




## ORIGINAL REPORT

# Patterns of opioid initiation at first visits for pain in United States primary care settings

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**Abstract**

**Purpose:** The primary objective of this study was to characterize variation in patterns of opioid prescribing within primary care settings at first visits for pain, and to describe variation by condition, geography, and patient characteristics.

**Methods:** 2014 healthcare utilization data from Optum's Clinformatics™ DataMart were used to evaluate individuals 18 years or older with an initial presentation to primary care for 1 of 10 common pain conditions. The main outcomes assessed were (1) the proportion of first visits for pain associated with an opioid prescription fill and (2) the proportion of opioid prescriptions with >7 days' supply.

**Results:** We identified 205 560 individuals who met inclusion criteria; 9.1% of all visits were associated with an opioid fill, ranging from 4.1% (headache) to 28.2% (dental pain). Approximately half (46%) of all opioid prescriptions supplied more than 7 days, and 10% of prescriptions supplied  $\geq 30$  days. We observed a 4-fold variation in rates of opioid initiation by state, with highest rates of prescribing in Alabama (16.6%) and lowest rates in New York (3.7%).

**Conclusions:** In 2014, nearly half of all patients filling opioid prescriptions received more than 7 days' of opioids in an initial prescription. Policies limiting initial supplies have the potential to substantially impact opioid prescribing in the primary care setting.

**KEYWORDS**

epidemiology, health policy, opioids, pain, pharmacoepidemiology, primary care

## 1 | BACKGROUND

In 2014, more than 10 million Americans misused prescription opioids.<sup>1</sup> During the same year, prescription opioids led to approximately 1000 emergency room visits per day, and more than 14 000 deaths.<sup>2-5</sup> Opioid initiation for pain, even when intended for short-term use, may lead to significant drug-drug interactions, future dependence, or diversion.<sup>6-14</sup>

Primary care clinicians represent the largest group of opioid prescribers.<sup>6</sup> Accordingly, guidelines recently issued by the Centers for

Disease Control and Prevention (CDC) have targeted primary care clinicians as key agents for containing the opioid epidemic.<sup>15</sup> The guidelines specify that primary care clinicians should avoid opioids when possible and prescribe no more than 7 days of opioids to patients without a prior history of opioid use. Based upon these recommendations, 5 states have already implemented policies limiting initial opioid supplies to 7 days.<sup>16</sup>

Despite the focus of such policies on opioid initiation, and the fact that primary care settings are a major source of prescription opioids, there is a lack of data describing recent patterns of opioid initiation in primary care settings.<sup>16-22</sup> We sought to characterize opioid initiation across a spectrum of pain conditions encountered in primary care settings, to better understand the potential impact of policies directed at the initiation of opioids.

This work was presented on April, 21, 2017 at the National Meeting for the Society of General Internal Medicine.

## 2 | METHODS

We used insurance claims data from the de-identified Clinformatics™ Datamart (OptumInsight, Eden Prairie, MN), a database derived from commercial insurance claims which contains a combination of inpatient and outpatient claims, pharmacy dispensing information, and patient demographics routinely collected during health insurance enrollment.<sup>23</sup> This study included patients with first visits for pain presenting to a primary care setting in 2014 for 1 of 10 conditions commonly managed in primary care settings: back pain with radiculopathy, back pain without radiculopathy, neck pain, joint pain, tendon/bursal pain, muscle strains/sprains, musculoskeletal injury such as ligamentous tears, urinary calculus, headache, and dental pain (see *Online Appendix, Table 1 for ICD9 codes*). These specific conditions were selected on the basis of occurring frequently within our dataset. We focused on first visits in order to quantify the tendency of primary care clinicians to prescribe opioids at early stages of pain management.

Patients were eligible for inclusion if they were at least 18 years of age at the beginning of the year and had a claim for an outpatient visit with a recorded new diagnosis for one of the pain conditions of interest. Patients were further required to have 6 months of continuous enrollment prior to the outpatient visit for pain, to ensure that the encounter was, in fact, a first visit and for 1 week after the visit to assess outcomes. We restricted the analysis to visits with primary care clinicians including generalist physicians (eg, internist, family practitioner), nurse practitioners, or physician assistants in an outpatient setting.

We excluded patients with history of prior opioid fills, admission to hospitals, nursing homes, ambulatory surgical facilities, or hospice/palliative care utilization in the 6 months prior to the outpatient visit of interest. We also excluded patients with a diagnosis of cancer or opioid-abuse/dependence anytime for up to 2 years prior to the outpatient visit, as these represent more specialized patient populations.

### 2.1 | Outcomes

We assessed 2 main outcomes relating to opioid initiation: (1) the proportion of first visits for a specific pain condition associated with initiation of opioids, determined by the presence of a prescription claim within 1 week of the visit and (2) the proportion of opioid prescriptions providing a supply greater than 7 days, the maximum initial supply as recommended in the CDC guidelines<sup>15</sup> (see *Online Appendix, Table 2 for opioids*).

In a post hoc exploratory analysis examining an additional outcome of long-term use by condition in relation to days of opioids initially supplied, we examined the subset of opioid recipients with at least 1 year of continuous health plan enrollment following the index date. We assessed the proportion who continued to use opioids chronically—which we defined as greater than or equal to a cumulative 180 days of opioid use in the year following the index date of opioid initiation.<sup>24</sup> We compared rates of long-term use for patients depending upon the duration of the index supply (ie,  $\leq 7$  days vs 8 days or more).

### 2.2 | Covariates

We extracted information on a number of variables that we anticipated might influence opioid initiation, including geography (ie, state),

### KEY POINTS

- In 2014, prior to the implementation of opioid prescribing guidelines, primary care clinicians prescribed opioids at varying frequencies for different pain complaints during the initial visit, ranging from 4.1% for headache to 28.2% for dental pain.
- When opioids were prescribed, approximately 46% of prescriptions provided more than a 7-day supply at a first visit for pain and 10% provided more than a 30-day supply.

demographics (ie, age, gender), certain chronic medical co-morbidities (ie, renal disease, COPD, or liver disease), and the Charlson comorbidity score. We evaluated any filled prescriptions for an antidepressant, benzodiazepine, muscle relaxant, gabapentanoid, and sedative/hypnotic (eg, zolpidem) in the month prior to the pain visit. We also assessed for evidence of psychiatric diagnoses (depression, anxiety, psychosis), history of alcohol or substance use disorder, and smoking in the previous 6 months.

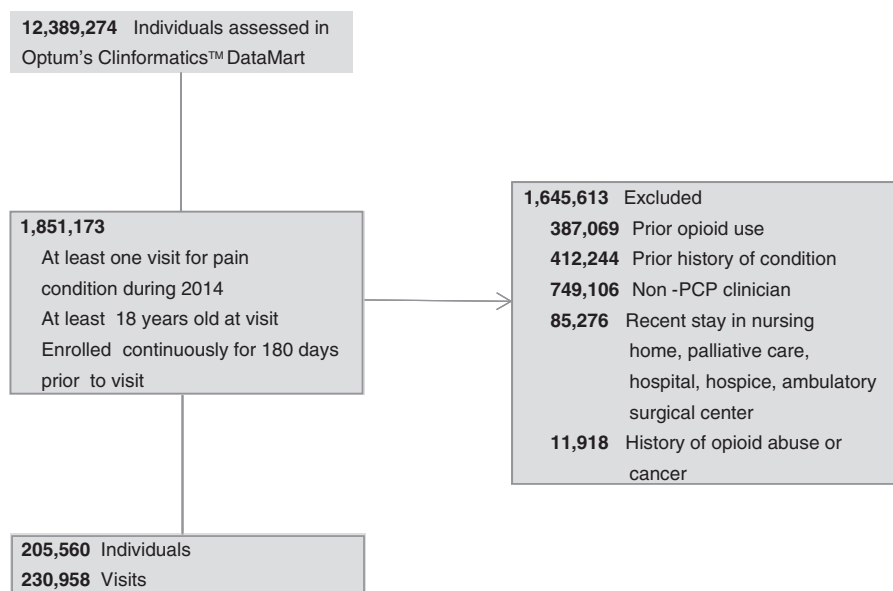
### 2.3 | Analysis

For our main outcomes, we assessed each pain condition individually, as well as overall, and reported the 10<sup>th</sup>, 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>, and 90<sup>th</sup> percentiles of variation in the total dose dispensed in milligrams of morphine equivalents (MME) as well as variation in the days of opioid supplied.<sup>25</sup> Using both univariate and multivariable logistic regression models, we evaluated the association between patient-level and provider-level factors and odds of opioid initiation and, among those prescribed opioids, the odds of receiving  $>7$ -d supply. Adjusted odds ratios (OR) with 95% confidence intervals (CI) summarize the association between opioid prescribing decisions and the covariates above. Finally, we evaluated state-level variation in opioid initiation in our study outcomes using mixed effects regression models that provided adjusted rates of our 2 primary outcomes by state, accounting for patient case mix, patient/clinician characteristics (fixed effects), and possible clustering by state (random effect).

We also described the association between initial days' supplied and chronic opioid use; we dichotomized initial use as  $\leq 7$  versus 8 days or more, and compared chronic use between the 2 groups by deriving a risk difference and 95% confidence interval, for each condition.

## 3 | RESULTS

Of the 12 389 274 individuals in the Optum Research Database during 2014, a total of 205 560 presented to primary care settings with a first visit for pain and met selection criteria (Figure 1). The mean age of the cohort was 44 (SD 13.2); approximately half of encounters involved female patients. Patients were treated by physicians for the majority of visits (97.8%), although a small number of visits were treated by nurse practitioners or physician assistants.



**FIGURE 1** Selection of patients into cohort from Optum's Clinformatics™ DataMart, 2014

The overall rate of opioid initiation was 9.1%. Across conditions, we observed substantial variation in rates of initiation, ranging from 4.1% for patients with headache, to 28.4% for patients with dental pain (Table 1). Among patients receiving opioids, the median initial days' supply of opioid was 7 (IQR 5 to 12), with 46% of opioid prescriptions supplying greater than 7 days of opioids in an initial fill. The most frequently dispensed opioid was hydrocodone (57.3%), followed by tramadol (31.9%) and oxycodone (10.2%); codeine and morphine were each dispensed less than 1% of the time.

We identified a number of factors that were independently associated with increased odds of a patient being prescribed an opioid at a first visit for pain (Table 2). Patients with dental pain, for instance, experienced 6-fold higher odds of receiving opioids at a first visit for pain

relative to patients with joint pain. Recent use of benzodiazepines and sedative hypnotics were also associated with increased odds of receiving opioids at a first visit, as was male gender. Among patients receiving opioids, several factors were significantly associated with increased odds of receiving an initial opioid supply of greater than 7 days, including advanced age and a higher comorbidity score (Table 3).

We observed marked variation in initiation of opioid initiation by state (Figure 2, Panel A), with the highest adjusted rates of initiation at first visits for pain occurring in the Southeast; specifically, states with the highest rates of opioid initiation were Alabama (17%), Arkansas (16%), and Mississippi (14%), while the lowest rates of initiation occurred in New York (4%), Connecticut (5%), New Jersey (5%), and Massachusetts (6%) (see *Online Appendix, Table 3 for crude and adjusted*

**TABLE 1** Frequency of opioid prescribing and quantity prescribed by primary care clinicians for 10 pain conditions in 2014

	Initial pain encounters n	Initial pain encounters with opioid fill <sup>a</sup> % (95% CI)	Days of opioid supplied <sup>b</sup> Median [10 <sup>th</sup> , 25 <sup>th</sup> , 75 <sup>th</sup> , 90 <sup>th</sup> percentile]	Total mg morphine equivalents <sup>b</sup> Median [10 <sup>th</sup> , 25 <sup>th</sup> , 75 <sup>th</sup> , 90 <sup>th</sup> percentile]
All conditions	230 958	9.1 (9.0–9.1)	7 [3, 5, 12, 30]	150 [90, 120, 300, 600]
Joint pain	71 735	6.6 (6.4–6.7)	8 [3, 5, 15, 30]	150 [100, 150, 300, 450]
Back pain without radiculopathy	54 682	14.5 (14.3–14.9)	7 [3, 5, 12, 25]	150 [90, 113, 300, 450]
Headache	40 005	4.1 (4.0–4.4)	7 [3, 4, 12, 24]	150 [75, 100, 300, 600]
Neck pain	18 957	10.2 (9.8–10.6)	7 [3, 5, 12, 23]	150 [75, 102, 300, 450]
Tendonitis/bursitis	18 888	4.9 (4.6–5.3)	7 [3, 5, 13, 30]	150 [90, 120, 300, 450]
Muscular strains/sprains	12 763	10.0 (9.5–10.5)	5 [3, 5, 8, 15]	150 [75, 100, 200, 300]
Back pain with radiculopathy	6983	20.2 (19.3–21.2)	7 [3, 5, 13, 30]	158 [100, 150, 300, 450]
Nephrolithiasis	3593	15.3 (14.2–16.5)	5 [3, 3, 8, 15]	150 [75, 100, 225, 338]
Musculoskeletal injury	2153	7.9 (6.8–9.1)	7 [3, 4, 10, 20]	200 [100, 150, 300, 450]
Dental pain	1199	28.4 (25.9–30.1)	4 [2, 3, 7, 10]	100 [60, 75, 150, 225]

<sup>a</sup>Opioid fill occurred within 1 wk of pain encounter.

<sup>b</sup>Limited to patients with opioid fill.

**TABLE 2** Characteristics of outpatient visits for pain and odds of filling an opioid prescription within 1 wk

	Initial pain encounters without opioid fill (N = 210 017)	Initial pain encounters with opioid fill (N = 20 941)	Univariate analysis: opioid fill	Multivariable analysis: opioid fill
	%	%	OR (95% CI)	OR (95% CI)
<i>Condition</i>				
Joint pain	31.9	22.5	Ref	Ref
Back pain without radiculopathy	22.3	38.0	2.42 (2.33, 2.52)	1.65 (1.58, 1.72)
Headache	18.3	8.0	0.62 (0.59, 0.66)	0.63 (0.59, 0.67)
Neck pain	8.1	9.2	1.61 (1.53, 1.71)	1.08 (1.02, 1.15)
Tendonitis/bursitis	8.6	4.5	0.74 (0.69, 0.80)	0.75 (0.69, 0.80)
Muscular strains/sprains	5.5	6.1	1.58 (1.48, 1.68)	1.51 (1.41, 1.61)
Back pain with radiculopathy	2.7	6.7	3.61 (3.38, 3.85)	2.57 (2.40, 2.75)
Nephrolithiasis	1.5	2.6	2.57 (2.34, 2.83)	2.66 (2.41, 2.93)
Musculoskeletal injury	0.9	0.8	1.21 (1.03, 1.42)	1.28 (1.09, 1.50)
Dental pain	0.4	1.6	5.64 (4.96, 6.41)	5.97 (5.24, 6.80)
<i>Clinician type</i>				
Physician	97.9	97.0	Ref	Ref
Nurse practitioner	1.9	2.6	1.41 (1.29, 1.55)	1.29 (1.18, 1.42)
Physician's Assistant	0.3	0.4	1.68 (1.34, 2.10)	1.55 (1.22, 1.96)
<i>Patient demographics</i>				
<i>Age (y)</i>				
18–45	51.7	51.0	Ref	Ref
46–55	26.0	27.8	1.09 (1.05, 1.12)	1.07 (1.04, 1.11)
56–65	18.9	18.4	0.99 (0.95, 1.03)	0.99 (0.95, 1.03)
>65	3.4	2.9	0.87 (0.80, 0.94)	0.93 (0.85, 1.01)
Male	48.9	56.1	1.34 (1.30, 1.38)	1.26 (1.22, 1.30)
<i>Other medications (in 1 mo prior to index visit)</i>				
Antidepressants	6.1	7.2	1.18 (1.12, 1.25)	1.15 (1.08, 1.22)
Benzodiazepines	3.3	6.4	1.99 (1.87, 2.11)	2.01 (1.87, 2.15)
Gabapentin	0.9	1.7	1.95 (1.74, 2.19)	1.57 (1.39, 1.77)
Muscle relaxants	9.5	32.4	4.56 (4.41, 4.71)	3.67 (3.54, 3.80)
Sedative hypnotic	2.4	2.8	1.20 (1.10, 1.30)	1.23 (1.12, 1.35)
<i>Chronic diseases (in 180 d prior to visit)</i>				
COPD/asthma	5.9	6.1	1.05 (0.99, 1.11)	0.98 (0.92, 1.05)
Liver disease	1.0	0.8	0.81 (0.70, 0.95)	0.79 (0.67, 0.93)
Renal disease	1.1	1.3	1.23 (1.08, 1.40)	1.16 (0.99, 1.35)
<i>Psychiatric disorders (in 180 d prior to visit)</i>				
Anxiety	6.4	6.5	1.01 (0.95, 1.07)	0.88 (0.83, 0.94)
Psychosis	0.2	0.1	0.74 (0.49, 1.13)	0.72 (0.47, 1.10)
Depression	6.0	6.1	1.02 (0.96, 1.08)	0.97 (0.91, 1.04)
<i>Non-prescription drug use (in 180 d prior to visit)</i>				
Smoking	2.4	3.1	1.34 (1.24, 1.46)	1.23 (1.13, 1.34)
Alcohol abuse/dependence	0.3	0.5	1.43 (1.17, 1.76)	1.25 (1.00, 1.55)
Drug abuse	0.1	0.2	1.24 (0.87, 1.77)	1.05 (0.72, 1.52)
<i>Charlson comorbidity score</i>				
0	86.9	86.2	Ref	Ref
1	10.6	11.1	1.06 (1.01, 1.10)	1.09 (1.03, 1.15)
2	1.9	2.1	1.11 (1.00, 1.23)	1.08 (0.97, 1.21)
3 +	0.5	0.6	1.19 (0.99, 1.43)	1.13 (0.91, 1.41)

rates). For our secondary outcome, Michigan and Nevada were the 2 states with the highest proportions of initial supplies exceeding 7 days (64% and 62%, respectively (Figure 2, Panel B) (see Online Appendix, Table 4 for crude and adjusted rates).

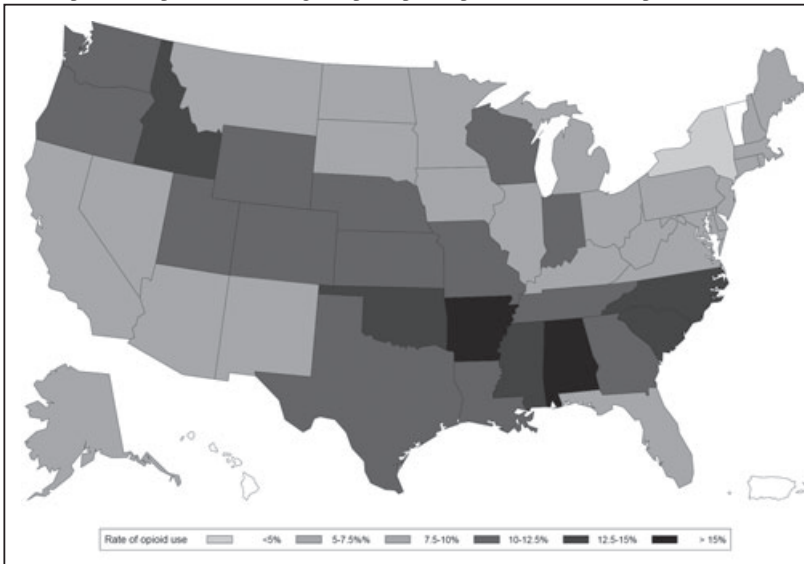
For some conditions, we observed a significant difference in long-term use in relation to initial days' supplied, with the largest risk differences observed for neck, back, and joint pain (Table 4). We observed either small or non-significant

**TABLE 3** Characteristics of initial encounters for pain resulting in >7-d opioid supply<sup>a</sup>

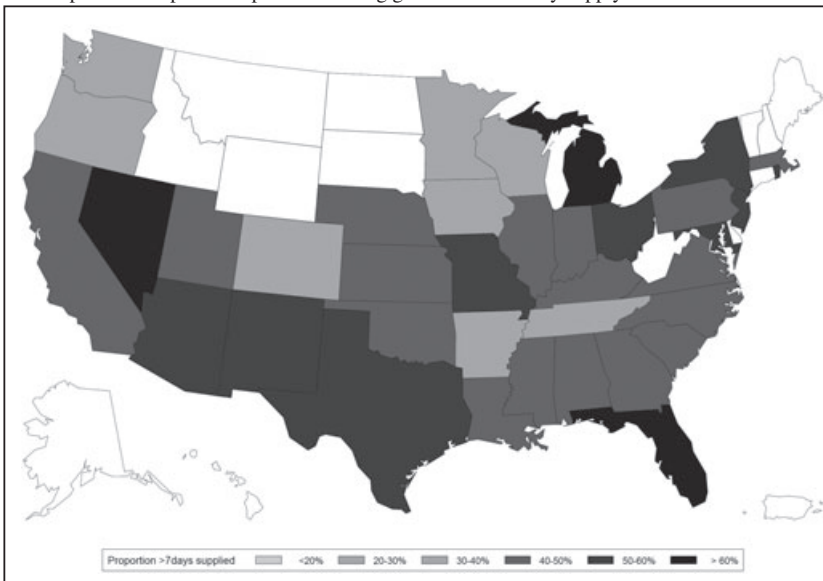
	Initial pain encounters with ≤7 d of opioid supplied (N = 11 273)	Initial pain encounters with >7 d of opioid supplied (N = 9668) >7 d	Univariate analysis: >7 d of opioid supplied	Multivariable analysis: >7 d opioid supplied
	%	%	OR (95% CI)	OR (95% CI)
<i>Condition</i>				
Joint pain	19.7	25.7	Ref	Ref
Back pain without radiculopathy	37.3	38.8	0.80 (0.74, 0.86)	0.94 (0.87, 1.01)
Headache	8.4	7.5	0.68 (0.61, 0.76)	0.74 (0.66, 0.83)
Neck pain	9.2	9.2	0.77 (0.69, 0.85)	0.91 (0.82, 1.02)
Tendonitis/bursitis	4.4	4.5	0.78 (0.68, 0.90)	0.80 (0.69, 0.92)
Muscular strains/sprains	7.9	3.9	0.38 (0.33, 0.43)	0.42 (0.37, 0.48)
Back pain with radiculopathy	6.3	7.2	0.87 (0.77, 0.98)	0.97 (0.85, 1.09)
Nephrolithiasis	3.4	1.7	0.38 (0.32, 0.46)	0.38 (0.32, 0.47)
Musculoskeletal injury	0.8	0.8	0.80 (0.59, 1.09)	0.81 (0.60, 1.11)
Dental pain	2.5	0.6	0.18 (0.13, 0.24)	0.20 (0.15, 0.26)
<i>Clinician type</i>				
Physician	96.4	97.6	Ref	Ref
Nurse practitioner	3.0	2.1	0.69 (0.58, 0.82)	0.72 (0.60, 0.87)
Physician's Assistant	0.5	0.3	0.56 (0.36, 0.87)	0.57(0.36, 0.90)
<i>Patient demographics</i>				
<i>Age (y)</i>				
18–45	56.2	44.9	Ref	Ref
46–55	25.7	30.2	1.47 (1.38, 1.57)	1.35 (1.26, 1.44)
56–65	16.0	21.1	1.65 (1.54, 1.78)	1.41 (1.31, 1.52)
>65	2.12	3.9	2.29 (1.93, 2.70)	1.79 (1.51, 2.13)
Male (% visits)	55.7	56.7	1.04 (0.98, 1.10)	1.07 (1.01, 1.13)
<i>Other medications (in 1 mo prior to index visit)</i>				
Antidepressants	6.8	7.6	1.12 (1.01, 1.24)	1.04 (0.92, 1.16)
Benzodiazepines	5.7	7.1	1.26 (1.13, 1.41)	1.12 (0.99, 1.26)
Gabapentin	1.3	2.2	1.71 (1.38, 2.12)	1.34 (1.08, 1.67)
Muscle relaxants	34.7	29.6	0.79 (0.75, 0.84)	0.74 (0.70, 0.79)
Sedative hypnotic	2.4	3.3	1.35 (1.15,1.59)	1.26 (1.07, 1.50)
<i>Chronic diseases (in 180 d prior to visit)</i>				
COPD/asthma	5.5	6.9	1.27 (1.27, 1.44)	0.87 (0.77, 1.00)
Liver disease	0.6	1.1	1.76 (1.29, 2.39)	1.36 (0.98, 1.87)
Renal disease	0.9	1.8	2.13 (1.66, 2.74)	1.35 (1.00, 1.81)
<i>Psychiatric disorders (in 180 d prior to visit)</i>				
Anxiety	6.0	7.1	1.21 (1.09, 1.35)	1.18 (1.05, 1.34)
Psychosis	0.1	0.1	0.83 (0.37, 1.88)	0.82 (0.35, 1.90)
Depression	6.1	6.2	1.01 (0.90, 1.13)	0.93 (0.82, 1.06)
<i>Non-prescription drug use(in 180 d prior to visit)</i>				
Smoking	2.8	3.6	1.30 (1.11, 1.52)	1.20 (1.02, 1.40)
Alcohol abuse/dependence	0.5	0.5	1.10 (0.75, 1.62)	0.88 (0.59, 1.31)
Drug abuse	0.2	0.2	1.16 (0.59,2.29)	1.10 (0.55, 2.19)
<i>Charlson comorbidity score</i>				
0	89.3	82.5	Ref	Ref
1	8.8	13.8	1.70 (1.56,1.86)	1.55 (1.40, 1.71)
2	1.5	2.8	2.00 (1.65, 2.43)	1.54 (1.24, 1.91)
3 +	0.4	0.9	2.75 (1.89, 4.00)	1.81 (1.18, 2.76)

<sup>a</sup>Restricted to pain visits with opioid fill within 1 wk.

A. Proportion of patients receiving an opioid prescription at first visit for pain\*



B. Proportion of opioid recipients receiving greater than a 7 day supply\*



**FIGURE 2** 2014 Geographic variation: opioid prescribing at first visits for pain in primary care settings. Panel A. Proportion of patients receiving an opioid prescription at first visit for pain\*. Panel B. Proportion of opioid recipients receiving greater than a 7-d supply\*

associations between initial days' supplied and long-term use for other conditions.

#### 4 | DISCUSSION

Our study represents the most recent, comprehensive, and policy-oriented description of opioid initiation in primary care settings in the United States. From a cohort of 210 017 adults presenting to a primary care setting in a first visit for pain, over 20 000 patients received opioids at a first visit for pain. When opioids were prescribed, patients received an initial opioid supply exceeding 7 days in nearly half of cases. Our findings suggest that policies imposing 7-day limits, if implemented nationwide, would have a substantial impact on opioid prescribing patterns.

We observed wide variation in opioid prescribing both within and across conditions that would be reduced by policies limiting initial opioid supplies. While this change might not be beneficial in all situations,

it would serve to eliminate certain prescribing practices that might be considered excessive.<sup>26</sup> Specifically, we found that approximately 1 in 10 opioid recipients in our cohort received an opioid supply of 30 days or greater—the equivalent of 80 tablets of 5-mg oxycodone—in an initial prescription. Even for patients initiating treatment for chronic pain, providing such quantities of opioids to patients without prior or recent experience with opioids, such as the individuals in our cohort, may be associated with risks of accidental overdose, misuse by household members, or diversion of leftover medication.<sup>27-29</sup> Thus, conceivable benefits of policies restricting initial supplies might be to eliminate outliers in prescribing, to promote a culture of providing only the minimum necessary, and to cultivate the expectation among patients that pain will need to be assessed more frequently.

While policies enforcing prescribing limits may confer some benefits, limits that are arbitrarily set at a certain value also run the risk of interfering with “best” clinical care.<sup>30</sup> Much of the variation in opioid prescribing that we observed, for example, might be considered appropriate responses to variation in acuity of pain, expected natural history of the

**TABLE 4** Long-term opioid use in the 1 y following index opioid fill<sup>a</sup>

	Long-term use among individuals with initial opioid fill $\leq 7$ d <sup>b</sup> Proportion (%)	Long-term use among individuals with initial opioid fill $> 7$ d <sup>b</sup> Proportion (%)	Risk difference (95% CI) %
Joint pain	16/1557 (1.0)	90/1751 (5.1)	4.1 (3.0, 5.3)
Back pain without radiculopathy	47/2955 (1.6)	151/2619 (5.8)	4.2 (3.2, 5.2)
Headache	1/642 (0.2)	10/496 (2.0)	1.8 (0.6, 3.5)
Neck pain	9/709 (1.3)	46/605 (7.6)	6.3 (4.2, 8.8)
Tendonitis/bursitis	4/345 (1.2)	14/304 (4.6)	3.4 (0.8, 6.5)
Muscular strains/sprains	1/630 (0.2)	5/263 (1.9)	1.7 (0.4, 4.2)
Back pain with radiculopathy	9/489 (1.8)	36/500 (7.2)	5.4 (2.8, 8.1)
Nephrolithiasis	0/277 (0)	2/120 (1.7)	1.7 (-0.1, 5.9)
Musculoskeletal injury	1/64 (1.6)	1/52 (1.9)	0.3 (-7.8, 10.1)
Dental pain	1/189 (0.5)	0/42 (0)	0.5 (-9.9, 3.4)

<sup>a</sup>Among opioid recipients only and patients with at least 365 d of continuous enrollment following the index fill.

<sup>b</sup>Long-term use defined as  $\geq 180$  d of opioid use.

condition, or logistical factors affecting patient access (eg, dependence on others for transportation in the case of elderly or disabled individuals). We also note that the majority of primary care clinicians in our cohort exhibited a generally cautious approach to opioid initiation, and 90% of the time did not prescribe opioids at a first visit for pain. Furthermore, when opioids were selected, most clinicians prescribed no more than 12 days of opioids, and for some conditions as few as 2. It is not surprising, then, that policies strictly enforcing limits on either days or quantities supplied have been met with criticism, particularly given the lack of data to support a using a threshold of 7 days.<sup>15,31</sup> Whether policies that rigidly enforce limits without enabling the inclusion of important patient-centric factors may lead to such unintended consequences as an increase in health care costs (eg, increased use of emergency rooms, more frequent office visits) and under-treatment of pain is something that will have to be defined. Finally, tighter restrictions on prescription opioids may feed directly into the growing problem of heroin abuse; New York and Massachusetts, states with the lowest rates of opioid initiation in our study and early adopters of the 7-day limits, have also been among the states to witness the greatest recent rise in heroin-related deaths, with such deaths increasing by 30% in each state over the period 2014 to 2015.<sup>16,32</sup>

Apart from the policy implications of our findings, other aspects of our results warrant further exploration. We observed, for instance, that patients with risk factors for developing an opioid use disorder or opioid-related adverse effects (eg, history of smoking, recent benzodiazepine use) were at higher odds of receiving opioids at a first visit for pain, indicating a potential need to strengthen existing risk assessment protocols in primary care settings.<sup>33-37</sup> We also found that even when adjusting for condition, age, and other measured differences, men had a 30% increased odds of receiving opioids at a first visit for pain relative to women, suggesting either objective differences in pain at first presentation or implicit gender bias in prescribing. We were struck by 4-fold geographic variation in opioid initiation by state that persisted even after adjusting for differences such as case-mix. Echoing more general data on prevalent opioid use by state, we observed lowest rates of initiation in the Northeast and highest initiation in the South.<sup>38</sup> Finally, we observed an association between initial days'

supplied and long-term opioid use for some conditions. While experts have advocated for limiting the initial supply of opioids dispensed to prevent the developed of dependence or addition, we are not able to describe the clinical factors that account for the pattern observed in our data. It may be explained by prescribing intent at the outset (ie, the clinician's decision to institute opioids as a chronic medication), severity of illness, or unmeasured confounders. Future research will need to further characterize the extent to which limiting the quantity of medication dispensed with the initial opioid prescriptions decreases chronic opioid use.

Our study has key limitations. First, we were not able to measure or adjust for factors such as pain severity using claims data, which may explain some of the observed variation in opioid prescribing. However, even self-reported pain-rating scales, the established standard used to quantify pain severity, are often difficult to interpret in the context of inconsistent agreement with objective assessments.<sup>39</sup> Second, given that claims data are available only for prescription drugs, we cannot measure use of over-the-counter medication medications prior to a visit. Third, our sample represents a commercially insured population that is relatively healthy and young. Therefore, our findings may not generalize to all populations, including the unemployed and the elderly. Finally, by focusing on primary care settings, our study does not clarify prescribing by other major prescribers such as surgeons, dentists, and emergency room physicians.<sup>6</sup>

The prescribing guidelines issued by the CDC represent the first set of recommendations regarding opioid prescribing that have ever been issued by a national public health agency.<sup>15</sup> Several states have already responded rapidly to these recommendations, and 5 states the Northeast—Massachusetts, New York, Connecticut, Maine, and Rhode Island—have passed new laws in 2016, limiting initial opioid prescriptions to a maximum of 7 days.<sup>16</sup> As opioid limits are considered in a wider number of states, dramatic changes in prescribing practices in the primary care setting can be anticipated, although the extent of this impact will vary based upon baseline patterns. As health systems implement more restrictive prescribing, measures must simultaneously be undertaken to ensure that individuals with pain are not undertreated.<sup>40</sup>

## ETHICS STATEMENT

IRB approval was obtained to conduct this work through the Brigham and Women's Institutional Review Board.

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## CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

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