INTRODUCTION

The illicit use of prescription opioids has been rising nationally and continues to be a major public health crisis representing a leading cause of morbidity and mortality in the United States. Despite the ongoing prevention efforts such as health screenings and policy reforms, opioid abuse remains accountable for the loss of many lives. From 1999 to 2015 alone, over 180,000 people in the United States died from prescription opioid related overdoses. According to the Centers for Disease Control and Prevention, opioid overdoses were responsible for the deaths of over 47,000 Americans in 2017, and two-thirds of overdoses in 2018 involved an opioid. Common uses of opioid drugs can be linked to treatment for pain. Patients seek relief after experiencing pain whether it be acute or chronic. This leads to the involvement of health care professionals, especially providers in the emergency department (ED) who are readily accessible to a large and diverse patient population and offer immediate medical care. Emergency medicine physicians are trained in appropriate pain management, so it is not surprising to see patients list pain as one of the most common chief complaints.

Pain relief often coincides with the use of potent opioid medications due to the severity and nature of cases presented to the ED. Emergency medicine providers treat high volumes of patients daily, often lacking a pre-established patient-provider relationship due to the nature of the emergency medicine specialty. Therefore, although clinicians are

ABSTRACT

Background: Ohio remains one of the most afflicted states nationally with 46.3 per 100,000 deaths due to drug overdose. Opioids are commonly administered in emergency departments for the management of pain. Given the high volume of patients presenting with pain, emergency clinicians must be cognizant of responsible opioid dispensing practices. Ohio established guidelines in April 2012 to provide a general approach for responsible opioid prescribing practices in the emergency setting. The purpose of this study assesses clinician opioid dispensing before and after the implementation of the Ohio Opioid Prescribing Guidelines.

Methods: The study design used retrospective data analysis of opioid medications ordered by emergency clinicians to be administered in the emergency room between January 1, 2007, to December 31, 2017, at the University of Toledo Medical Center. A segmented regression analysis with an interrupted time series was used to determine impact.

Results: All opioid medication usage showed a significant decrease after guideline implementation except for morphine and fentanyl which showed statistically significant increases in administration over time ($P < 0.05$).

Conclusion: There was a significant decrease in the use of opioids since the implementation of the Ohio Opioid Prescribing Guidelines, yet morphine and fentanyl use has generally increased across all age groups. Age demographics frequently receiving opioids in the emergency room have seemed to shift over time as well as specific opioid drugs dispensed for the management of pain in certain age groups. Further study is needed to evaluate the use of opioids prescribed by emergency physicians after discharge from the emergency department.

Keywords: Opioid; Emergency; Acute; Dispense; Ohio
aware of the importance of balancing patient safety and quality care, there is growing hesitation among the emergency medicine community as providers attempt to discern the role of opioid drugs in managing pain and weighing the risks of under-treatment versus opioid over-use. This issue is especially prevalent in Northwest Ohio which has one of the greatest amounts of prescription opioid overdoses in the state. In 2015, Lucas County had the eighth highest number of fentanyl-related overdoses in the state with 41 deaths. This national issue is relevant to the Toledo area as many residents, families, and providers in the community are continually combating the struggles of opioid addiction. The patient demographics of Toledo can be extrapolated to represent major urban centers found across the state.

In April 2012, the Ohio Governor’s Cabinet Opioid Action Team instituted opioid prescribing guidelines for emergency health care providers in order to provide a general approach for responsibly prescribing opioids and other controlled substances. These guidelines were not intended to take the place of clinical judgement but, rather, assist emergency providers when assessing the need for opioids in the ED. The guidelines address several facets of opioid prescribing practices and their application in the acute emergency setting including management of chronic pain issues, replacement of past opioid prescriptions, utilization of the Ohio Automated Rx Reporting System (OARRS) database, patient-physician pain management agreements, and discussion with patients about the risks and benefits of using opioids for pain management. This study aims to analyze the effects of the 2012 prescribing guidelines on opioid dispensing in the emergency room.

METHODS

Setting
The University of Toledo Medical Center Emergency Department is an academic urban level 1 trauma center with an annual census of approximately 36,000 patients.

Design
The design was a retrospective chart review analysis of opioid prescriptions written by ED physicians between January 1, 2007, to December 31, 2017, at the University of Toledo Medical Center.

Participants
Subjects included in the study were ED patients greater than 18 years of age who received opioid orders (N = 9,598) in the ED for treatment of pain. Participants were administered at least one opioid medication at the University of Toledo Medical Center prior to discharge from the emergency room. The study excluded children, prisoners, pregnant women, mentally incapacitated, and palliative care/hospice patients due to risk factors associated with those populations.

Procedures
This study was approved by the University of Toledo Institutional Review Board. Medications dispensed in the ED were obtained from the University of Toledo Medical Center drug dispensing database. The records contain dispense level, limited data set that include patient ID, gender, race, birth date, date the medication was dispensed, quantity dispensed, and drug name.

Measures
The primary study outcome evaluates the existence of positive or negative change in opioid dispensing practices at the University of Toledo emergency room using the implementation of the 2012 Ohio Opioid Prescribing Guidelines as a time reference for comparison. The overall opioid dispense rate in addition to specific opioid medications were analyzed. Additional measures were included to evaluate the relationship between patient demographics and opioid dispensing behaviors.

Statistical Analysis
Descriptive statistics were used to characterize opioid dispenses by demographic variables.

The data points for the time-series were aggregated per month. The rate of opioid administrations in the ED per month was calculated before (January 2006 to April 2012) and after (until December 2017) the new regulations were released. The time periods were divided into monthly intervals versus yearly intervals to observe drug dispensing acute and chronic progression before and after guideline implementation. The rate of other commonly administered drugs per month was also determined for comparison with the corresponding opioid data.

An interrupted time series analysis was utilized to compare the monthly number of opioid dispense orders in the ED in the pre- and post-guideline time periods. To determine the impact of the intervention, a segmented regression analysis with an interrupted time series design was used. The difference in monthly ED administered opioids orders between the pre-intervention and post-intervention periods can be interpreted as a microcosm that demonstrates the impact of state opioid-regulating legislation.

The analyses were stratified by gender, race, and age group. Age stratification was performed to compare populations of interest and accommodate for generational influences between young adults versus early/middle-aged versus older adults. In addition to studying the impact of the rules on all opioids, we individually assessed the most commonly administered opioids: hydrocodone, oxycodone, morphine, fentanyl, and hydromorphone. Three other non-opioid drugs (albuterol, azithromycin, and ondansetron) were used for comparison as they are commonly prescribed in the ED, especially for conditions associated with chief complaints regarding pain.

Opioid prescription doses for pre-intervention and post-intervention were described as mean dosage in milligrams (mg) of opioid dispenses per month with standard deviation and median dosage in mg of opioid dispenses per month (interquartile range) and compared using Mann-Whitney U test. All analyses were performed using SAS version 9.4 (SAS Institute Inc.) and R statistical software version 3.4.1 (R Foundation for Statistical Computing). Statistical significance was evaluated at \(\alpha = 0.05\) and all testing were 2-sided.
RESULTS

The annual number of ED opioid dispenses ranged from a high of 4,784 in 2011 to a low of 2,332 in 2017. The percentage of opioids dispensed in the ED based on age was found to be statistically significant with the youngest age group (48.8%) less likely to receive opioids compared to older age groups. The highest percentage of dispensed opioids was among the age group 30 to 49 years (60.2%). The percentage of opioid dispenses for males (57.5%) was significantly higher than that for females (53.2%). With regard to race/ethnicity, Hispanic patients had the highest percentage of opioid dispenses (65.5%) compared to White (55.5%), Black (55.2%), and Other (52.2%) patients. Patient characteristics by opioid dispenses are summarized in Table 1.

Following the Ohio Opioid Prescribing Guidelines, from May 2012 until December 2017, there were sustained reductions in monthly prescription narcotic use from March 2012 (83 dispenses per month) to December 2017 (53 dispenses per month) (Figure 1).

Table 1. Frequency of Emergency Department Opioid Utilization by Demographic Variables Between 2007-2017

|                     | Opioid dispenses a | All dispenses b | % Opioid | P value * * |
|---------------------|-------------------|-----------------|----------|------------|
| **Age group**       |                   |                 |          |            |
| 18-29               | 249               | 510             | 48.8     | 0.00001    |
| 30-49               | 15,986            | 26,554          | 60.2     |            |
| 50-64               | 16,794            | 30,798          | 54.5     |            |
| 65+                 | 8286              | 16,869          | 49.1     |            |
| **Gender**          |                   |                 |          |            |
| Male                | 20,861            | 36,286          | 57.5     | 0.0001     |
| Female              | 20,454            | 38,445          | 53.2     |            |
| **Race/Ethnicity**  |                   |                 |          |            |
| White               | 21,256            | 38,294          | 55.5     | 0.0001     |
| Black               | 12,137            | 21,980          | 55.2     |            |
| Hispanic            | 1831              | 2795            | 65.5     |            |
| Other *             | 6091              | 11,662          | 52.2     |            |

* Morphine, hydrocodone, hydromorphone, and oxycodone, other (tramadol, methadone, propoxyphene, buprenorphine, pentazocine, sufentanil, opium alkaloids)

* Encompasses all non-opioid drug dispenses administered in the University of Toledo Medical Center Emergency Department during this time frame

* P value < 0.05 is significant

* Includes missing values for race
Table 2 presents opioid dosing (in mg) before and after the Ohio Opioid Prescribing Guidelines stratified by demographic variables. Non-significant reduction in ED opioid dosing was observed among the age groups 30 to 49 years (-1.30 mg) and 50 to 64 years (-1.51 mg). A significant increase was observed in the age group 65 and over (+0.73 mg). Both genders exhibited non-significant reductions in dispensing doses when comparing doses before and after guideline implementation (males -1.16 mg; females -0.96 mg). With regard to race/ethnicity, the reduction in dispensing dose was borderline significant only for Whites (-1.31 mg).

Dispensing doses for selected opioid drugs before and after the Ohio Opioid Prescribing Guidelines are presented in Table 3. There were significant increases in the average dose for morphine (+0.3 mg) and fentanyl (+0.04 mg). Conversely, there were significant decreases in the average doses for hydrocodone (-0.41 mg), hydrocodone (-0.29 mg), and oxycodone (-1.38 mg). There were significant increases in overall dispense dose for albuterol (+1.09 mg) and azithromycin (+101.2 mg). On the other hand, overall dispense dose for ondansetron was found to be significantly lower (-0.52 mg).

**DISCUSSION**

There has been a significant decrease in the orders of dispenses and doses of various opioids since the implementation of the Ohio Opioid Prescribing Guidelines, yet the dose of morphine and fentanyl has continued to increase. There could be several reasons as to why the use of morphine in emergency settings has increased including but not limited to its ease of administration, quick onset of action, and demonstrated safety profile. Fentanyl is also a short acting analgesic agent with a better hemodynamic safety profile. A significant decrease in total opioid dispenses is further demonstrated by comparing opioid dispenses to total ED prescriptions including non-narcotics. The frequency of narcotics dispensed in the ED was also found to have significantly decreased which may be argued to represent less overall addiction potential, although this finding may indicate that clinicians are not dispensing proper doses of pain medication. Further analysis of patient pain relief would be required to elucidate the impact of opioid dispensing frequency with regard to patient pain control in the ED.

Males showed an increased number of narcotic dose dispenses compared to females in the population studied. While this could possibly reflect differences in pain tolerances and health care provider perception on the significance of patients’ clinical pain, further study would be necessary to validate this claim. Variations in chief complaints could also influence provider decision making on the appropriateness of opioid dispensing in the ED. For example, abdominal pain complaints in females may not be perceived by physicians as requiring immediate administration of narcotics due to confounding differential diagnosis considerations such as pregnancy or menstruation pain. Trends suggest an overall increase in opioid dispensing dose in Hispanics compared to other groups. The data presented in Table 2 suggests that opioid dispensing practices to Hispanic patients have become more standardized and less variable (Mean 4.99 mg, SD 8.2 mg) when compared to dispensing dose practices before the implementation of the Ohio Opioid Prescribing Guidelines (Mean 4.56 mg, SD 9.4 mg). While the Ohio Opioid Prescribing Guidelines serve as a general framework with the goal of promoting safe opioid dispensing practices, further analysis would be required to determine the impact of various other modifiers affecting physician opioid dispensing and dosage practices such as pain management of non-English speaking patients or managing pain in patients that cannot communicate with the provider due to pre-existing conditions such as dementia or MRDD (mental retardation developmental delay).

| Table 2. Dosage of Emergency Department Opioids Before and After Ohio Opioid Prescribing Guidelines |
|-----------------------------------|----------------|----------------|----------------|-----------------|-----------------|-----------------|
|                                   | Pre-intervention | Post-intervention | Difference In Means in mg | P value* |
| Age group                         | Median dose in mg (IQR) | Mean dose in mg (SD) | Median dose in mg (IQR) | Mean dose in mg (SD) |                          |                |
| 18-29                             | 5 (19)           | 11.34 (14.4)     | 10 (25)           | 17.8 (20.3)     | +6.46            | 0.4676          |
| 30-49                             | 2 (9)            | 6.88 (14.3)      | 4 (4)             | 5.58 (10.6)     | -1.3             | 0.4781          |
| 50-64                             | 2 (4)            | 6.90 (13)        | 4 (4)             | 5.39 (10.5)     | -1.51            | 0.5576          |
| 65+                               | 2 (4)            | 4.80 (10.6)      | 4 (4)             | 5.53 (10.4)     | +0.73            | 0.0001          |
| Gender                            |                 |                |                  |                  |                  |                |
| Male                              | 2 (4)            | 6.10 (11.9)      | 4 (4)             | 4.94 (9.5)      | -1.16            | 0.1190          |
| Female                            | 2 (9)            | 7.03 (14.5)      | 4 (4)             | 6.07 (11.5)     | -0.96            | 0.3343          |
| Race                              |                 |                |                  |                  |                  |                |
| White                             | 2 (4)            | 6.39 (14.0)      | 4 (4)             | 5.08 (9.6)      | -1.31            | 0.0566          |
| Black                             | 2 (9)            | 6.95 (12.7)      | 4 (4)             | 6.10 (11.58)    | -0.85            | 0.6597          |
| Hispanic                          | 2 (3)            | 4.56 (9.4)       | 4 (3)             | 4.99 (8.2)      | +0.43            | 0.0005          |
| Other*                            | 2 (3)            | 6.98 (12.9)      | 4 (4)             | 5.85 (11.8)     | -1.13            | 0.2357          |

Abbreviations: IQR, interquartile range; SD, standard deviation
*P value < 0.05 is significant
*Includes missing values for race/ethnicity
Age demographics of patients receiving opioids in the ED appear to have shifted over time along with the most frequently administered opioid drugs dispensed for specific age groups. The implementation of the 2012 Ohio Opioid Prescribing Guidelines showed statistically non-significant decreases in ED opioid dispensing doses among middle-aged patients (age 30 to 64). These trends, although statistically nonsignificant, represent particular importance as middle-aged individuals encompass a key demographic being affected by the national opioid epidemic. By increasing awareness of the national opioid epidemic and implementing guidelines to address opioid dispensing practices, physicians can be more cognizant of the addiction potential when considering options for pain management in these vulnerable patient populations.

This retrospective analysis has some limitations. The population used in this study included patients that frequented a moderately sized, academic level 1 emergency room in urban, inner-city Toledo. There exists intrinsic limitation in this research study’s scope and extrapolation of data and conclusions when applied to rural or suburban settings, which represent key demographics affected by the opioid epidemic. Since this study evaluated opioid dispensing practices in an acute care setting, further study is required to analyze the impact of opioid prescribing practices upon patient discharge from the ED. Furthermore, the study did not control for individuals who may have received multiple opioid dispenses during the study period. In addition, this study does not incorporate patient chief complaints into the analysis of opioid dispensing behavior nor does it distinguish between the management of acute versus chronic pain in the ED. Further subset analysis of specific opioids dispensed stratified by age group would add value to this research study. This study may raise concern for bias regarding opioid dispenses before and after guideline implementations due to missing racial/ethnic groups categorized as “Other” in Tables 1 and 2. Finally, this study aims to demonstrate the impact of the 2012 Ohio Opioid Prescribing Guidelines on the opioid dispensing practices in the ED setting, but acknowledges that the opioid crisis response has been multifactorial and this study’s data cannot be entirely attributed to the implementation of these specific guidelines.

**PUBLIC HEALTH IMPLICATIONS**

This study aimed to explore the change in emergency physician opioid dispensing habits after the implementation of a statewide guideline initiative in 2012. The results indicate that the prescribing guidelines had a positive effect on opioid dispensing practices, in the context of less overall opiates being dispensed in the ED, specifically in the Toledo inner-city setting. Based on the results of this study, opioid dispensing practices in the ED can be influenced by statewide legislation and policies aimed at increasing public awareness and implementing guidelines to promote responsible and practical opioid prescribing practices.

The design of this study can potentially be applied to the analysis of opioid dispensing practices on other state and national levels, such as, but not limited to, the CDC guidelines for Opioid Use released in 2016 as well as mandatory OARRS reporting implemented in 2015. These guidelines could influence drug seeking

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**Table 3. Opioid and Non-opioid Medication Dispense Doses Before and After Ohio Opioid Prescribing Guidelines**

|                        | Pre-intervention | Post-intervention | Difference in Means | P value** |
|------------------------|------------------|-------------------|---------------------|-----------|
|                        | Total number of dispenses | Median dose in mg (IQR) | Mean dose in mg (SD) | Total number of dispenses | Median dose in mg (IQR) | Mean dose in mg (SD) |                   |
| **Opioids**            |                  |                   |                     |                       |                      |                      |                   |
| Oxycodone              | 446              | 5 (5)             | 7.89 (7.42)         | 773                   | 5 (5)                  | 6.51 (3.67)           | -1.38              | 0.0001              |
| Hydrocodone            | 289              | 5 (5)             | 6.38 (2.24)         | 350                   | 5 (0)                  | 5.97 (1.95)           | -0.41              | 0.0200              |
| Hydromorphone          | 1051             | 1 (0)             | 1.38 (0.93)         | 696                   | 1 (0)                  | 1.09 (0.44)           | -0.29              | 0.0001              |
| Morphine               | 1248             | 2 (2)             | 3.3 (3.4)           | 1484                  | 4 (2)                  | 3.6 (2.7)            | +0.3               | 0.0001              |
| Fentanyl               | 713              | 0.05 (0.05)       | 0.09 (0.12)         | 638                   | 0.1 (0)                | 0.13 (0.15)           | +0.04              | 0.0001              |
| **Non-opioids**        |                  |                   |                     |                       |                      |                      |                   |
| Albuterol              | 1288             | 2.5 (0)           | 2.87 (1.94)         | 435                   | 2.5 (0)                | 3.96 (3.49)           | +1.09              | 0.0001              |
| Azithromycin           | 275              | 500 (250)         | 545 (278)           | 287                   | 500 (500)              | 646 (254)            | +101               | 0.0001              |
| Ondansetron            | 1985             | 4 (0)             | 4.79 (1.81)         | 2430                  | 4 (0)                  | 4.27 (1.39)           | -0.52              | 0.0001              |

Abbreviations: IQR, interquartile range; SD, standard deviation

* P value < 0.05 is significant
behavior as national and state databases provide increased safeguards for providers to monitor for these types of patient behavior patterns. Future studies can also assess prescribing and dispensing practices of pain medication alternatives used in the acute care setting such as nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, gabapentin, topical lidocaine, muscle relaxers, or capsaicin creams in addition to nonpharmacological treatments such as acupuncture, massage therapy, and physical therapy. The 2012 Ohio Opioid Prescribing Guidelines produced an initial impact on opioid prescribing rates in the acute care setting and served as a foundation for further interventions to combat the national opioid crisis on a state level.

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