

Pharmacology in Emergency Medicine



CHANGES IN PROVIDER PRESCRIBING PATTERNS AFTER IMPLEMENTATION OF AN EMERGENCY DEPARTMENT PRESCRIPTION OPIOID POLICY

Scott R. Osborn, MD, Julianna Yu, MD, Barbara Williams, PHD, Maria Vasilyadis, MD, and C. Craig Blackmore, MD, MPH

Virginia Mason Medical Center, Seattle, Washington

Reprint Address: Scott R. Osborn, MD, Virginia Mason Medical Center, 1010 Spring Street, Seattle, WA 98101

Abstract—Background: Prescription opioid-associated abuse and overdose is a significant cause of morbidity and mortality in the United States. Opioid prescriptions generated from emergency departments (EDs) nationwide have increased dramatically over the past 20 years, and opioid-related overdose deaths have become an epidemic, according to the Centers for Disease Control and Prevention. **Objective:** Our aim was to determine the effectiveness of implementing a prescription policy for opioids on overall opioid prescribing patterns in a hospital ED. **Methods:** The ED provider group of an academic, non-university-affiliated urban hospital with 23,000 annual patient visits agreed to opioid prescribing guidelines for chronic pain with the goal of limiting prescriptions that may be used for abuse or diversion. These guidelines were instituted in the ED through collaborative staff meetings and educational and training sessions. We used the electronic medical record to analyze the number and type of opioid discharge prescriptions during the study period from 2006–2014, before and after the prescribing guidelines were instituted in the ED. **Results:** The number of patients discharged with a prescription for opioids decreased 39.6% (25.7% to 15.6%; absolute decrease 10.2%; 95% confidence interval [CI] 9.6–10.7; $p < 0.001$) after the intervention. The improvements were sustained 2.5 years after the intervention. Decreases were seen in all major opioids (hydrocodone, oxycodone, hydromorphone, and codeine). The number of pills per prescription also decreased 14.8%, from 19.5% to 16.6% (absolute decrease 2.9; 95% CI 2.6–3.1; $p < 0.001$). **Conclusions:** Implementation of an ED prescription opioid policy was associated with a significant reduction in total opioid prescriptions and in the number of pills per prescription. © 2016 Elsevier Inc. All rights reserved.

Keywords—opioid; narcotic; overdose; chronic pain; prescription policy

INTRODUCTION

The Centers for Disease Control and Prevention has classified prescription drug abuse as an epidemic due to the recent dramatic increase in prescription drug overdose deaths in the past decade, with >13,000 deaths nationally since 2007 (1,2). The prescription of opioids for noncancer pain has also raised concerns for substance abuse, prescription drug diversion, increase in emergency department (ED) visits, overutilization of ED resources, and traumatic injuries caused by nonmedical use of prescription opioids. Among individuals who abused prescription opioids upon entering methadone treatment, 13% reported obtaining their opioids from EDs (3). Prescription opioid pain relievers are the leading cause of overdose deaths in the United States, accounting for 73.8% of prescription drug overdose deaths in 2008 (4). Opioid deaths surpassed motor-vehicle-related injuries as the highest cause of injury and death for the past several years (5). ED visits for prescription opioid misuse or diversion account for an estimated 950,000 ED visits each year (1).

Of particular concern, Washington State Department of Health (WADOH) data suggested higher rates of drug overdose deaths and a higher percentage of nonmedical use of prescription pain medication in Washington State compared to the rest of the nation (6,7). Several

potentially important factors in this increase include deregulation of prescription opioids in the mid-1990s, promotion of pain control initiatives as the fifth vital sign by The Joint Commission in 2001 with associated changes in provider prescribing patterns and creation of a long-acting formulation of oxycodone (6,8,9).

WADOH formed the ED Opioid Abuse Workgroup in 2009, a multi-stakeholder collaboration including the Washington State Hospital Association, Washington State Medical Association, and WA-ACEP (Washington State Chapter of American College of Emergency Physicians). This initiative led to the draft Opioid Prescribing Guidelines by mid-2010, designed to help curb the rapidly increasing opioid prescribing patterns and overdose rates (6).

Importance

There has been little analysis of the impact of an ED Opioid Prescribing Policy. Given the scope of this public health concern, implementing effective policies will be critical in reducing opioid prescription-related abuses and overdoses.

Goals of This Investigation

Our objective was to determine the effectiveness of implementing an opioid prescription policy on reducing opioid prescribing patterns at an urban, teaching, non-university-affiliated hospital.

MATERIALS AND METHODS

Setting

This study was conducted as part of a quality-improvement project, resulting in a waiver by the Institutional Review Board. The setting is a 336-bed nonuniversity, teaching hospital serving primarily adults in the Pacific Northwest, with approximately 23,000 ED visits per year and about 16,000 ED visits per year that result in outpatient discharges.

Study Design

We performed a pre- and post-intervention time series study in which ED opioid prescription rates were compared during a 7-year period. The primary outcome was the ED opioid prescription rate, defined as the number of ED visits with an opioid prescription at discharge, as a proportion of the total number of ED visits. A secondary outcome was the dispensing quantity (number of tablets or capsules prescribed per prescription). To insure that observed differences were not related to changes in providers, we performed a subanalysis on

dispensing quantity limited to the providers who were on staff in the ED throughout the entire study timeframe.

The study was based on clinical and pharmacy data for ED visits retrieved retrospectively from the electronic medical record (EMR) (Cerner Corporation, Kansas City, MO), and included all pharmacy prescriptions for opioid tablets or capsules, including hydrocodone, oxycodone, codeine, hydromorphone, and tramadol. The presence or absence of potential confounders, including payer; level of services provided (Current Procedure Terminology code); and demographic information, including age, sex, ED length of stay, and discharge disposition; was also determined from the EMR. Medications were included in the analysis if they were prescribed by 1 of 34 ED providers, including both physician's assistants and physicians. If there were two opioid prescriptions during the same visit, the first prescription was used. Less than 1% of all ED visits had two opioid prescriptions, and a chart review revealed that there was no consistent pattern as to which prescription was more reliable. Medications administered in the ED were not considered for the outcome measures.

We included patients aged 18 years and older who had an ED visit between January 2007 and June 2014 and who were not admitted to the hospital or the observation unit. The primary analysis of ED opioid use was based on comparing the time period before the intervention (January 2007–September 2010) with the time period after intervention (January 2012–June 2014). The time-frame from October 2010 to December 2011 was the period in which the quality-improvement intervention occurred and was therefore excluded from the pre- and post-comparison. Means for continuous variables were compared using *t*-tests and proportions were compared with χ^2 test.

To define underlying trends and changes over time that might not be related to the quality-improvement intervention, the data for the entire time period (January 2007 to June 2014) were assessed graphically using statistical process control charts. Statistical process control charts allow determination of whether variability in data in a time series can be attributed to random variation or to systematic change, and represent a method of choice for analyzing quality-improvement data (10,11). All statistics were performed using STATA MP, version 12 (StataCorp, College Station, TX).

Intervention

We adopted prescribing guidelines between fall 2010 and spring 2011 based on the Washington ED Opioid Abuse Work Group set of guidelines, in line with other medical systems within Washington state (Figure 1) (6).

Washington ED Opioid Prescribing Guidelines (Abridged)

1. One medical provider should provide all opioids to treat a patient's chronic pain
2. The administration of intravenous and intramuscular opioids in the ED for the relief of acute exacerbations of chronic pain is discouraged
3. Emergency medical providers should not provide replacement prescriptions for controlled substances that were lost, destroyed, or stolen
4. Emergency medical providers should not provide replacement doses of methadone for patients in a methadone treatment program
5. Long-acting or controlled-release opioids (such as OxyContin®, fentanyl patches, and methadone) should not be prescribed from the ED
6. EDs are encouraged to share the ED visit history of patients with other emergency physicians who are treating the patient using an Emergency Department Information Exchange (EDIE) system
7. Physicians should send patient pain agreements to local EDs and work to include a plan for pain treatment in the ED
8. Prescriptions for controlled substances from the ED should state that the patient is required to provide a government-issued picture identification (ID) to the pharmacy filling the prescription
9. EDs are encouraged to photograph patients who present for pain-related complaints without a government-issued photo ID
10. EDs should coordinate the care of patients who frequently visit the ED using an ED care coordination program
11. EDs should maintain a list of clinics that provide primary care for patients of all payer types
12. EDs should perform screening, brief interventions, and treatment referrals for patients with suspected prescription opioid abuse problems
13. The administration of Demerol® (meperidine) in the ED is discouraged
14. For exacerbations of chronic pain, the emergency medical provider should contact the patient's primary opioid prescriber or pharmacy. The emergency medical provider should only prescribe enough pills to last until the office of the patient's primary opioid prescriber opens
15. Prescriptions for opioid pain medication from the ED for acute injuries, such as fractured bones, in most cases should not exceed 30 pills
16. ED patients should be screened for substance abuse prior to prescribing opioid medication for acute pain
17. The emergency physician is required by law to evaluate an ED patient who reports pain. The law allows the emergency physician to use their clinical judgment when treating pain and does not require the use of opioids

Figure 1. Washington Emergency Department (ED) Opioid Prescribing Guidelines (Abridged).

The opioid prescribing guidelines were presented at the ED section meeting in 2010 and approved by the provider group as a whole. They were subsequently approved by the Hospital Pharmacy and Therapeutics Committee. Implementation of the guidelines included development of patient education pamphlets and provider education focused on changing practice patterns. It was gradually implemented and universally adopted by all providers over the course of 2011.

Practice recommendations were instituted through collaborative meetings with other hospitals in the area, didactic departmental lectures, and continuing education to nurses and providers. The pharmacy provided feedback in the form of comparisons that illustrated individual practice patterns in comparison with the group. There were no opioid formulary changes at the hospital pharmacies during the study period. Nursing staff education took place in daily huddles, e-mail communication, and educational fliers. There was a collaboration with the Communications Department to make patient-friendly fliers for staff to hand out to patients and placards to post.

Placards outlining the opioid prescribing guidelines were posted in ED treatment rooms and in the waiting room. In January 2013, the South Carolina Hospital Association presented a concern to the Centers for Medicare and Medicaid Services regarding the practice of posting such placards in the ED waiting room and treatment areas as a possible violation of federal Emergency Medical Treatment and Active Labor Act law. As a result, the majority of Washington State EDs—ours included—elected to remove these placards (12).

RESULTS

Between January 2007 and June 2014, there were 116,676 ED patient visits and 25,219 prescriptions for opioids. There were 34 providers who prescribed opioids in the ED, 11 were physician’s assistants (PA) and 23 were physicians. Mean (standard deviation [SD]) patient age was 51.8 (20.2) years (range 18–106 years) and 61,693 (53%) were female. Patients after the intervention were slightly older (52.2 vs. 51.3 years; $p < 0.001$), and there were small differences in diagnosis categories (Table 1).

Table 1. Description of All Patients Evaluated in the Emergency Department

	Total	Before Intervention	During Intervention	After Intervention
Dates	1/2007–6/2014	1/2007–9/2010	10/2010–12/2011	1/2012–6/2014
Patient visits, n	116,676	62,817	17,665	36,194
Visit characteristics				
Age, y, mean (SD)	51.8 (20.2)	51.3 (20.0)	52.6 (20.4)	52.2 (20.4)
Female, n (%)	61,693 (53)	33,126 (53)	9,503 (54)	19,064 (53)
Payor type, n (%)				
Commercial	48,715 (42)	26,349 (42)	7,449 (42)	14,917 (41)
Medicare	34,103 (29)	17,501 (28)	5,385 (30)	11,217 (31)
Medicaid	13,616 (12)	7,440 (12)	1,997 (11)	4,179 (12)
Uninsured	12,001 (10)	6,160 (10)	1,897 (11)	3,944 (11)
Other/unknown	8,241 (7)	5,367 (9)	937 (5)	1,937 (5)
LOS, min, mean (SD)	184 (118)	188 (122)	184 (110)	176 (113)
LOS ≥ 3 h, n (%)	50,226 (43)	27,898 (45)	7,728 (44)	14,600 (40)
Discharge disposition, n (%)				
Home	111,143 (95)	60,017 (96)	16,762 (95)	34,364 (95)
Against medical advice	3,083 (3)	1,534 (2)	434 (2)	1,115 (3)
Other	2,450 (2)	1,266 (2)	469 (3)	715 (2)
CPT code, n (%)				
99281, 1 service	420 (1)	334 (1)	51 (1)	35 (1)
99282, 2 services	5,545 (5)	1,615 (3)	1,052 (6)	2,878 (8)
99283, 2 services	36,200 (31)	21,823 (35)	4,820 (27)	9,557 (26)
99284, 5 services	43,919 (38)	23,123 (37)	5,313 (30)	15,483 (43)
99285, 8 services	25,003 (21)	13,358 (21)	5,900 (33)	5,745 (16)
Other/unknown	5,589 (5)	2,564 (4)	529 (3)	2,496 (7)
Primary ICD-9 diagnosis,* n (%)				
Ill-defined conditions	35,575 (30)	19,893 (32)	5,393 (31)	10,289 (28)
Injury and poison	24,990 (21)	13,811 (22)	3,703 (21)	7,476 (21)
Musculoskeletal	9,542 (8)	5,166 (8)	1,463 (8)	2,913 (8)
Digestive	6,242 (5)	3,413 (5)	942 (5)	1,887 (5)
Genitourinary	6,001 (5)	3,135 (5)	1,006 (6)	1,860 (5)
Other/unknown	34,326 (29)	17,399 (28)	5,158 (29)	11,769 (33)

CPT = Current Procedural Terminology; LOS = length of stay; SD = standard deviation.

All comparisons between before and after intervention are significant $p < 0.001$, except for sex.

* For five most common International Classification of Diseases, 9th revision (ICD-9) diagnosis groups: 780–799 ill-defined conditions, 800–999 injury and poison, 710–739 musculoskeletal, 520–579 digestive, and 580–629 genitourinary.

After the intervention, there was a 39.6% decrease in the proportion of ED visits resulting in a discharge opioid prescription (from 25.7% to 15.6%, absolute decrease 10.2 percentage points; 95% CI 9.6–10.7; $p < 0.001$, Table 2). This decrease was temporally associated with the opioid prescription intervention, and was sustained after the intervention, when evaluated using statistical process control charts plotted by quarter (Figure 2). Decreases were greatest in oxycodone (7.3; 95% CI 6.9–7.7), but were also substantial in hydrocodone (2.4; 95% CI 2.0–2.8), hydromorphone (0.5; 95% CI 0.4–0.6), and codeine (0.2; 95% CI 0.1–0.3) (Table 2). These reductions were observed in patients with the primary International Classification of Diseases, 9th revision (ICD-9) diagnoses of musculoskeletal problems, including low back pain, limb pain, and joint pain (Table 2). The largest reduction was seen in patients aged 18–49 years (from 31.6% to 17.5% prescribed), while the group with the smallest reduction were those older than age 65 years (14.4% to 11.1% prescribed).

Table 2. Visits with Opioid Prescriptions Before and After the Intervention

Variable	Before Intervention	After Intervention
Dates	1/2007–9/2010	1/2012–6/2014
Patient visits, n	62,817	36,194
Visit with prescription, n (%)	16,174 (25.7)	5,633 (15.6)
Opioid prescribed, n (%)		
Hydrocodone/Vicodin	7,225 (11.5)	3,311 (9.1)
Oxycodone/Percocet	7,811 (12.4)	1,862 (5.1)
Hydromorphone	554 (0.9)	147 (0.4)
Codeine	425 (0.7)	164 (0.5)
Other*	159 (0.3)	149 (0.4)
No. of pills per prescription, mean (SD)	19.5 (8.6)	16.6 (7.2)
No. of pills prescribed ≥ 20 , n (%)	9,207 (56.9)	2,352 (41.7)
Primary diagnosis with prescription, † n (%)		
Ill-defined conditions	3,359 (16.9)	1,015 (9.9)
Injury and poison	5,668 (41.0)	1,848 (24.7)
Musculoskeletal	2,507 (48.5)	894 (30.7)
Digestive	1,191 (34.9)	378 (20.0)
Genitourinary	1,131 (36.1)	572 (30.8)
Other/unknown	2,318 (13.3)	926 (7.9)
Age group, n (%)		
18–49 years	10,164 (31.6)	3,075 (17.5)
50–64 years	3,819 (25.4)	1,476 (16.7)
65+ years	2,191 (14.1)	1,081 (11.1)

SD = standard deviation.

All comparisons between before and after intervention are significant $p < 0.001$.

* Other drugs include tramadol ($n = 194$), morphine ($n = 77$), methadone ($n = 25$), meperidine ($n = 11$), and fentanyl ($n = 1$).

† For five most common International Classification of Diseases, 9th revision diagnosis groups: 780–799 ill-defined conditions, 800–999 injury and poison, 710–739 musculoskeletal, 520–579 digestive, and 580–629 genitourinary.

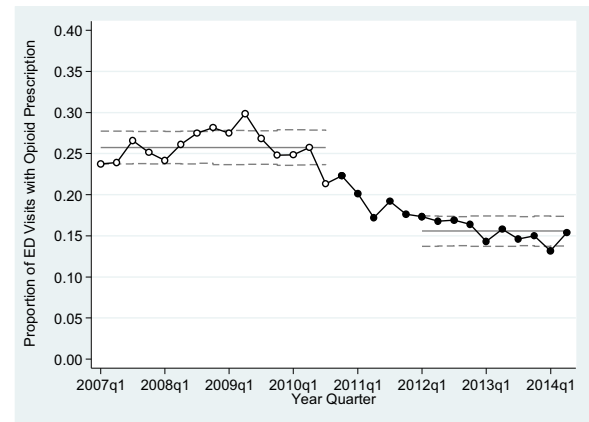


Figure 2. Statistical process control chart of opioid prescription rates by quarter. ED = emergency department.

The decrease in proportion of visits with an opioid was sustained for 2.5 years of follow-up (Figure 2).

We also identified a significant change in the number of pills per opioid prescription after the intervention. The mean number of pills per prescription decreased 14.8%, from 19.5 to 16.6 (absolute decrease 2.9; 95% CI 2.6–3.1; $p < 0.001$) (Table 2). The decrease in prescription size was temporally associated with the intervention and was also sustained for 2.5 years of follow-up (Figure 2).

To show that the decrease in the number of pills prescribed was not the result of staff turnover, we compared changes in the number of pills for only providers who had practiced in the ED during the entire time period (2007–2014; $n = 12$) (Figure 3). Mean number of pills per prescription decreased from 19.7 to 17.6 (absolute decrease 2.1; 95% CI 1.8–2.5; $p < 0.001$). The decrease was consistent across providers, with the 10 providers with the greatest number of opioid prescriptions all decreasing (statistically significant at $p < 0.001$ for 9 of 10). For providers with continuous service, the mean (SD) number of pills prescribed by physicians decreased from 21.0 (9.8) to 18.3 (7.8) ($p < 0.001$), while that prescribed by PAs decreased from 17.0 (6.5) to 14.3 (6.7) ($p < 0.001$).

DISCUSSION

Our study provides evidence of the effectiveness of an ED opioid prescribing policy with reductions in the rate of opioid prescribing and the number of doses per prescription in the setting of state initiatives aimed at reducing opioid prescriptions. The improvements were sustained through 2.5 years after the intervention. Prescriptions for oxycodone decreased most dramatically, with lesser decreases in hydrocodone, now the most commonly prescribed opioid and a designated Schedule III drug at the time with a lower potential for abuse. Although the

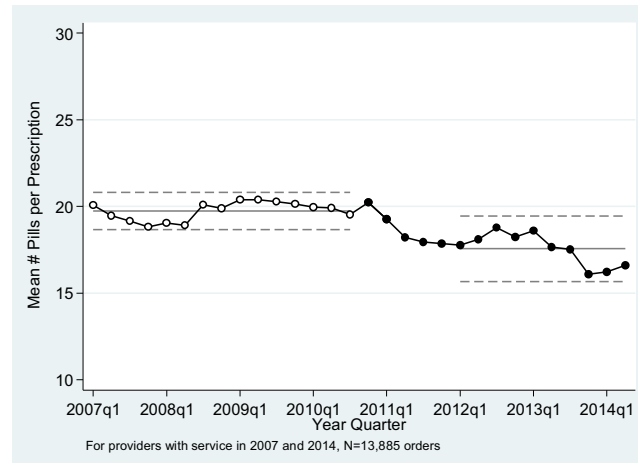


Figure 3. Statistical process control chart of number of pills per prescription by quarter for providers practicing in the emergency department during the entire study period.

decrease in pill count dropped only 14.8% on average, when applied to the entire sum of prescriptions written from an ED, this accounts for a considerable quantity of opioid medication.

Franklin and colleagues have reported decreases in use of long-acting opioids and in the number of unintentional opioid-related deaths in the worker's compensation patients in Washington State after implementation of the state opioid prescribing guidelines (2). They also performed a survey of primary care providers in Washington State, identifying a decrease in provider self-reported opioid prescribing (13,14). However, they were not able to directly measure actual prescribing in the non-worker's compensation population. Previously, Gugelmann and colleagues have reported success with a computer order-entry system-based intervention on decreasing the use of ED opioid "discharge packs," and Baehren et al. reported a decrease in opioid use after implementation of a statewide prescription monitoring program (15,16). In addition, Fox and colleagues found a decrease in ED opioid prescribing after implementing a department guideline specifically targeted to dental pain (8). Our work looks more broadly at the effect of a multicomponent intervention, on both the rate of prescribing and the number of pills for all adult ED patients.

The setting likely affected the success of the program. Our ED is part of an institution with a long track record of focus on Lean management principles (17,18). The institutional culture strongly supports uniform adoption of standardized processes and use of Lean quality-improvement events to effect change (19,20). This likely facilitated adoption of the new ED opioid policy.

Our ED opioid program must be viewed in the context of the Washington State initiatives. The ED Opioid Abuse Workgroup Opioid Prescribing Guidelines were endorsed

broadly by state medical professional and hospital groups, with 90% of EDs reporting adoption of either all or most of the guidelines (6). In Seattle, one ED staff advocated an "Oxy-Free ED" in an effort to limit prescription Schedule II drugs (6). Our opioid prescription policy involved a similar transparent policy at triage with patient education placards and materials designed to reduce patient conflict with staff about the prescription of these drugs. Additional programs, such as the Emergency Department Information Exchange and the Prescription Monitoring Program, have also been adopted across the state. However, we do not have data to show whether or not these other institutions have had similar success in reducing opiate prescriptions.

In 2012, subsequent to our intervention, the Washington State Congress passed legislation to require hospitals to support the exchange of patient information between EDs, the implementation of the WA-ACEP ED Opioid Prescribing Guidelines, and creation of individualized ED care plans for patients requiring care (10). Similar efforts in other states have included the New York City Discharge Opioid Prescribing Guidelines that recommend prescribing no more than 3 days of short-acting opioid analgesics for non-cancer pain management, checking in with primary care providers about prescriptions from the ED, and restricting the use of opioids in patients already taking opioids or benzodiazepines, given the risk of further respiratory depression (21,22). Prescription drug monitoring programs are also becoming more prevalent across the United States (23).

The findings seen with this performance improvement place further importance on the implementation of opioid prescribing guidelines and the overall improvements in prescription patterns expanded to a larger urban setting as in our hospital. With continued increasing awareness

and education on the effects of opioids, hospitals in conjunction with patients and their advocates can appropriately manage pain with prescribing guidelines across the United States.

Limitations

This study identifies correlation rather than causation. Other concurrent ED initiatives included the formation of the WADOH ED Opioid Abuse Work Group with guidelines beginning in April 2009 and the Washington State legislation in 2012, which set forth best practices, including “adoption of strict guidelines for the prescribing of narcotics,” where “hospitals have also attested they have trained ED physicians in how to enforce these guidelines.” These measures informed our own efforts, and their contribution to the success of our program cannot be separated. In addition, although we are unable to assess whether high visit-frequency patients formerly seen at our institution are now seeking care (and opiates) elsewhere, the state-level initiatives would seem to mitigate this potential bias.

A limitation of this study was the change in the proportion of PA to MD providers in the ED in August 2009. There were changes to the ED staffing before the ED opioid intervention with replacement of daytime PA hours with physician coverage. PAs in our ED primarily evaluate lower-acuity patients. Some of the observed reductions in opioid prescription in mid-2009 may be related to differing practice patterns between the PA and MD providers (13). However, we found significant decreases in the number of pills prescribed in both PA and MD providers when limiting the analysis to providers with continuous service between 2007 and 2014. We were unable to perform a similar analysis for the prescription rates, so it is possible that new or different providers contributed to the differences identified.

Another limitation is that our primary data source was the EMR, which is an incomplete source of information. Our EMR does capture all prescriptions written in the ED, but we cannot confirm whether or not they were actually filled. Our ED intervention was directed toward decreasing opioid discharge prescriptions for pain. However, our EMR data sources were insufficient to accurately determine when pain was the primary reason for the ED visit. We include all ED patients in the study to avoid any bias in coding. Also, we are only able to characterize patient diagnoses in broad categories defined by discharge ICD-9 codes, with a limited ability to compare different subgroups. In addition, there were differences between the pre- and post-intervention group demographics (Table 1), which, although small in magnitude, were statistically significant due to the large sample size.

We evaluated success of the opioid guidelines in terms of reduction in opioids prescribed and not in terms of the impact on patient pain management. Although the guidelines are explicitly aimed at reduction in prescriptions for chronic, non-cancer pain, we have no ability to gauge whether the measured reductions are clinically appropriate. It is possible that an additional outcome of implementation of an opioid policy is poorer pain management in patients who could have been more adequately treated. Further, after the intervention, there was a new apparent plateau in the rate of narcotic prescriptions. However, we cannot confirm whether this is the appropriate level of prescribing without longer-term outcomes data, including on abuse rates. Finally, the narcotic policy might have contributed to a decrease in the number of ED visits, with economic consequences.

CONCLUSIONS

The prescription of opioids for patients with chronic non-cancer pain has dramatically increased during the course of the past 2 decades in the United States, resulting in a national epidemic of mortality associated with unintentional overdose, dependence, and abuse. Our study demonstrates that a formal ED policy with provider education can decrease ED opioid prescribing by nearly 40%. To help manage patient expectations, we placed the policy openly throughout the ED so that staff could review the policy with patients as necessary. This program, in conjunction with statewide policies, can help reduce the number of opioid prescriptions from the ED and might have an effect on overall abuse and overdose patterns.

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ARTICLE SUMMARY

1. Why is this topic important?

Opioid abuse is a significant, nationwide epidemic and as yet there are few proven strategies to address it.

2. What does this study attempt to show?

This study shows that implementation of a prescription policy in the setting of statewide initiatives can significantly reduce the number of opioid prescriptions from an emergency department.

3. What are the key findings?

There was a significant drop in the number of opioid prescriptions per discharged patient, the number of pills per prescription, and a change to less potent opioids.

4. How is patient care impacted?

Reduction in opioid prescriptions from the emergency department for chronic pain can contribute to lowering opioid dependence and related morbidity and mortality.