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Association between initial opioid prescription diagnosis type and subsequent chronic prescription opioid use in Rhode Island: a population-based cohort study

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ABSTRACT

Objective To identify initial diagnoses associated with elevated risk of chronic prescription opioid use.

Design Population-based, retrospective cohort study.

Setting State of Rhode Island.

Participants Rhode Island residents with an initial opioid prescription dispensed between 1 April 2019 and 31 March 2020.

Primary outcome measure Subsequent chronic prescription opioid use, defined as receiving 60 or more days' supply of opioids in the 90 days following an initial opioid prescription.

Results Among the 87 055 patients with an initial opioid prescription, 3199 (3.7%) subsequently became chronic users. Patients who become chronic users tended to receive a longer days' supply, greater quantity dispensed, but a lower morphine milligram equivalents on the initial opioid prescription. Patients prescribed an initial opioid prescription for diseases of the musculoskeletal system and connective tissue (adjusted OR (aOR): 5.9, 95% CI: 4.7 to 7.6), diseases of the nervous system (aOR: 6.3, 95% CI: 4.9 to 8.0) and neoplasms (aOR: 5.6, 95% CI: 4.2 to 7.5) had higher odds of subsequent chronic prescription opioid use, compared with a referent group that included all diagnosis types with fewer than 15 chronic opioid users, after adjusting for confounders.

Conclusions By focusing interventions and prescribing guidelines on specific types of diagnoses that carry a high risk of chronic prescription opioid use and diagnoses that would benefit equally or more from alternative management approaches, states and healthcare organisations may more efficiently decrease inappropriate opioid prescribing while improving the quality of patient care.

Strengths and limitations of this study

► This study included all Rhode Island residents with an initial opioid prescription dispensed by a licensed retail pharmacy during the 12-month study period, which decreases selection bias and provides more generalisable results.

► A high percentage (36%) of initial opioid prescriptions had a missing diagnosis code during the analysis period, which may bias our results.

► Identifying logical, simple and accurate ways to collapse International Classification of Disease codes, 10th revision (ICD-10), into meaningful groups is difficult.

the Centers for Disease Control and Prevention estimated that approximately 50 million Americans are burdened with chronic pain, and of those, 19.6 million have pain that frequently impacts their life or work activities.[2] While prescription opioids may be effective at relieving pain, they fail to alleviate the underlying cause of pain, and the evidence supporting their effectiveness at relieving chronic pain is controversial.[3] Additionally, chronic prescription opioid use can cause dependence in some individuals, which may lead to addiction, overdose, and/or death.

To help define safe prescribing practices, many studies have tried to identify factors associated with prolonged opioid use following specific diagnoses or procedures, including childbirth, major surgeries or chronic conditions.[4–6] While many studies have identified patient-level risk factors associated with chronic opioid use among those with a specific diagnosis (eg, higher doses, history of substance abuse, anxiety or tobacco use), none have attempted to identify initial

INTRODUCTION

In developed countries, pain is one of the most common reasons people seek medical care and managing this pain appropriately can be clinically challenging.[1] An analysis of the National Health Interview Survey by

diagnoses associated with elevated risk of chronic opioid use overall.[5–7]

Previous regulations limiting opioid prescribing have been effective at reducing inappropriate or unsafe opioid prescribing practices.[8] Properly characterising the underlying diagnoses and procedures that resulted in chronic prescription opioid use could inform targeted prescribing guidelines, particularly if those underlying diagnoses and procedures can be managed effectively with non-opioid therapies. To inform these knowledge gaps, we leveraged population-based controlled substance prescribing data to estimate the association between the diagnosis type on the initial opioid prescription and subsequent chronic prescription opioid use.

METHODS

Study design and population

We conducted a population-based retrospective cohort study utilising data from the Rhode Island Prescription Drug Monitoring Programme (PDMP). Our cohort included all Rhode Island residents with an initial opioid prescription dispensed by a retail pharmacy with a controlled substance registration between 1 April 2019 and 31 March 2020.

We identified opioid prescriptions using the American Hospital Formulary Service Pharmacologic—Therapeutic Classification Code (TCC) associated with the National Drug Code of each product in the IBM Micromedex RED BOOK, including opiate agonists (TCC 28:08.08), opiate partial agonists (TCC 28:08.12) and tramadol products (TCC 28:08.92.00.50). We excluded antitussive and antidiarrhoeal medications and buprenorphine products that were only approved by the US Food and Drug Administration for medication-assisted treatment for opioid use disorder as of 30 July 2020 due to our interest in opioids prescribed for pain management. We defined an initial opioid prescription as either (1) the patient's first opioid prescription or (2) an opioid prescription that started at least 60 days after the patient's previous opioid prescription ended. When defining initial opioid prescriptions, we utilised prescriptions filled on/after 1 January 2019 to ensure there was a 'look-back' of at least 90 days for all patients. For patients with more than one initial opioid prescription during the analysis period, we randomly selected one initial prescription for inclusion in the analysis to maintain independence of observations.

In 2018, Rhode Island began requiring prescribers to include the primary International Classification of Disease codes, 10th revision (ICD-10), on all prescriptions for a controlled substance.[9] In this study, our primary exposure was the diagnosis type associated with the primary ICD-10 code on the initial opioid prescription. We classified ICD-10 codes into 20 major diagnostic groups based on ICD-10 code chapters and separately presented specific ICD-10 codes associated with at least 15 chronic opioid users. Our primary outcome was subsequent chronic prescription opioid use, defined as ≥60 days' supply of

opioids dispensed in the 90 days following the fill date of an individual's initial opioid prescription (including the days' supply of the initial prescription).[10] When monitoring subsequent chronic opioid prescription use, we utilised prescription data through 1 July 2020 to ensure at least 90 days of follow-up following the initial opioid prescription for all patients.

We excluded veterinary prescriptions based on an indicator for veterinary prescriptions, an animal name field and the degrees listed with the prescriber's last name (ie, DVM or VMD). Additionally, we excluded initial opioid prescriptions filled by pharmacies for which ICD-10 codes were missing for more than 80% of their dispensed opioid prescriptions due to concerns about bias among the ICD-10 codes that were entered. We defined unique patients based on the first five letters of the last name, the first three letters of the first name and the date of birth on each prescription.

Statistical analysis

We estimated the association between the diagnosis type on the initial opioid prescription and subsequent chronic prescription opioid use using logistic regression, adjusting for potential confounders. The diagnosis categories with fewer than 15 chronic opioid users were collapsed and used as the reference group. Patients with missing diagnosis type were excluded from the model. We selected the following potential confounders a priori: age (continuous) and sex. Characteristics of the initial prescription (eg, type of opioid, days' supply, quantity dispensed, daily morphine milligram equivalents (MME)) were not considered confounders because they are determined by the prescriber based on the diagnosis and, thus, are in the causal pathway between the diagnosis type and subsequent chronic opioid use. While other sociodemographic and clinical factors likely impact chronic opioid use (eg, socioeconomic status), these variables are not recorded in the Rhode Island PDMP database. To understand the potential impact of missing diagnosis category information, we compared the characteristics of initial opioid prescriptions with and without a diagnosis.

All analyses were conducted in SAS V.9.4 (Cary, North Carolina, USA).

Patient and public involvement

No patient or public involvement.

RESULTS

Between 1 April 2019 and 31 March 2020, there were a total of 113 398 initial opioid prescriptions dispensed to 99 129 unique Rhode Island residents. Of these, 98 883 initial opioid prescriptions to 87 055 unique people were dispensed by pharmacies with <80% of initial opioid prescriptions missing an ICD-10 code. After randomly selecting one initial opioid prescription for each of the 10 294 patients with more than one during this period,

Table 1 Baseline characteristics of Rhode Island residents dispensed initial opioid prescriptions, 1 April 2019 to 31 March 2020¶

Characteristics	Overall N=87 055 n (%)†	Subsequent chronic prescription opioid use*	
		Yes N=3199 n (%)†	No N=83 856 n (%)†
Patient Characteristics			
Age	53 (36–66)‡	63 (53–73)‡	53 (36–65)‡
Sex			
Female	50 399 (57.89)	1850 (57.83)	48 549 (57.90)
Male	36 652 (42.10)	1349 (42.17)	35 303 (42.10)
Unknown	<5	0 (0.00)	<5
Payment method			
Private insurance	52 491 (60.30)	1416 (44.26)	51 075 (60.91)
Medicare	12 948 (14.87)	881 (27.54)	12 067 (14.39)
Medicaid	10 829 (12.44)	343 (10.72)	10 486 (12.50)
Cash	8079 (9.29)	389 (12.16)	7690 (9.17)
Workers' compensation	433 (0.50)	22 (0.69)	411 (0.49)
Unknown	2275 (2.61)	148 (4.63)	2127 (2.54)
Prescription Characteristics			
Opioid type			
Oxycodone	37 631 (42.23)	1072 (33.51)	36 559 (43.60)
Hydrocodone	24 261 (27.87)	628 (19.63)	23 633 (28.18)
Tramadol	12 590 (14.46)	1089 (34.04)	11 501 (13.72)
Codeine	9525 (10.94)	135 (4.22)	9390 (11.20)
Morphine	2327 (2.67)	110 (3.44)	2217 (2.64)
Hydromorphone	494 (0.57)	40 (1.25)	454 (0.54)
Buprenorphine (pain)§	91 (0.10)	61 (1.91)	30 (0.04)
Methadone	42 (0.05)	27 (0.84)	15 (0.02)
Fentanyl	28 (0.03)	19 (0.59)	9 (0.01)
Tapentadol	27 (0.03)	8 (0.25)	19 (0.02)
Opium	22 (0.03)	5 (0.16)	17 (0.02)
Oxymorphone	6 (0.01)	<5	5 (0.01)
Butorphanol	<5	<5	<5
Pentazocine	<5	0 (0.00)	<5
Dihydrocodeine	<5	<5	0 (0.00)
Meperidine	<5	<5	<5
Initial opioid prescription			
Days' supply	4 (3–5)‡	10 (5–30)‡	4 (3–5)‡
Quantity prescribed	15 (10–20)‡	20 (20–60)‡	15 (10–20)‡
MME	22.5 (18.0–30.0)‡	20 (10.0–30.0)‡	24.0 (18.8–30.0)‡
90-day follow-up period			
Total days dispensed	5 (3–9)‡	85 (66–100)‡	5 (3–8)‡
Initial MME	23.3 (18.0–30.0)‡	20.0 (10.0–30.0)‡	25.0 (18.8–30.0)‡
Final MME	25.0 (18.0–30.0)‡	20.0 (10.0–40.0)‡	25.0 (18.8–30.0)‡
Prescriber type			
Physician	38 240 (43.93)	2105 (65.80)	36 135 (43.09)

Continued

Table 1 Continued

| | Overall | Subsequent chronic prescription opioid use* | |
| | | Yes | No |
Characteristics	N=87055 n (%)†	N=3199 n (%)†	N=83856 n (%)†
Advanced nurse	11973 (13.75)	541 (16.91)	11432 (13.63)
Physician assistant	13077 (15.02)	372 (11.63)	12705 (15.15)
Dental professional	14262 (16.38)	22 (0.69)	14240 (16.98)
Unknown	9503 (10.92)	159 (4.97)	9344 (11.14)

*Chronic prescription opioid use defined as ≥60 days' supply of opioids dispensed in the 90 days following the fill date of an individual's initial opioid prescription (including the days' supply of the initial prescription).
†Unless otherwise specified.
‡Median (IQR).
§This analysis excluded buprenorphine products only FDA-approved for medication-assisted treatment of opioid use disorder.
¶Initial opioid prescriptions defined as either the patient's first opioid prescription or an opioid prescription that started at least 60 days after the patient's previous opioid prescription ended. For patients with more than one initial opioid prescription during this period, we randomly selected one for inclusion in this analysis.
MME, morphine milligram equivalent.

there were 87055 initial opioid prescriptions dispensed to 87055 unique people in the final study population.

Baseline characteristics of initial opioid prescriptions

The median age of patients receiving an initial opioid prescription was 53 years (IQR=36–66), and a majority (57.9%) of patients were female. Most patients paid for the initial opioid prescription with private insurance (60.3%), followed by Medicare (14.9%) and Medicaid (12.4%). The most common types of opioids prescribed on the initial prescription were oxycodone (42.2%), hydrocodone (27.9%), tramadol (14.5%) and codeine (10.9%). The median days' supply prescribed, and quantity prescribed were 4 days (IQR=3–5) and 15 units (IQR=10–20), respectively. The median daily MME was 22.5 (IQR=18.0–30.0, table 1). Most of the initial opioid prescriptions were prescribed by physicians (43.9%).

Patients with and without subsequent chronic prescription opioid use following the initial prescription differed on all baseline characteristics compared, except for sex and the median MME on their initial opioid prescription. Of note, patients with versus without subsequent chronic prescription opioid use following the initial prescription tended to be older (median: 63 vs 53 years), more likely to have paid for their initial opioid prescription with Medicare (27.5% vs 14.4%), and less likely to have paid with private insurance (44.3% vs 60.9%). Additionally, patients with versus without subsequent chronic use were somewhat more likely to have been prescribed tramadol (34.0% vs 13.7%), hydromorphone (1.3% vs 0.5%) or buprenorphine pain (1.9% vs 0.0%) products; and had a longer median days' supply (10 vs 4 days) and greater quantity dispensed (20 vs 15 units). Finally, patients with versus without subsequent chronic use were somewhat more likely to have been prescribed their initial opioid prescription by a physician (65.8% vs 43.1%) or an advanced nurse (16.9% vs 13.6%) rather than a dentist (0.7% vs 17.0%) or a physician assistant (11.6% vs 15.2%).

Overall, 32574 (36.27%) patients were missing diagnosis code information on their initial opioid prescription. The most common diagnosis codes for the remaining 55481 patients included diseases of the musculoskeletal system and connective tissue (n=15525, 17.8%), diseases of the nervous system (n=8377, 9.6%) and diseases of the digestive system (n=7552, 8.7%; table 2). Notably, patients with unknown versus known diagnosis type were somewhat more likely to pay for their initial opioid prescription with cash (11.2% vs 8.2%), to have received hydrocodone (32.6% vs 25.2%) or codeine (15.2% vs 8.5%) products on their initial opioid prescription, and to have received their initial opioid prescription from a dental professional (29.0% vs 9.2%, table 3).

Opioid prescribing during the 90-day follow-up period

In the 90 days following the start of the initial opioid prescription, the daily MME increased slightly from a median of 23.3 MME (IQR=18.0–30.0) on the first day of opioids prescribed to 25.0 (IQR=18.0–30.0) on the last day of opioids prescribed. Overall, patients were prescribed a median of 5 days (IQR=3–9) of opioids total during the 90-day follow-up period.

Among the 87055 patients with an initial opioid prescription, 3199 (3.7%) subsequently had chronic prescription opioid use per our definition. Similarly, among the 55481 patients with an initial opioid prescription that included a known diagnosis type, 2305 (4.2%) subsequently had chronic prescription opioid use (table 4). When compared with patients prescribed an initial opioid prescription in the referent group (ie, all diagnosis categories with fewer than 15 chronic opioid users), those with diseases of the musculoskeletal system and connective tissue (adjusted OR (aOR): 5.9, 95% CI:

Table 2 Diagnosis type on initial opioid prescriptions dispensed to Rhode Island residents, 1 April 2019 to 31 March 2020*

Diagnosis type	Overall N=87 055 n (%)	Subsequent chronic prescription opioid use	
		Yes N=3199 n (%)	No N=83 856 n (%)
Unknown	31 574 (36.27)	894 (27.95)	30 680 (36.59)
Diseases of the musculoskeletal system and connective tissue	15 525 (17.83)	1157 (36.17)	14 368 (17.13)
Diseases of the nervous system	8377 (9.62)	601 (18.79)	7776 (9.27)
Diseases of the digestive system	7552 (8.67)	34 (1.06)	7518 (8.97)
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	7133 (8.19)	158 (4.94)	6975 (8.32)
Factors influencing health status and contact with health services	3833 (4.40)	63 (1.97)	3770 (4.50)
Injury, poisoning and certain other consequences of external causes	3290 (3.78)	55 (1.72)	3235 (3.86)
Diseases of the genitourinary system	2974 (3.42)	12 (0.38)	2962 (3.53)
Neoplasms	1960 (2.25)	148 (4.63)	1812 (2.16)
Pregnancy, childbirth and the puerperium	1246 (1.43)	<5	1244 (1.48)
Diseases of the respiratory system	811 (0.93)	12 (0.38)	799 (0.95)
Diseases of the skin and subcutaneous tissue	756 (0.87)	15 (0.47)	741 (0.88)
Diseases of the circulatory system	479 (0.55)	16 (0.50)	463 (0.55)
Certain infectious and parasitic diseases	416 (0.48)	5 (0.16)	411 (0.49)
Diseases of the eye and adnexa	277 (0.32)	<5	275 (0.33)
Mental and behavioural disorders	272 (0.31)	9 (0.28)	263 (0.31)
Endocrine, nutritional and metabolic diseases	267 (0.31)	6 (0.19)	261 (0.31)
Congenital malformations, deformations and chromosomal abnormalities	145 (0.17)	5 (0.16)	140 (0.17)
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	85 (0.10)	<5	81 (0.10)
External causes of morbidity and mortality	82 (0.09)	<5	81 (0.09)
Certain conditions originating in the perinatal period	<5	0 (0.00)	<5

*Initial opioid prescriptions were defined as either the patient's first opioid prescription or an opioid prescription that started at least 60 days after the patient's previous opioid prescription ended. For patients with more than one initial opioid prescription during this period, we randomly selected one for inclusion in this analysis.

4.7 to 7.6), diseases of the nervous system (aOR: 6.3, 95% CI: 4.9 to 8.0) and neoplasms (aOR: 5.6, 95% CI: 4.2 to 7.5) had higher odds of subsequent chronic prescription opioid use after adjusting for age and sex, and had an elevated percentage of patients with chronic use when compared with the overall average (7.5%, 7.2% and 7.6%, respectively, when compared with 1.0%).

When looking at the specific ICD-10 codes with at least 15 patients with subsequent chronic prescription opioid use, pain not elsewhere classified (G89; 592/2305, 25.7%), dorsalgia (M54; 477/2305, 20.7%), pain, unspecified (R52; 95/2305, 4.1%) and other joint disorders not elsewhere classified (M25; 94/2305, 4.1%) had the highest number of chronic users (table 5). Notably, specific diagnoses that had a relatively high percentage of patients who progressed to chronic use following the

initial opioid prescription included: intraoperative and postprocedural complications and disorders of musculoskeletal system, not elsewhere classified (31/89, 34.8%); polyosteoarthritis (38/205, 18.5%); rheumatoid arthritis (15/84, 17.9%); and spondylosis (69/407, 17.0%).

DISCUSSION

In the 12-month study period, nearly 10% of Rhode Island residents received at least one initial opioid prescription, of whom 3.7% went on to become chronic prescription opioid users based on our study definition. Tramadol, hydromorphone and buprenorphine pain products were more often prescribed on the initial opioid prescription to people who became chronic prescription opioid users. Moreover, chronic users tended to receive a longer days'

Table 3 Characteristics associated with unknown diagnosis type on initial opioid prescriptions dispensed to Rhode Island residents, 1 April 2019 to 31 March 2020§

Characteristics	Known diagnosis type N=55481 N (%)*	Unknown diagnosis type N=31574 N (%)*
Patient characteristics		
Age	54 (37–66)†	52 (34–65)†
Sex		
Female	33007 (59.49)	17392 (55.08)
Male	22474 (40.51)	14178 (44.90)
Unknown	0 (0.0)	<5
Payment method		
Private insurance	33777 (60.88)	18714 (59.27)
Medicare	8358 (15.06)	4590 (14.54)
Medicaid	6861 (12.37)	3968 (12.57)
Cash	4552 (8.20)	3527 (11.17)
Workers' compensation	241 (0.43)	192 (0.61)
Unknown	1692 (3.05)	583 (1.85)
Prescription characteristics		
Opioid type		
Oxycodone	26422 (47.62)	11209 (35.50)
Hydrocodone	13955 (25.15)	10306 (32.64)
Tramadol	8417 (15.17)	4173 (13.22)
Codeine	4719 (8.51)	4806 (15.22)
Morphine	1483 (2.67)	844 (2.67)
Hydromorphone	314 (0.57)	180 (0.57)
Buprenorphine (pain)‡	70 (0.13)	21 (0.07)
Methadone	32 (0.06)	10 (0.03)
Fentanyl	25 (0.05)	<5
Tapentadol	16 (0.03)	11 (0.03)
Opium	18 (0.03)	<5
Oxymorphone	<5	<5
Butorphanol	<5	<5
Pentazocine	0 (0.00)	<5
Dihydrocodeine	<5	0 (0.00)
Meperidine	<5	<5
Chronic opioid use		
Yes	472 (0.85)	175 (0.55)
No	55009 (99.15)	31399 (99.45)
Initial opioid prescription		
Days' supply	5 (3–5)†	4 (3–5)†
Quantity prescribed	18 (10–20)†	15 (10–20)†
Daily MME	25.0 (18.8–30.0)†	22.5 (18.0–30.0)†
90-day follow-up period		
Total days prescribed	5 (3–5)†	5 (3–7)†
Initial MME	25.0 (18.8–30.0)†	22.5 (18.0–30.0)†
Final MME	25.0 (18.8–30.0)†	22.5 (18.0–30.0)†
Prescriber type		
Physician	26083 (47.01)	12157 (38.50)
Physician assistant	8954 (16.14)	4123 (13.06)

Table 3 Continued

Characteristics	Known diagnosis type N=55481 N (%)*	Unknown diagnosis type N=31574 N (%)*
Advanced nurse	8458 (15.24)	3515 (11.13)
Dental professional	5101 (9.19)	9161 (29.01)
Unknown	6885 (12.41)	2618 (8.29)

*Unless otherwise specified.
†Median (IQR).
‡This analysis excluded buprenorphine products that were only FDA-approved for medication-assisted treatment of opioid use disorder.
§Initial opioid prescriptions were defined as either the patient's first opioid prescription or an opioid prescription that started at least 60 days after the patient's previous opioid prescription ended. For patients with more than one initial opioid prescription during this period, we randomly selected one for inclusion in this analysis.
MME, morphine milligram equivalent.

supply, greater quantity dispensed, but a lower MME on the initial opioid prescription. Physicians and advanced nurses more often prescribed the initial opioid prescription of patients who become chronic prescription opioid users. Overall, initial opioid prescriptions were most often prescribed for diseases of the musculoskeletal system and connective tissue, diseases of the nervous system and diseases of the digestive system, and these diagnoses were strongly associated with subsequent chronic prescription opioid use. Among ICD-10 codes with at least 15 chronic users, the percentage of patients who went on to develop chronic prescription opioid use following the initial prescription ranged from 1.9% to 34.8% by the specific ICD-10 code.

While prior work has focused on chronic prescription opioid use following specific diagnoses or procedures, our population-based study evaluated chronic prescription opioid use among all patients receiving initial opioid prescriptions in Rhode Island.[4–6] Despite differences in methodology, other studies estimating the frequency of chronic prescription opioid use after childbirth (1.7%–2.2%), dental procedures (2.4%–4.1%), elective surgeries (3.0%–8.0%) or cancer treatment (8.3%) identified a similar percentage of patients with chronic use compared with our study of all patients receiving initial opioid prescriptions (3.67%).[4–7 11–14] In the absence of similar population-based studies, these comparisons suggest that the percentage of patients experiencing subsequent chronic prescription opioid use in our study was generally similar to what might be expected based on prior work. While other studies often define chronic use as one or more claims for opioid prescriptions 0–90 and 90–180 days after the procedure/diagnosis, we defined chronic use as at least 60 days' supply of opioids dispensed in the 90 days following the fill date of an individual's initial opioid prescription (including the days' supply of the initial prescription).[5 7 9 10] We used this relatively strict definition of chronic prescription opioid in an attempt to exclude patients who intermittently used opioids and to focus our analysis on opioid prescribing patterns most

Table 4 Association between the diagnosis type on the initial opioid prescription and subsequent chronic prescription opioid use among Rhode Island residents, 1 April 2019 to 31 March 2020†, *

Diagnosis type	Subsequent chronic prescription opioid use		Adjusted OR (95% CI)‡
	No N=53 176 n (row %)	Yes N=2305 n (row %)	
Diseases of the musculoskeletal system and connective tissue	14 368 (92.55)	1157 (7.45)	**5.94 (4.68–7.56)**
Diseases of the nervous system	7776 (92.83)	601 (7.17)	**6.26 (4.90–8.01)**
Diseases of the digestive system	7518 (99.55)	34 (0.45)	**0.43 (0.29–0.65)**
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	6975 (97.78)	158 (2.22)	**1.96 (1.48–2.60)**
Factors influencing health status and contact with health services	3770 (98.36)	55 (1.67)	1.34 (0.96–1.89)
Injury, poisoning and certain other consequences of external causes	3235 (98.33)	55 (1.67)	1.38 (0.97–1.96)
Neoplasms	1812 (92.45)	148 (7.55)	**5.60 (4.20–7.47)**
Diseases of the circulatory system	463 (96.66)	16 (3.34)	**2.05 (1.18–3.57)**
Other§	7259 (99.00)	73 (1.00)	Ref

Significant adjusted odds ratios where p<0.05 are bolded

*Initial opioid prescriptions defined as either the patient's first opioid prescription or an opioid prescription that started at least 60 days after the patient's previous opioid prescription ended. For patients with more than one initial opioid prescription during this period, we randomly selected one for inclusion in this analysis.

†Chronic prescription opioid use defined as ≥60 days' supply of opioids dispensed in the 90 days following the fill date of an individual's initial opioid prescription (including the days' supply of the initial prescription).

‡Adjusted for potential confounders selected a priori: age (continuous) and sex.

§Other includes all initial opioid prescriptions for diagnosis types with 15 or less chronic users, including: certain conditions originating in the perinatal period, certain infectious and parasitic diseases, congenital malformations, deformations and chromosomal abnormalities, diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism, diseases of the eye and adnexa, external causes of morbidity and mortality, pregnancy, childbirth and the puerperium, mental and behavioural disorders, endocrine, nutritional and metabolic diseases, diseases of the skin and subcutaneous tissue, diseases of the respiratory system and diseases of the genitourinary system.

likely to represent chronic use and carry the greatest risk of opioid addiction.[15]

Unfortunately, the Rhode Island PDMP only recently started collecting ICD-10 codes on controlled substance prescriptions, and as such, we do not know if the percentage of patients who developed chronic prescription opioid use following an initial prescription has changed over time. Additionally, it is possible that the 'legacy population' of long-term prescription opioid users in Rhode Island began their chronic use through different diagnoses than those reported here, particularly given changes in prescribing patterns over the past 5–10 years. The Rhode Island Department of Health, in collaboration with other sister state agencies and community-based organisations, has launched several interventions that may have reduced the chronic prescription opioid use over time, including one-on-one targeted prescriber education on responsible prescribing, appropriate regulation regarding prescribing, and provider reimbursement for the use of non-opioid pain management strategies.[9 16 17]

A primary benefit of categorising diagnosis type through ICD-10 codes in this population-based study is the ability to systematically review opioid prescribing patterns among patients with different diseases or sources of pain. Previous studies have shown the dangers of inappropriate prescribing, but effectively targeting interventions and prescribing guidelines to minimise risk of chronic opioid use while appropriately managing pain is challenging.[18] Our study identified a few diagnosis types on initial opioid prescriptions that are associated with greater odds of subsequent chronic prescription opioid use in Rhode Island, which allows our state to prioritise interventions that target specific practice areas. For instance, we found that diseases of the musculoskeletal system and connective tissue were highly associated with subsequent chronic prescription opioid use, and initial opioid prescriptions with ICD-10 codes for polyosteoarthritis, rheumatoid arthritis, spondylosis and intraoperative/postprocedural complications and disorders of the musculoskeletal system had a particularly high percentage of patients develop chronic use after initiation. Given that many patients with musculoskeletal pain can improve over time independent of treatment, prior work has suggested that non-pharmacological treatments be utilised first (eg, physical therapy, acupuncture, massages), followed by or with anti-inflammatory medications, and if patients are still experiencing pain,

Table 5 ICD-10 codes on initial opioid prescriptions with the highest number of subsequent chronic prescription opioid users, Rhode Island residents—1 April 2019 to 31 March 2020*

	Subsequent chronic prescription opioid use	
	N=2305 n (row %)	N=53 176 n (row %)
Diagnosis	**Yes**	**No**
Pain, not elsewhere classified (G89)	592 (7.86)	6087 (92.14)
Dorsalgia (M54)	477 (9.75)	4416 (90.25)
Pain, unspecified (R52)	95 (2.27)	4081 (97.73)
Other joint disorder, not elsewhere classified (M25)	94 (4.76)	1880 (95.24)
Spondylosis (M47)	69 (16.95)	338 (83.05)
Thoracic, thoracolumbar, and lumbosacral intervertebral disc disorders (M51)	67 (13.76)	420 (86.24)
Osteoarthritis of knee (M17)	59 (7.11)	771 (92.89)
Other and unspecified soft tissue disorders, not elsewhere classified (M79)	58 (5.48)	1001 (94.52)
Other and unspecified osteoarthritis (M19)	50 (12.17)	361 (87.83)
Other spondylopathies (M48)	42 (8.11)	476 (91.89)
Polyosteoarthritis (M15)	38 (18.54)	167 (81.46)
Intraoperative and postprocedural complications and disorders of musculoskeletal system, not elsewhere classified (M96)	31 (34.83)	58 (65.17)
Abdominal and pelvic pain (R10)	23 (2.03)	1108 (97.97)
Oseoarthritis of hip (M16)	22 (5.46)	381 (94.54)
Malignant neoplasm of bronchus and lung (C34)	22 (14.29)	132 (85.71)
Presence of other functional implants (Z96)	17 (3.83)	427 (96.17)
Other deforming dorsopathies (M43)	15 (8.77)	156 (91.23)
Other rheumatoid arthritis (M06)	15 (17.86)	69 (82.14)
All other ICD-10 codes	592 (1.88)	30 847 (98.12)

*Initial opioid prescriptions were defined as either the patient's first opioid prescription or an opioid prescription that started at least 60 days after the patient's previous opioid prescription ended. For patients with more than one initial opioid prescription during this period, we randomly selected one for inclusion in this analysis.

prescription opioids.[19][20] Importantly, as the pathophysiology of musculoskeletal diseases is inflammatory, a prescription opioid to block pain is not clinically appropriate, and if pharmacological therapy is necessary, anti-inflammatory medications may be more efficacious than opioids.[21] This is true for diagnoses of polyosteoarthritis, rheumatoid arthritis and spondylosis, which are generally inflammatory in nature, and depending on the diagnosis standard treatment guidelines recommend treatment with non-steroidal anti-inflammatory drugs, corticosteroids, muscle relaxants, steroids, disease-modifying anti-rheumatic drugs, biologics, anti-seizure medications, warming therapy, exercise and/or antidepressants rather than opioid pain management.[22] By focusing interventions and prescribing guidelines on specific types of diagnoses that carry a high risk of chronic opioid use and benefit equally or more for alternative management approaches, states and healthcare organisations may efficiently decrease inappropriate opioid prescribing while improving the quality of patient care. Our study suggests that interventions focused on appropriate management of musculoskeletal conditions, including polyosteoarthritis,

rheumatoid arthritis and spondylosis, may be particularly beneficial given the overall association with chronic use and the high percentage of patients who develop chronic use after an initial opioid prescription for one of these diagnoses.

This study can serve as an example for other states looking to undertake a similar analysis of new chronic prescription opioid use in their population and highlights the added value of collecting ICD-10 codes associated with prescriptions in PDMPs. Replicating this study in other regions could inform the standard of care for pain management and hopefully lead to safer prescribing patterns.

A major strength of this study is the inclusion of all opioid prescriptions dispensed to Rhode Island residents by licensed retail pharmacies for the 12-month study period through the Rhode Island PDMP. The use of a large, population-based study decreases selection bias and provides more generalisable results, although we are not able to identify specific subpopulations with unique risk profiles using this approach. Additionally, our restrictive definition of chronic prescription opioid use

likely minimised the inclusion of intermittent prescription opioid users in this group, improving the specificity of our outcome. Finally, this study demonstrates the utility of collecting ICD-10 codes in PDMPs, as this allows for consideration of the *reason* for prescriptions in population-based epidemiologic studies. This highlights for us the advantage of increasing ICD-10 reporting. As reporting increases, this dataset provides a way to systematically identify the diagnoses associated with all opioid prescriptions dispensed to Rhode Island residents.

Despite the advantages of having ICD-10 codes in the Rhode Island PDMP, the largest limitation of this study was the high percentage (36%) of opioid initiate prescriptions with a missing diagnosis code during the analysis period. Unfortunately, we are not able to determine whether the prescriber neglected to provide an ICD-10 code on the prescription, or the pharmacy neglected to include the ICD-10 code when reporting to the PDMP. Although initial opioid prescriptions with and without ICD-10 codes were significantly different on all characteristics compared, our sample size was large, and the most meaningful difference was that prescriptions missing ICD-10 codes were more often written by dental professionals. It may be useful to support dental professionals in the reporting of ICD-10 codes, including sharing the results of these types of studies, to improve the completeness of reporting. Additionally, this analysis is limited to opioids dispensed by retail pharmacies and does not include those dispensed at hospitals or by Veterans Affairs, which may modify our results. Finally, due to variation in the specificity of ICD-10 codes, identifying logical, simple and accurate ways to collapse them into meaningful groups is difficult. Improved systematic methods for categorising ICD-10 codes into clinically meaningful groups would be useful for future epidemiologic studies.

CONCLUSIONS

Despite nearly 10% of Rhode Island residents receiving an initial opioid prescription in the 12-month study period, 3.7% went on to become chronic prescription opioid users based on our study definition. Diseases of the musculoskeletal system and connective tissue, diseases of the nervous system and neoplasms carried a high risk of subsequent chronic opioid use. For diagnoses in these groups that would benefit equally or more from alternative management approaches, we can create targeted interventions and prescribing guidelines to efficiently decrease inappropriate opioid prescribing while improving the quality of patient care.

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