

Opioid-Prescribing Metrics in Washington State: Trends and Challenges

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ABSTRACT

Context: Analyses of prescribing trends using prescription drug monitoring programs (PDMP) are impacted by changes in reporting requirements and in the scheduling of medications by the Drug Enforcement Administration. In 2014, the Drug Enforcement Administration changed the status of tramadol from an unscheduled to a scheduled medication. The addition of tramadol to the PDMP may affect the prevalence of opioid-prescribing metrics and the interpretation of prescribing trends.

Objective: The objectives were to (1) examine trends in opioid prescribing in Washington State between 2012 and 2017, (2) assess the potential impact of adding tramadol to PDMP on these trends, and (3) describe challenges in defining and implementing opioid-prescribing metrics.

Design: Analysis of quarterly summary statistics of opioid prescribing.

Setting: Washington State.

Participants: Washington State residents.

Main Outcome Measures: The metrics include measures of opioid prescribing overall and by age group, chronic opioid prescribing, high-dose prescribing among those on chronic opioid therapy, prescribing of concurrent opioids and sedatives, days' supply of new opioid prescriptions, and transition from short-term to long-term use of opioids.

Results: In Washington, the prevalence of any opioid prescribing, chronic opioid prescribing, high-dose opioid prescribing, and prescribing of concurrent opioids and sedatives declined between 2012 and 2017. The prevalence of opioid prescribing was higher in older than in younger age groups. The addition of tramadol to the Washington PDMP in 2014 affected the observed prevalence of all opioid metrics and of all opioid-prescribing trends. Conclusions about trends in opioid prescribing differ substantially depending on whether tramadol is included or not, particularly in 2014 and 2015.

Conclusions: The development of opioid-prescribing metrics is relatively new. There is likely much benefit of standard definitions of opioid metrics at the state and national levels to track important trends and compare progress from state to state.

KEY WORDS: analgesics, epidemiologic surveillance, hypnotics and sedatives, opioid, prescribing patterns

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Although the percentage of opioid overdose deaths involving prescription opioids has declined,^{1,2} the overall rate of overdose deaths associated with prescription opioids remains high.^{3,4} High opioid doses, chronic use, and concurrent use of opioids and sedatives have been associated with a higher risk of fatal and nonfatal opioid overdoses.⁵⁻⁸ Opioid-prescribing guidelines and use of prescription drug monitoring programs (PDMP) are 2

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of the strategies being used to address the share of the opioid epidemic attributable to prescription opioids. In 2016, the Centers for Disease Control and Prevention published national prescribing guidelines.⁹ Many individual states have published opioid-prescribing guidelines, including Washington State, which has published comprehensive guidelines on prescribing opioids for pain.¹⁰ As of 2018, 49 of 50 states operate statewide PDMPs to track controlled substance prescriptions. Guidelines and PDMPs have been associated with decreases in opioid prescribing overall as well as reductions in high-dose prescribing, inappropriate prescribing, and opioid misuse.¹¹⁻¹³

Utilizing consistent methods to track opioid prescribing may help health care providers and insurers improve prescribing practice and decrease morbidity and mortality associated with opioid overdoses. As one promising example, the Bree Collaborative,¹⁴ a partnership of public and private health care sector stakeholders in Washington, developed and adopted a set of opioid-prescribing metrics in 2017¹⁵ to support and track the impact of state efforts to reverse the opioid epidemic.

State PDMPs are one source of data to monitor prescribing trends.¹⁶⁻¹⁹ However, analyses of prescribing trends using PDMP data are impacted by changes in PDMP reporting requirements and changes in the scheduling of medications by the Drug Enforcement Administration (DEA). One example is tramadol, a pain medication that was originally considered low risk. However, because of concerns about abuse and addiction, on August 18, 2014, the DEA changed the status of tramadol from being an unscheduled medication to a scheduled medication. In Washington, tramadol prescriptions were added to the state PDMP at that time and tramadol prescriptions filled prior to this date were not reported to the PDMP. The addition of tramadol to the PDMP may affect the prevalence of all opioid-prescribing metrics and may impact the interpretation of changes in prescribing trends.

The purpose of this article is to (1) examine trends in opioid prescribing in Washington State between 2012 and 2017, (2) assess the potential impact of adding tramadol to PDMPs on these trends, and (3) describe challenges in defining and implementing opioid-prescribing metrics.

Methods

Opioid-prescribing metrics

The Washington State Bree Collaborative developed 6 opioid-prescribing metrics through expert consensus with public input.^{14,15} For this analysis, we

present Washington opioid-prescribing metrics, as implemented by the Department of Health Washington Tracking Network,²⁰ a source of state and county public health data. The metrics include measures of opioid prescribing overall and by age group, chronic opioid prescribing, high-dose prescribing among those on chronic opioid therapy, prescribing of concurrent opioids and sedatives, days' supply of new opioid prescriptions, and transition from short-term to long-term use of opioids. The Department of Health definitions of the metrics are shown in the Table. Each metric was calculated by calendar quarter and the population denominators were determined as of April 1 of each year.²¹ Prevalence of opioid use was defined as the number of patients who filled at least 1 opioid prescription during the calendar quarter divided by the Washington population as of April 1²¹ of that calendar year. The prevalence of having at least 1 opioid prescription in a quarter was also calculated by age group (0-9, 10-17, 18-24, 25-34, 35-44, 45-54, 55-64, 65-74, and 75+ years). Chronic use was defined as having a 60 days' or longer supply of opioids dispensed in a calendar quarter. Among those prescribed chronic opioids, 3 high-dose categories were constructed: an average of at least 50, at least 90, or at least 120 morphine milligram equivalents (MME), which is a measure of opioid dosage relative to morphine, per day over the calendar quarter. To calculate the average MME, the total MME dispensed per person during the calendar quarter was divided by the number of days in the quarter (89-92 days). Concurrent sedatives was defined as having at least 1 day of overlap of opioid and sedative prescriptions during the quarter. Lists of medications classified as sedatives, including hypnotics, benzodiazepines, carisoprodol, and barbiturates, are available in the Opioid Prescribing Metrics document on the Washington State Bree Collaborative Web site.¹⁵ If a patient did not have opioids dispensed in a previous quarter, the patient was considered to have new opioid use in the current calendar quarter. For these new patients, the days' supply of the first prescription was assessed. The transition from acute to chronic use was defined as the number of new opioid users in one quarter who had at least 60 days' worth of opioids dispensed in the next calendar quarter. Opioid medications were identified using National Drug Codes. Buprenorphine, which is used to treat opioid addiction, was excluded from the calculation of all metrics.

Data sources

The Washington State Prescription Monitoring Program began collecting prescription data in late 2011; provider access and data availability began January 1,

TABLE
Washington State Opioid-Prescribing Metrics: Washington Tracking Network

Opioid-Prescribing Metrics	Numerator	Denominator
Any opioid prescription	Number of patients with ≥ 1 opioid Rx filled	Number in population
Chronic opioid prescriptions		
Prevalence of chronic opioid users	Number of patients with ≥ 60 d supply from opioid Rx filled	Number in population
High-dose chronic opioid prescriptions		
Prevalence of chronic opioid users prescribed ≥ 120 , ≥ 90 , or ≥ 50 MME/d	Number of patients with chronic opioids with dose ≥ 120 , ≥ 90 , or ≥ 50 MME/d	Number in population
Concurrent opioids and sedatives		
Prevalence of opioid users with at least 1 d of overlap with a sedative	Number of patients with overlapping supply of opioids and sedatives	Number in population
Days' supply on first opioid prescription		
Percent with ≤ 3 , 4–7, 8–13, and ≥ 14 d supply on the first opioid prescription among new opioid users ^a	Number of new users with ≤ 3 , 4–7, 8–13, and ≥ 14 d supply on the first opioid prescription	Number of new opioid users in quarter with no opioid Rx in prior quarter
Transition from acute to chronic opioid prescriptions		
Incidence of new users ^a transitioning to chronic users	Number of opioid users with ≥ 60 d in current quarter who were new users in previous quarter	Number in population

Abbreviations: MME, morphine milligram equivalents. Rx, prescription.

^aNew users: No opioid prescription in prior quarter and 1+ opioid prescription in current quarter (with respect to indicated quarter).

2012. For controlled substances, dispensers (primarily pharmacies) provide the medication name, National Drug Codes, dose, the date the medication was dispensed, and days' supply to the PDMP. For this analysis, we analyzed quarterly summary data from January 1, 2012, through December 31, 2017. Because this analysis used only summary data, institutional review board review was not required.

Statistical analysis

We examined prescribing trends in several different ways, in part because various states and organizations use different denominators for opioid-prescribing metrics. To assess the impact of the tramadol scheduling change, we described prescribing trends in Washington with and without including tramadol in the construction of the metrics. Generally, we presented the prevalence or incidence per 1000 population for each metric. However, for the metric on chronic opioid prescribing, we also presented the percentage of patients with chronic opioids among patients with any opioid prescription, in addition to presenting the rate per 1000. Direct standardization using the 2000 US Census population proportions for gender and 5-year age groups was employed to obtain age- and gender-adjusted estimates for most metrics (except for prevalence by age group and days' supply of the first prescription).

Results

Trends in opioid-prescribing metrics (excluding tramadol)

Between 2012 and 2017, the trend in the overall prevalence of the population in Washington state with an opioid prescription (excluding tramadol) decreased from 98.2 per 1,000 in the first quarter of 2012 to 69.8 per 1,000 in the fourth quarter of 2017 (Figure 1). The prevalence of the population with chronic opioid prescriptions was 19.3 per 1000 population in the first quarter of 2012 and began to decrease after 2015 with a prevalence of 15.7 per 1000 at the end of 2017. The prevalence of patients with chronic opioids with high doses decreased slightly from 2012 through 2014 and began to decrease more rapidly after 2015. Using the 120 MME level, the prevalence decreased from 3.2 per 1000 in 2012 to 1.6 per 1000 in 2017. The prevalence of concurrent opioids and sedatives decreased from 19.5 per 1000 in the first quarter of 2012 to 11.6 per 1000 in the fourth quarter of 2017. Among patients with new opioid prescriptions in the first quarter of 2012, approximately 8% were dispensed with at least a 14 days' supply and the percentage remained fairly constant between 2012 and 2017. The transition from acute to chronic opioids decreased from approximately 1.2 per 1000 in 2012 to 0.5 per 1000 in 2017.

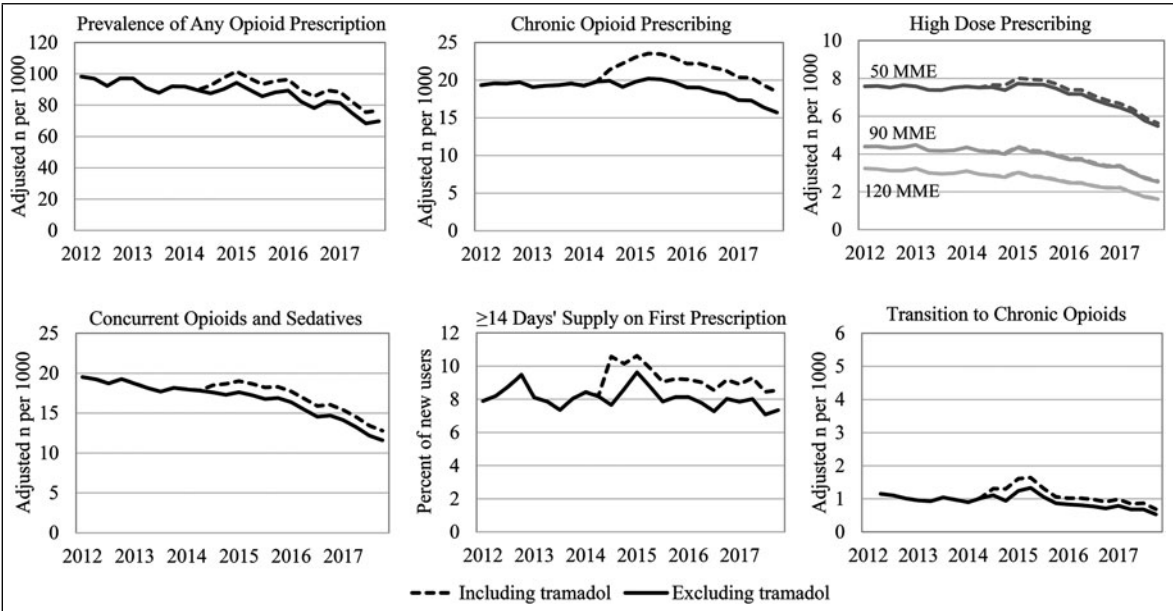


FIGURE 1 Trends in Opioid-Prescribing Metrics With and Without Tramadol—Washington Tracking Network: 2012-2017^a
^aAdjusted estimates were calculated using direct standardization and the 2000 US Census population proportions for gender and 5-year age groups.

Trends in opioid-prescribing metrics including tramadol

Conclusions about opioid-prescribing trends were quite different when tramadol was included in the analysis. When examining the trends in the prevalence of all opioids including tramadol, it appeared that the prevalence of the population with an opioid prescription increased in 2014 before decreasing in later years. The prevalence of chronic opioids also appeared to increase substantially in 2014 with the addition of tramadol to the PDMP. The prevalence of high-dose opioids did not differ much with and without tramadol, although the prevalence for 50 MME or more was slightly higher with tramadol.

The prevalence of concurrent prescribing of opioids and sedatives also appeared to increase in 2014 when tramadol was included.

Trends in opioid prescribing by age

The prevalence of prescription opioids was higher in older than in younger age groups (Figures 2A and 2B). As an example, in the first quarter of 2012, the prevalence of opioid prescribing in the 55- to 64-year-old age group (151.2/1000) was about twice as high as the prevalence in the 18- to 24-year-old age group (75.7/1000). Between 2012 and 2017, the prevalence of opioid prescriptions (excluding tramadol) decreased in all age groups (Figure 2A). When tramadol

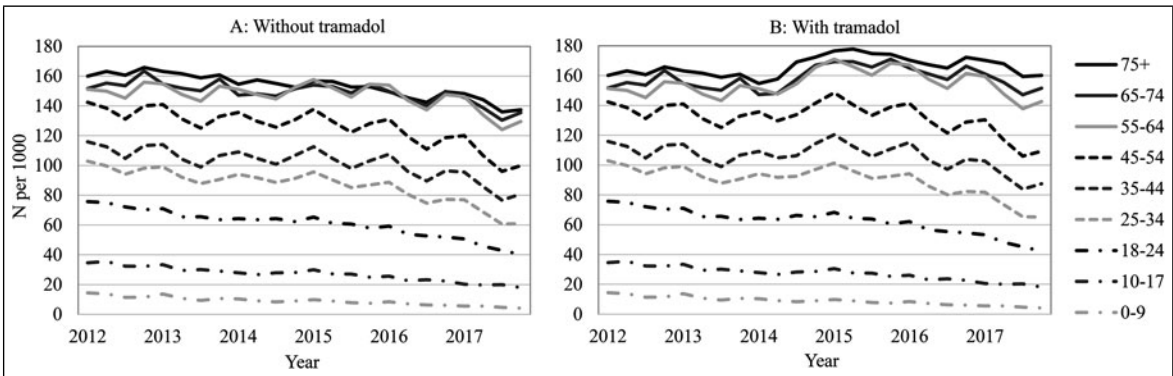


FIGURE 2 A and B, Age-Specific Prevalence of Any Opioid Prescription With and Without Tramadol—Washington Tracking Network: 2012-2017

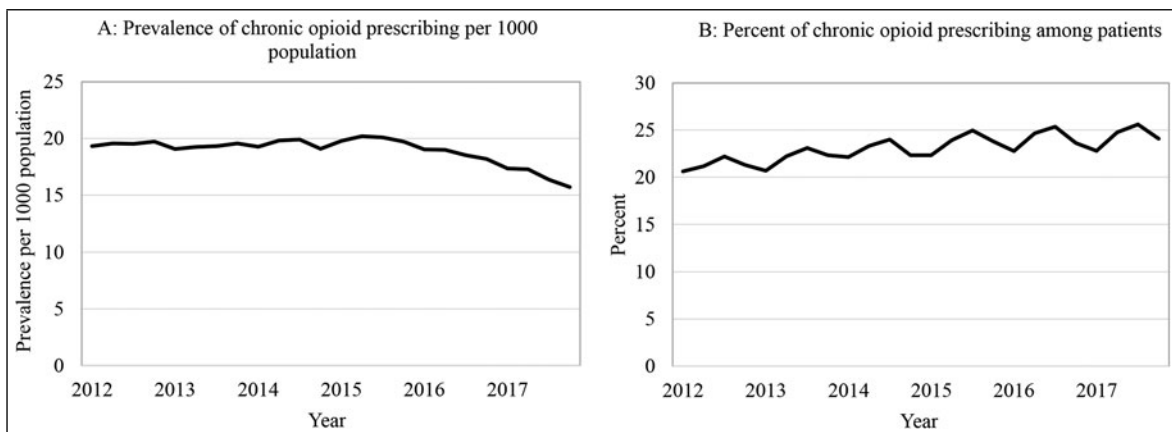


FIGURE 3 A and B, Difference in Trends When Calculating Chronic Opioid Prescribing Using Prevalence Versus Percent

was included, it appeared that opioid prescribing increased in 2014 and 2015, especially in older age groups (Figure 2B).

Comparing trends calculated as rates versus percentages

The opioid-prescribing metrics can be calculated as the prevalence or incidence per 1000,²⁰ or alternatively, as the percentage of opioid users or percentage of those on chronic opioids.^{15,22} We compared the trends using the prevalence and using percentages for each of the opioid-prescribing metrics. Although the trends for most measures were similar (data not shown), the conclusions about trends in chronic opioid prescribing were dependent on the method used. In Figure 3A, the prevalence of chronic opioid prescribing per 1000 population was relatively steady between 2012 and 2015 and then began to decline. When this metric was calculated as the percentage with chronic opioid prescriptions among those with any opioid prescription (Figure 3B), chronic opioid prescribing appeared to increase (from about 20% to about 24%).

Discussion

In Washington, the prevalence of any opioid prescribing, chronic opioid prescribing, high-dose opioid prescribing, prescribing of concurrent opioids and sedatives, and transition from acute to chronic use all declined between 2012 and 2017. This is consistent with recent state and national trends.^{13,23–27} We also found that the prevalence of opioid prescriptions was higher in older than in younger age groups, which is similar to the patterns observed in Iowa,²⁸ in Minnesota,²⁹ and in nationally representative commercially insured samples.^{30,31} The persistently high

prescribing in all 3 older age groups may be important sentinel information related to the recently reported increasing mortality and increasing nonfatal overdoses reported in this population.³² Examination of these opioid-prescribing trends in Washington identified a number of issues that may affect the quality of the data used and interpretation of the results.

The addition of tramadol to the Washington PDMP in 2014 affected the observed prevalence of all opioid metrics and of all opioid-prescribing trends. When using the Washington PDMP data, conclusions about trends in opioid prescribing differ substantially depending on whether tramadol is included or not, particularly in 2014 and 2015. Because tramadol was newly required to be reported to the PDMP in August 2014, when it became a scheduled medication, and because tramadol prescriptions were not included in the PDMP prior to that, using PDMP data to assess opioid-prescribing trends without accounting for tramadol could be misleading, depending on the time period involved. When tramadol was included, there was an observed increase in most measures of opioid prescribing in 2014 and 2015. However, these patterns are an artifact of which medications were required to be reported to the PDMP during these years. When tramadol was excluded from the analysis, there were decreases in the prevalence of prescribing any opioids, in the prevalence of chronic opioid prescribing, and in the prevalence of prescribing concurrent opioids and sedatives between 2012 and 2017. To evaluate any changes in opioid-prescribing trends that use PDMP data and encompass DEA schedule changes in 2014, we recommend excluding tramadol to have a stable list of medications over time. Alternatively, if starting in 2015 or later, analyses of trends can include tramadol and all other opioids. Some states present trends in opioid prescribing with and without tramadol,²⁷ others include a description

of changes (eg, scheduling tramadol and rescheduling hydrocodone),^{19,20} and others begin analysis after these changes occurred.¹⁸ Because tramadol was not included in the PDMP prior to 2014, we are unable to determine whether there were changes in tramadol prescribing in Washington after it was scheduled by the DEA. However, in 2014, the DEA also changed hydrocodone from a schedule III medication to a schedule II medication. Using a large commercial insurance database, the hydrocodone schedule change was associated with a decrease in hydrocodone prescribing between 2013 and 2015, but there was no change in tramadol prescribing during the same years.³⁰

Another data issue is that seasonal “cycling” can occur, which can make it difficult to interpret prescribing trends over a year. This was most evident in the prevalence of any opioid prescribing (Figure 1) but occurred with each metric. This pattern could occur if the annual population denominator overestimated the total population for the early part of the year and underestimated the population at the end of the year. It can also occur if there are seasonal variations in health care access and use in the population, such as having new insurance coverage at the beginning of the year or after meeting deductibles later in the year.²⁴

In the course of this analysis, we also observed increases in the prevalence of some of the metrics (eg, transition from acute to chronic opioids and high dose) in 2015 even after accounting for the addition of tramadol to the PDMP in 2014. One possible explanation could be that the Veterans Administration began reporting prescriptions to the PDMP in March of 2015; however, we are unable to assess the impact of the inclusion of Veterans Administration prescriptions with the available data.

Concurrent use of opioids and sedative-hypnotics has been associated with a high risk of opioid overdose.⁸ Guidelines recommend against prescribing benzodiazepines or other sedatives with opioids and the Food and Drug Administration requires a black box warning,³³ but opioids and sedatives are often prescribed concurrently. Estimates of concurrent prescribing vary on the basis of how the overlap is defined and which medications are included. For example, using the National Ambulatory Care Survey, of patients prescribed opioids between 2001 and 2010, 8% with acute pain and 16% with chronic pain were coprescribed opioids and benzodiazepines, while 33% with acute pain and 36% with chronic pain were prescribed opioids and any sedative hypnotics concurrently.³⁴ Similarly, using the IMS Health Total Patient Tracker, concomitant opioids and benzodiazepines were relatively rare in non-chronic opioid users (3%-4%) but were very common (about 40%) in those with chronic opioids.³⁵ Among

Medicare beneficiaries, about 25% of patients with at least 1 opioid prescription had at least 5 days overlap with a benzodiazepine, although there was substantial variation by state.³⁶ There are various ways to measure concurrent prescribing of opioids and sedatives. One method is to determine whether there is at least 1 overlapping day²⁰ or at least 5 days³⁶ of opioid and sedative prescriptions. Another method is to measure opioids and sedatives dispensed at the same time.³⁷ Others focus on concurrent sedatives among patients with chronic opioids.¹⁵ In addition, the definition of sedatives has varied. Some states (eg, Pennsylvania³⁸ and Rhode Island³⁹) and the Centers for Disease Control and Prevention clinical quality improvement opioid-prescribing measures focus on benzodiazepines.²² Washington State uses a generalized category of sedating drugs (inclusive of sedative hypnotics, benzodiazepines, carisoprodol, and/or barbiturates).^{15,20} Differences in these definitions make it difficult to compare estimates of concurrent opioids and sedatives from various sources.

There are other issues to consider when comparing opioid-prescribing rates across states and nationally including whether the rates are calculated per month, per quarter, or per year; whether the numerator used to calculate opioid-prescribing rates is the number of opioid prescriptions or the number of individuals with at least 1 opioid prescription; and whether the denominator used to calculate opioid-prescribing rates is the number of people in the population or the number of opioid users. For example, the Centers for Disease Control and Prevention recently reported an overall prescribing prevalence of 58.7 per 100 persons in 2017, which was calculated by dividing the number of opioid *prescriptions* per year by the population.²⁶ In contrast, in 2017 in Washington, the overall prescribing prevalence was 69.8 per 1000, which was calculated by dividing the number of *people* with at least 1 opioid prescription in the calendar quarter by the population. In addition, the conclusions about trends in chronic opioid prescribing differ depending on whether the metric is calculated as the prevalence per 1000 or as the percentage of opioid users. The prevalence of chronic opioid prescribing in this population decreased between 2012 and 2017 but the percentage of chronic opioid use among opioid users increased over the same years. This pattern can occur if the level of acute prescribing is decreasing so that chronic prescribing accounts for a larger percentage of all opioid prescriptions. These examples show how different definitions may make it difficult to compare measures across jurisdictions and may lead to different conclusions about the magnitude of prescribing or trends in opioid prescribing and highlight the potential benefit of standardizing definitions.

There are a number of limitations in this analysis of opioid-prescribing trends and of the use of PDMP data to monitor opioid prescribing. First, there are no clinical data included in the PDMP, so it is difficult to determine whether prescriptions, dosages, or transitions to chronic opioids (ie, cancer, end of life) are appropriate and, therefore, we do not have a target or goal for the appropriate level of prescribing for many of the metrics. Another limitation is that all calculations are based on the dispensed amounts, rather than the amount consumed. Although some patients may not take any of the opioids or may take more or less than what was prescribed, the calculations assume that patients are taking the maximum prescribed dose. Also, using these opioid-prescribing metrics, patients who fill an opioid prescription one quarter and then have a gap of at least 1 calendar quarter without filling an opioid prescription will be considered a new user the next time they fill a prescription. Similar to other changes with administrative data (eg, the transition from *International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] to *International Classification of Diseases, Tenth Revision, Clinical Modification* [ICD-10-CM]),⁴⁰ when there are changes to pharmacy data such as a medication is scheduled or rescheduled by the DEA, when a new drug comes on the market, or when there are changes to required reporting to the PDMPs (eg, Veterans Administration), there may be changes in prescribing trends that are difficult to interpret. In addition, tramadol-prescribing practices may have changed after it was scheduled by the DEA, but because tramadol was not included in the PDMP prior to being scheduled, we are unable to assess changes in tramadol prescribing using PDMP data prior to 2014. Commercial or public insurance databases may be more complete sources of prescribing data in some circumstances, since all pharmacy bills would be included, not just those required to be reported to the PDMP.

Conclusions

We have demonstrated that monitoring temporal trends in opioid prescribing can signal how states, counties, health plans, or public programs are faring in efforts to reverse the opioid epidemic. There are promising downward trends in prevalence of any opioid prescribing, chronic opioid prescribing, high-dose opioid prescribing, prescribing of concurrent opioids and sedatives, and transition from acute to chronic prescribing. These trends should translate into fewer fatal and nonfatal overdoses associated with prescription opioids and fewer people developing opioid use disorder.

Implications for Policy & Practice

- Utilizing consistent methods to track opioid prescribing may help improve prescribing and decrease opioid-related morbidity and mortality.
- Prescribing trends are impacted by changes in PDMP reporting requirements and DEA scheduling of medications.
- The scheduling of tramadol by the DEA and the addition of tramadol to the PDMP in 2014 affected the observed prevalence of all opioid metrics.
- To account for the addition of tramadol to the PDMP in 2014, states can present opioid-prescribing trends with and without tramadol included, can present trends beginning in 2015, or can include a description of reporting changes.

The development of opioid-prescribing metrics is relatively new. Although there is similarity in many of the overall concepts measured⁴¹ (eg, high dose, concurrent opioids/sedatives), metric definitions vary within Washington State, across states, and nationally.^{15,20,27,31,41-43} As practice guidelines and analysis of PDMP data become increasingly robust and more detailed opioid-prescribing information becomes available, there is likely much benefit to be gained by standardizing definitions of opioid metrics at the state and national levels to track important trends and compare progress from state to state.

References

1. Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and opioid-involved overdose deaths—United States, 2013–2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(5152):1419–1427.
2. Hedegaard H, Bastian BA, Trinidad JP, Spencer M, Warner M. Drugs most frequently involved in drug overdose deaths: United States, 2011–2016. *Natl Vital Stat Rep*. 2018;67(9):1–14.
3. Vivolo-Kantor AM, Seth P, Gladden RM, et al. Vital signs: trends in emergency department visits for suspected opioid overdoses—United States, July 2016–September 2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(9):279–285.
4. O'Donnell JK, Gladden RM, Seth P. Trends in deaths involving heroin and synthetic opioids excluding methadone, and law enforcement drug product reports, by census region—United States, 2006–2015. *MMWR Morb Mortal Wkly Rep*. 2017;66(34):897–903.
5. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Ann Intern Med*. 2010;152(2):85–92.
6. Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*. 2011;305(13):1315–1321.
7. Gomes T, Mamdani MM, Dhalla IA, Paterson JM, Juurlink DN. Opioid dose and drug-related mortality in patients with nonmalignant pain. *Arch Intern Med*. 2011;171(7):686–691.
8. Garg RK, Fulton-Kehoe D, Franklin GM. Patterns of opioid use and risk of opioid overdose death among Medicaid patients. *Med Care*. 2017;55(7):661–668.
9. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain 2016. <https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm#suggestedcitation>. Published 2016. Accessed July 19, 2018.

10. Washington Agency Medical Directors' Group. Interagency guideline on prescribing opioids for pain. <http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf>. Published 2015. Accessed August 28, 2019.
11. The Pew Charitable Trusts. Prescription drug monitoring programs; evidence-based practices to optimize prescriber use. <http://www.pewtrusts.org/en/research-and-analysis/reports/2016/12/prescription-drug-monitoring-programs/>. Published 2016. Accessed July 20, 2018.
12. Haegerich TM, Paulozzi LJ, Manns BJ, Jones CM. What we know, and don't know, about the impact of state policy and systems-level interventions on prescription drug overdose. *Drug Alcohol Depend*. 2014;145:34-47.
13. Bohnert ASB, Guy GP Jr, Losby JL. Opioid prescribing in the United States before and after the Centers for Disease Control and Prevention's 2016 Opioid Guideline. *Ann Intern Med*. 2018;169(6):367-375.
14. The Bree Collaborative. <http://www.breecollaborative.org/>. Accessed July 19, 2018.
15. Dr Robert Bree Collaborative. Opioid prescribing metrics. <http://www.breecollaborative.org/wp-content/uploads/Bree-Opioid-Prescribing-Metrics-Final-2017.pdf>. Published 2017. Accessed July 19, 2018.
16. Hedberg K, Bui LT, Livingston C, Shields LM, Van Otterloo J. Integrating public health and health care strategies to address the opioid epidemic: the Oregon Health Authority's Opioid Initiative. *J Public Health Manag Pract*. 2019;25(3):214-220.
17. Luu H, Slavova S, Freeman PR, Lofwall M, Browning S, Bush H. Trends and patterns of opioid analgesic prescribing: regional and rural-urban variations in Kentucky from 2012 to 2015. *J Rural Health*. 2019;35(1):97-107.
18. Winstanley EL, Zhang Y, Mashni R, et al. Mandatory review of a prescription drug monitoring program and impact on opioid and benzodiazepine dispensing. *Drug Alcohol Depend*. 2018;188:169-174.
19. Kuschel LM, Mort JM. Impact of the hydrocodone schedule change on opioid prescription patterns in South Dakota. *S D Med*. 2017;70(10):449-455.
20. Washington State Department of Health. Washington tracking network—opioids. <https://www.doh.wa.gov/DataandStatisticalReports/EnvironmentalHealth/WashingtonTrackingNetworkWTN/Opioids>. Accessed July 19, 2018.
21. Washington State Office of Financial Management. April 1 official population estimates. <https://ofm.wa.gov/washington-data-research/population-demographics/population-estimates/april-1-official-population-estimates>. Published 2019. Accessed August 6, 2019.
22. Centers for Disease Control and Prevention. Quality improvement and care coordination: implementing the CDC guideline for prescribing opioids for chronic pain. <https://www.cdc.gov/drugoverdose/pdf/prescribing/CDC-DUIP-QualityImprovementAndCareCoordination-508.pdf>. Published 2018. Accessed December 28, 2018.
23. Guy GP Jr, Zhang K, Bohm MK, et al. Vital signs: changes in opioid prescribing in the United States, 2006-2015. *MMWR Morb Mortal Wkly Rep*. 2017;66(26):697-704.
24. Zhu W, Chernew ME, Sherry TB, Maestas N. Initial opioid prescriptions among U.S. commercially insured patients, 2012-2017. *N Engl J Med*. 2019;380(11):1043-1052.
25. Schieber LZ, Guy GP Jr, Seth P, et al. Trends and patterns of geographic variation in opioid prescribing practices by state, United States, 2006-2017. *JAMA Netw Open*. 2019;2(3):e190665.
26. Guy GP Jr, Zhang K, Schieber LZ, Young R, Dowell D. County-level opioid prescribing in the United States, 2015 and 2017. *JAMA Intern Med*. 2019;179(4):574-576.
27. Oregon Health Authority. Opioid overdose data dashboard. <https://www.oregon.gov/oha/PH/PreventionWellness/SubstanceUse/OPIOIDS/Pages/data.aspx>. Accessed August 8, 2018.
28. Ranapurwala SI, Carnahan RM, Brown G, Hinman J, Casteel C. Impact of Iowa's prescription monitoring program on opioid pain reliever prescribing patterns: an interrupted time series study 2003-2014. *Pain Med*. 2019;20(2):290-300.
29. Zhong W, Maradit-Kremers H, St Sauver JL, et al. Age and sex patterns of drug prescribing in a defined American population. *Mayo Clinic Proc*. 2013;88(7):697-707.
30. Raji MA, Kuo YF, Adhikari D, Baillargeon J, Goodwin JS. Decline in opioid prescribing after federal rescheduling of hydrocodone products. *Pharmacoepidemiol Drug Saf*. 2018;27(5):513-519.
31. Jeffery MM, Hooten WM, Henk HJ, et al. Trends in opioid use in commercially insured and Medicare advantage populations in 2007-16: retrospective cohort study. *BMJ*. 2018;362:k2833.
32. Weiss AJ, Heslin KC, Barrett ML, Izar R, Bierman AS. Opioid-related inpatient stays and emergency department visits among patients aged 65 years and older, 2010 and 2015: statistical brief #244. *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs*. Rockville, MD: Agency for Healthcare Research and Quality; 2018.
33. US Food and Drug Administration. FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. <https://www.fda.gov/media/99761/download>. Published 2016. Accessed August 15, 2019.
34. Larochelle MR, Zhang F, Ross-Degnan D, Wharam JF. Trends in opioid prescribing and co-prescribing of sedative hypnotics for acute and chronic musculoskeletal pain: 2001-2010. *Pharmacoepidemiol Drug Saf*. 2015;24(8):885-892.
35. Hwang CS, Kang EM, Kornegay CJ, Staffa JA, Jones CM, McAninch JK. Trends in the concomitant prescribing of opioids and benzodiazepines, 2002-2014. *Am J Prev Med*. 2016;51(2):151-160.
36. Hernandez I, He M, Zhang Y. Comparing state, regional, and local variation in concurrent opioid and benzodiazepine use. *Drug Alcohol Depend*. 2018;191:141-144.
37. Dasgupta N, Funk MJ, Proescholdbell S, Hirsch A, Ribisl KM, Marshall S. Cohort study of the impact of high-dose opioid analgesics on overdose mortality. *Pain Med*. 2016;17(1):85-98.
38. Pennsylvania PDMP interactive data. <https://www.health.pa.gov/topics/programs/PDMP/Pages/Data.aspx>. Published 2019. Accessed April 24, 2019.
39. Raimondo GM. Rhode Island overdose prevention and intervention task force action plan. <http://www.governor.ri.gov/documents/press/051116.pdf>. Published 2016. Accessed April 24, 2019.
40. Khera R, Dorsey KB, Krumholz HM. Transition to the ICD-10 in the United States: an emerging data chasm. *JAMA*. 2018;320(2):133-134.
41. Cochran G, Lo-Ciganic WH, Gellad WF, et al. Prescription opioid quality measures applied among Pennsylvania Medicaid enrollees. *J Manag Care Spec Pharm*. 2018;24(9):875-885.
42. Pharmacy Quality Alliance. Pharmacy quality alliance opioid core measure set. <https://www.pqaalliance.org/opioid-core-measure-set>. Accessed September 12, 2018.
43. Washington State Health Care Authority. Washington State common measure set. <https://www.hca.wa.gov/assets/Washington-State-Common-Measure-Set-2018.pdf>. Published 2018. Accessed September 12, 2018.