issue with current prescription limits is that basing policy on days supplied is imprecise. A common dosing order for oxycodone 5 mg is to take 1–2 tablets every 4–6 hours as needed for pain. With these instructions a 7-day prescription could vary anywhere from 1 tablet to 84 tablets or 7.5 to 630 morphine milligram equivalents.⁸ Therefore, the impact of policies to limit the days supplied on reducing the total number of opioid tablets and morphine milligram equivalents entering the community remains unclear, particularly if clinicians respond by writing for the same number of tablets but to be taken over fewer days.

Goals of this Investigation

To guide opioid stewardship efforts by benchmarking variation in prescribing and to generate clearer evidence on the risks of features of initial opioid prescriptions, we analyzed

commercial insurance claims from opioid-naïve patients treated in the emergency department (ED) for ankle sprains. We chose this indication and setting for three reasons. First, ankle sprains are common minor injuries for which pain rapidly improves within two weeks.⁹ Therefore, any risk of subsequent opioid misuse is likely to outweigh the treatment benefit given that non-opioid analgesics have been found to be equally effective for acute pain management.^{10,11} Second, although initial opioid prescriptions written in the ED are more consistent with current prescribing guidelines than those from non-ED settings and are typically for smaller quantities, (and thus less likely to progress to long-term use), EDs remain a common source of acute opioid prescriptions.^{12,13} Finally, there is still significant variability in opioid prescribing by emergency physicians and patient assignment is essentially random.^{6,13} This both represents an opportunity for quality improvement and also reduces the potential bias of downstream prescriptions being associated with characteristics of the initial prescriber.

We sought to determine the degree of patient- and state-level variation in opioid prescribing in this setting and the association between the variation in morphine milligram equivalents prescribed and transition to prolonged opioid use. We hypothesized variation in prescribing would be substantial and that larger opioid prescriptions would be associated with higher likelihood of prolonged use.

METHODS

Study Population

We employed a cohort study design in a retrospective analysis of the Clinformatics Data Mart Database (OptumInsight), which is comprised of administrative claims of 13 million privately insured enrollees throughout the U.S.^{14–16} This population is similar to the US population of commercially insured people in age, race or ethnicity, and sex and has a median continuous enrollment period of 24 months.¹⁶

We identified all index ED encounters for ankle sprains in patients aged 18 years old that occurred from January 1, 2011 to December 31, 2015. The index visit was defined as the earliest visit in which the enrollee had a provider claim by an emergency physician with a place of service designation in the emergency department and a diagnosis code of ankle sprain (ICD-9 code 845.00–09 and ICD10 S93.4). We excluded patients who had any other injury diagnoses as defined by State and Territorial Injury Prevention Directors Association consensus definitions,^{17–19} and those who had recurrent visits for ankle sprain during the study period to decrease the likelihood that future prescriptions were associated with a more severe initial presentation. To restrict the study population to those who are likely to be prescription opioid-naïve, we excluded all patients who were not continuously enrolled for 6 months prior to the index ED visit and those who had filled an opioid prescription in these prior 6 months.^{6,12}

Definition of Opioid Prescriptions

We identified prescription claims corresponding to an opioid according to National Drug Codes (excluding methadone and non-tablet formulations) filled within 3 days of the index

ED visit. We excluded any encounters for patients who had intervening medical claims for ankle sprains within 3 days of the ED visit.

Outcomes

The primary outcome was opioid prescription rate defined as the proportion of adult opioid-naïve patients treated for ankle sprains that filled an opioid prescription with 3 days of the ED visit. Secondary outcomes included characteristics of the initial prescription and continued opioid use beyond the initial prescription.

Characteristics of the initial prescription included number of tablets, days supplied, and morphine milligram equivalents (MME) per prescription.²⁰ The days supplied on the pharmacy prescription claims are entered at the point of sale by the pharmacist based on dosing instructions and number of tablets dispensed.²¹

We measured prolonged opioid use in the 30–180 days following the index ED visit given pain from ankle sprains rapidly improves within 2 weeks.⁹ We defined prolonged use as filling 4 or more subsequent opioid prescriptions during this time period,^{22,23} and used alternative specifications in our sensitivity analyses. Limiting the follow-up period to six months captures high-risk individuals who drop out of the dataset by virtue of losing employment, and thus insurance coverage, due to an opioid use disorder if longer follow up periods were used.^{24,25} Indeed, in our final study sample the insurance enrollment attrition rate between 6 and 12 months of follow-up was 1.5% (95% CI: 0.4%, 2.5%) higher among those who were prescribed opioids (16.7%) compared with those who did not fill opioids (15.2%). To further validate our outcome, we tabulated the most common first listed medical diagnosis codes within the 7 days prior to new opioid prescription fills 30–180 days after the index encounter. This analysis allowed us to explore the extent to which new prescriptions could be attributed to persistent ankle pain rather than another condition completely unrelated to the index ankle sprain.

Patient Covariates

We extracted information on patients' age, sex, highest level of education, and race. We also identified the patients' Elixhauser comorbidities, as well as diagnosis codes for drug abuse, alcohol abuse, depression, and psychoses as gathered from diagnosis codes on the index ED visit and any medical claims filed in the previous 6 months.²⁶

Statistical Analysis

First, we tabulated patient characteristics according to whether an opioid prescription was filled or not. Among those who filled opioids, we stratified patient characteristics according to whether a prescription was above or below the median total MME prescribed in the sample. We compared the magnitude of differences in patient and prescription characteristics between groups using 95% confidence intervals for the differences.

Second, we described the variation in the opioid prescription rate and characteristics at the patient- and state-level and over time. Prescriptions were aggregated by state according to the

state associated with the prescribers' de-identified National Provider Identifier (NPI) number.

Next, we calculated the patients' expected probability of receiving an opioid prescription using a logistic regression model adjusting for age, sex, highest level of education, race, the total number of Elixhauser comorbidities, a history of drug abuse, alcohol abuse, depression, or psychosis, and year. We then estimated observed-to-expected state-level prescribing ratios with 95% confidence intervals, with values over 1 indicating patients in that state were more likely than expected to fill opioid prescriptions and less than 1 indicating patients in states that were less likely than expected to fill opioid prescriptions.²⁷ For these state-level analyses we excluded states with less than 25 patients in the study sample.

We then quantified the number of tablets that would be prevented from entering the community from reducing excessive variation by: 1) reducing all states with above-median opioid prescribing rates to the median rate for ankle sprains; and 2) leveling all above-median opioid prescriptions supplies for ankle sprains to the median.

Finally, we quantified the association between the initial MME prescribed among those who filled a prescription and prolonged use. MME cutoffs were selected based on common tablet quantities dispensed for the most potent opioid prescribed, oxycodone 5 mg: 1–75 MME (≤ 10 tabs), 76–150 (11–20 tabs), 151–225 MME (21–30 tabs), and >225 MME (>30 tabs). We quantified the association using a logistic regression model adjusting for age, sex, highest level of education, race, the total number of Elixhauser comorbidities, a history of drug abuse, alcohol abuse, depression, or psychosis, year, and state. We then performed sensitivity analyses to assess the robustness of our findings, including: 1) using tablets dispensed (adjusted for MME/tablet), and days supplied as the independent measure of interest; and 2) limiting the exposure to just prescriptions for hydrocodone and oxycodone; and 3) considering alternative measures of prolonged use based on the number of prescriptions filled in the follow-up window. The University of Pennsylvania Institutional Review Board (IRB) determined that this study was eligible for IRB exemption. Stata 14.1 (StataCorp, College Station, TX) and SAS 9.4 (SAS Institute, Cary, NC) were used to conduct the statistical analyses.

RESULTS

Characteristics of the Study Subjects

Our sample consisted of 30,832 patients with an ED visit for an isolated injury of ankle sprain who had not filled an opioid prescription in the prior 6 months (Figure 1). The overall opioid prescribing rate in this sample was 25.1% ($n=7,739$). Among the 25,849 patients who had continuous enrollment for 6 months after the ED visit, the prescribing rate was similar (25.0%, $n=6,463$). Demographic and clinical characteristics were similar between those who were prescribed an opioid vs. those who were not as well as those who received above vs. below median (100) total MME prescriptions (Table 1).

Main Results

Hydrocodone was the most commonly prescribed opioid (64.9%), followed by tramadol (16.2%), oxycodone (14.4%), and codeine (5.5%). The median number of tablets prescribed for all opioid prescriptions was 16 with an interquartile range of 12 to 20 tablets. The median total MME was 100 (IQR 75–112.5) and median days supplied was 3 (IQR 2–4). However, only 5% of those who were prescribed opioids were given more than 30 tablets or greater than 200 MME total (Figure 2). The overall prescription rate declined modestly over the study period from 28.1% (95% CI: 27.1–29.1%) in 2011 to 20.4% (95% CI: 19.2–22.6%) in 2015 (Figure 3).

State-specific prescription rates varied by a factor of 14.2, ranging from 40.0% in Arkansas to 2.8% in North Dakota with a national median prescribing rate of 24.1% (Figure 4). There was less state-level variation in the MME per prescription (median 98.9 [range 77.5–136.3]) and quantity supplied per patient (median 18.2 [range 13.6–40.0]) for those who received prescriptions. After adjustment for case-mix and volume, the prescription rate variation persisted in 2014–15. States in the southern U.S. accounted for most of the higher than expected prescribing rates (Figure 4, eFigure 1).

There were a total of 143,064 opioid tablets prescribed for those who filled prescriptions in the study sample. Just reducing the excess variation in the state-level prescription rates by bringing states with above average prescribing rates to the median of 24.1% would have resulted in 18,260 fewer opioid tablets being prescribed. On the other hand, reducing the excess variation in prescription quantities by bringing prescriptions above the median to the median of 16 tablets would have resulted in an even bigger reduction, 32,177 less tablets prescribed.

Prolonged opioid use (4 or more new opioid prescriptions 30 days after the initial prescription) was slightly higher among those prescribed any opioid, 0.73% (95% CI: 0.63%–0.84%), versus those who were not prescribed opioids, 0.50% (95% CI: 0.40–0.59%). Only small proportion of subsequent prescriptions among those who went on to high-risk prolonged use were due to first listed diagnoses of non-traumatic joint disorders (7.5%) and sprains and strains (5.8%) of any kind. In contrast, subsequent prescriptions were more likely to be associated with other diagnosis codes (>80%) such as connective tissue disease (7.8%), back problems (5.8%), medical examination (3.6%), headache (2.6%), abdominal pain (2.0%), urinary tract infections (2.0%), and dozens of other conditions (eTable 1).

After multivariate risk adjustment, the associated probability of high-risk prolonged use among those who received a total of MME of 75 or less was 1.10% (95% CI: 0.72–1.53%) and remained similar for those who received up to 225 MME. However, above that threshold there was increased association with prolonged use 4.9% (95% CI: 1.8–8.1%) (Figure 5a).

When restricting the population to just those prescribed the higher potency drugs, hydrocodone and oxycodone, the dose-response relationship between total MME of the initial prescription and high-risk prolonged use was stronger (Figure 5b). Those prescribed >225 total MME in this group had a 6.3% (95% CI: 2.1–10.5%) probability of developing high-risk prolonged use vs. those prescribed <75 MME (1.2 %; 95% CI: 0.7–1.6%)

Female sex, age 35–44 years old, higher comorbidity burden, and previous history of drug abuse were also independently associated with transition to high-risk prolonged use (see full model results in eTable 1). Other sensitivity analyses varying alternative ways to measure prolonged use and initial prescription intensity confirmed the robustness of our findings (eAppendix).

LIMITATIONS

There are several limitations to this study. First, unmeasured differences between patients could have accounted for the observed associations. Arguing against this possibility is the observation that, among patients who were prescribed an opioid, measured patient characteristics were not significantly different according to prescription intensity. Furthermore, limiting the population to ankle sprains reduces the possibility that continued use was due to the development of chronic pain since the vast majority of ankle sprains resolve within 2–3 weeks regardless of initial pain severity.⁹ This is supported by the fact we found that <14% of new prescriptions among those with prolonged use were associated with sprains, strains, and non-traumatic joint pain of any type.

Second, we made the assumption that prescriptions were written for ankle sprains by limiting this analysis to claims with ankle sprains as the only injury diagnosis. It is possible that there were prescriptions for other indications that were not coded. Relatedly, data limitations preclude us from unequivocally attributing the prescription to ED clinicians. We addressed this by excluding patients who had other intervening medical claims for ankle sprains within the 3-day attribution window.

Third, we likely underestimated the opioid prescription rate if some patients filled prescriptions by paying out of pocket instead of using health insurance.²⁸ Finally, if data from 2017 were available and used to replicate this analysis, there may be a lower measured association with prolonged use due to the increase in prescription drug monitoring programs (PDMPs),^{29,30} prescribing guidelines,³¹ and the explosion in the availability and use of low-cost illicit opioids.^{32,33} All these factors increase the likelihood of an earlier transition to illicit opioids rather than seeking repeated prescription fills for individuals developing a new opioid use disorder after exposure to a prescription opioid.^{34–36} Given the recent explosion in deaths from illicit opioids,³⁷ this further highlights the importance of keeping opioid-naïve patients opioid-naïve when possible.

DISCUSSION

In this national study of 30,832 commercially insured, opioid-naïve patients treated in the ED for ankle sprains in 2011–15 we found opioid prescribing was common and that there was significant patient- and state-level variation in prescribing patterns. Although declining over time, 20% of opioid-naïve ankle sprain patients were prescribed opioids in 2015, and the prescribing rate was over 10 times higher in some states versus others. This is concerning because ankle sprains are a minor, self-limited condition for which there is likely to be little clinical benefit from opioids.¹⁰

While there was significant variation in the intensity of prescriptions written, less than 5% of prescriptions were written above a clinically significant threshold of more than 225 MME. We found that prescriptions above this threshold were associated with nearly a fivefold increased probability of transition to prolonged use. The interpretation of this finding is that for approximately every 26 patients exposed to greater than 225 MME (the equivalent of more than 30 tabs of oxycodone 5 mg) instead of 75 MME or less (equivalent to 10 tablets of oxycodone 5 mg) 1 additional patient transitioned to prolonged use. While there is room for improvement in promoting opioid stewardship for this minor condition in the ED, the majority of prescriptions written were concordant with guidelines for a 3-day supply^{12,13,31} and had a low total MME of 100 or less. Therefore, more research is urgently needed to examine the relationship between total MME, prolonged use, and adverse events in other contexts, such as for post-operative pain, where prescriptions are much larger.¹²

Our findings make several novel contributions to the growing understanding of opioid prescribing and downstream risks. First, this analysis addresses limitations of previous analyses⁵⁻⁷ in which prolonged opioid use could be caused by the development of a new chronic pain condition at the time of index prescription. By focusing on ankle sprains, an isolated, acute injury that is readily apparent on exam and that rapidly improves within two weeks,⁹ we decreased the likelihood that future opioid prescriptions beginning one month after injury are related to the index condition for which the original opioid was prescribed. Nonsteroidal anti-inflammatory drugs, rather than opioids are first-line treatment for ankle sprains^{38,39} and are just as effective as opioids in pain reduction.¹⁰ We confirmed that the majority of subsequent prescriptions were unlikely to be related to the initial ankle sprain or chronic ankle pain. This suggests that association between larger prescriptions and increased likelihood of prolonged use could be due to other factors such as patients requesting opioids as default pain control, or the development of dependence or misuse. More research is needed to better understand the underlying mechanisms between exposure to larger prescriptions and increased downstream prescription fills. Furthermore, our study population with a median age of 39 is also younger than previous populations that have been studied.⁵⁻⁷ For example, a prior rigorously conducted study using Medicare data⁶ may underestimate the relationship between initial prescription and long term use since opioid prescriptions carry increased acute side effects for elderly patients and are generally prescribed with more caution in this population.⁴⁰ Additionally, younger and middle-aged populations are at highest risk of developing a new opioid use disorder after exposure to opioid prescriptions,^{41,42} and for diverting unused tablets.⁴³

While our study was not designed to evaluate the association between being prescribed any opioid and prolonged use, our findings that those prescribed opioids were more likely to go on to prolonged use compared with those who did not fill opioids is consistent with previous research,^{6,7,44,45} and supports the importance of keeping opioid-naïve patients opioid-naïve.

Second, our study contributes actionable evidence for policy makers, health systems, and clinicians. The significant statewide variation in ED ankle sprain opioid prescribing rates with a concentration of higher prescribing in the southern U.S. is consistent with geographic variation in prescribing for all indications.⁴⁶ By limiting this analysis to a single minor condition for which opioids are not first line treatment, and adjusting for case-mix, our study

suggests ample opportunity to reduce excessive prescribing. Over 140,000 opioid tablets could have been prevented from entering the community if opioids had not been prescribed for our study sample. Substantial reductions in tablets being prescribed could be accomplished with efforts aimed at decreasing excessive variation in the prescribing rate and quantity supplied. This study demonstrates how well defined prescribing indications can be used to promote benchmarks for opioid stewardship efforts. More research is needed to understand the patient, clinician, and environmental causes of this geographic variation and its contributions to the opioid epidemic.

Despite most current guidelines and prescription limit policies being written around days supplied, there is a lack of specificity as to how many tablets and morphine milligram equivalents of common opioid prescriptions such as hydrocodone or oxycodone constitutes a day's supply. This is problematic since we demonstrate higher risk prescriptions of >225 MME could still fall within 5- or 7-day supply limit policies aimed at promoting safer opioid prescribing. The days supplied can be specified by the prescriber based on the start and end date of the prescription, or if this information is not provided, the pharmacist calculates this before claim submission based on the brand label dosing instructions. Therefore, the number of tablets dispensed per prescription is subject to manipulation and can be quite variable for the same number of days supplied. Furthermore, the number of tablets is more clinically relevant. Large numbers of tablets are commonly left over after prescriptions for acute pain and surgical procedures and are poorly secured.^{47–49} Decreasing leftover tablets is critical to reducing diversion and overdoses.⁴³ A promising approach is implementing lower electronic medical record order default opioid quantities (e.g. 10 tablets), which was recently shown to significantly shift ED discharge prescribing patterns towards the default quantity.⁵⁰ More research is needed to investigate whether prescribing limit policies should incorporate total MME or quantity limits.

In summary, our findings continue to support efforts to keep opioid-naïve patients opioid-naïve and to use the smallest quantities of opioid possible when clinically indicated for treatment of acute pain. Prescriptions exceeding 30 tablets of oxycodone 5mg or a total of 225 MME were associated with transition to prolonged use 30–180 days after an initial encounter for ankle sprain among those who had not previously filled an opioid prescription. Opioid prescribing for ankle sprains remains common and is highly variable at the state- and patient-level even though opioids are not first-line treatments for this condition. Given deaths from prescription and illicit opioids continue to increase, this suggests multiple opportunities for clinical, health system, and state-level interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Meetings

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Figure 1.
Study Sample

Figure 2.

These histograms display the patient-level variation in the quantity prescribed for opioid-naïve patients with ankle sprains. A) Displays the total morphine milligram equivalents (MME) per prescription of all patients who received opioid prescriptions ($n = 6,464$, median = 100). B) Displays the number of tablets prescribed for those who received hydrocodone ($n = 4,197$, median = 15). C) Displays the number of tablets prescribed for those who received oxycodone ($n = 928$, median = 16).

Figure 3.

This figure displays the proportion of opioid-naïve patients treated in the ED for ankle sprains who were prescribed opioids according to year of ED visit. The whiskers indicate 95% confidence intervals.

Figure 4.

The map displays the state-level variation in the emergency department opioid prescribing rate for ankle sprains in 2014–15 among patients who were opioid-naïve. The median state-level prescribing rate during these years was 21.3%. The observed prescribed rate is displayed within each state. States with higher than expected prescribing rates based on case mix are highlighted in red and states with lower than expected prescribing rates are shown in blue (see eFigure 1 for caterpillar plot). Case-mix was adjusted for age, sex, race, ethnicity, education, comorbid conditions, and year using multivariate logistic regression.

Figure 5.

A) Association between total morphine milligram equivalents (MME) prescribed and the probability of filling 4 or more new opioid prescriptions 30–180 days after the index visit for ankle sprain among those who were previously opioid-naïve. The whiskers indicate 95% confidence intervals. The logistic regression model adjusted for age, sex, race, ethnicity, educational level, Elixhauser comorbidity score, history of drug abuse, depression, psychoses, state, and year (model area under the curve [AUC] = 0.78). In **B)** the population is limited to just those prescribed hydrocodone and oxycodone (model area under the curve [AUC] = 0.81). For reference, 225 MME is the equivalent of 30 tablets of oxycodone 5 mg and the baseline rate of prolonged use among those who were not prescribed opioids, was 0.5% (95% CI: 0.4–0.6%). See eAppendix for full model estimates and sensitivity analyses of model specifications and outcomes.

Table 1:

Characteristics of Opioid-Naïve Patients Treated for Ankle Sprains

Patient Characteristics	No opioid (n =19,386)	Filled opioid (n= 6,463)	Filled opioid, ≤ 100 MME (n = 4,576)	Filled opioid, > 100 MME (n = 1,887)
Median Age (IQR)	39 (25–56)	38 (28–52)	38 (25–52)	40 (29–52)
Female (%)	10,915 (56.3)	3,392 (52.5)	2,492 (54.5)	900 (47.7)
Race/ethnicity (%)				
Non-Hispanic White	13,165 (67.9)	4,595 (71.1)	3,235 (70.7)	1,360 (72.1)
Hispanic White	2,073 (10.7)	652 (10.1)	468 (10.2)	184 (9.8)
Black	2,483 (12.8)	826 (12.8)	599 (13.1)	227 (12.0)
Asian	554 (2.9)	116 (1.8)	90 (2.0)	26 (1.4)
Unknown	470 (2.4)	104 (1.6)	70 (1.5)	34 (1.8)
Highest education level (%)				
<12 th grade	88 (0.5)	33 (0.5)	23 (0.5)	10 (0.5)
12 th grade	5,818 (30.0)	1,960 (30.3)	1,389 (30.4)	571 (30.3)
<Bachelor's	9,723 (50.2)	3,346 (51.8)	2,392 (52.3)	954 (50.6)
Bachelor's	3,287 (17.0)	1,020 (15.8)	702 (15.3)	318 (16.9)
Unknown	470 (2.4)	104 (1.6)	70 (1.5)	34 (1.8)
Mean No. of Elixhauser Comorbidities (SD)	0.98 (1.62)	0.94 (1.52)	0.93 (1.50)	0.97 (1.57)
Hypertension (%)	4,206 (21.7)	1,459 (22.6)	1,004 (21.9)	455 (24.1)
Depression (%)	1,770 (9.1)	629 (9.7)	452 (9.9)	177 (9.4)
Diabetes, Uncomplicated (%)	1,708 (8.8)	579 (9.0)	401 (8.8)	178 (9.4)
Chronic Pulmonary Disease (%)	1,829 (9.4)	563 (8.7)	414 (9.0)	149 (7.9)
Hypothyroidism (%)	1,484 (7.7)	454 (7.0)	321 (7.0)	133 (7.0)
Obesity (%)	943 (4.9)	367 (5.7)	252 (5.5)	115 (6.1)
Cardiac Arrhythmias (%)	941 (4.9)	250 (3.9)	172 (3.8)	78 (4.1)
Diabetes, Complicated (%)	449 (2.3)	147 (2.3)	101 (2.2)	46 (2.4)
Fluid and Electrolyte Disorders (%)	503 (2.6)	139 (2.2)	92 (2.0)	47 (2.5)
Renal Failure (%)	471 (2.4)	136 (2.1)	89 (1.9)	47 (2.5)
Alcohol Abuse (%)	180 (0.9)	73 (1.1)	51 (1.1)	22 (1.2)
Drug Abuse (%)	203 (1.0)	73 (1.1)	55 (1.2)	18 (1.0)
Prescription characteristics				
Drug name (%)				
Hydrocodone (%)		4,197 (64.9)	3,267 (71.4)	930 (49.3)
Oxycodone (%)		928 (14.4)	255 (5.6)	673 (35.7)
Codeine (%)		353 (5.5)	272 (5.9)	81 (4.3)
Tramadol (%)		1,050 (16.2)	782 (17.1)	268 (14.2)
Other (%)		8 (0.1)	2 (0.0)	6 (0.3)

Patient Characteristics	No opioid (n =19,386)	Filled opioid (n= 6,463)	Filled opioid, ≤ 100 MME (n = 4,576)	Filled opioid, > 100 MME (n = 1,887)
Median number of tablets (IQR)		16 (12–20)	15 (12–20)	24 (20–30)
Median days supplied (IQR)		3 (2–4)	3 (2–4)	4 (3–5)