

ORIGINAL RESEARCH



The impact of coronavirus disease 2019 (COVID-19) on alternatives to opioids protocol for opioid reduction in emergency department

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Abstract

The United States (US) is in the midst of both an opioid epidemic and COVID-19 pandemic. The Alternatives to Opioids (ALTO) approach is a useful strategy of utilizing non-opioid options as the first-line pain therapy in the emergency department (ED). Since the COVID-19 pandemic began, more than 40 states have reported a rise in opioid-related deaths. Since there is a potential increasing need for pain management due to limited outpatient resources during the COVID-19 pandemic, it is unclear whether the COVID-19 has affected the effectiveness of the ALTO protocol in reducing opioid administration in the ED. To investigate the impact of COVID-19 on the usage of the ALTO protocol for opioid reduction, this retrospective cohort study was performed to compare patients receiving pain medication in an urban ED during the COVID-19 pandemic (March to August 2020) and patients during the same period from one year prior. The primary outcome was the change in ED opioid administration and outpatient opioid prescriptions. All opioid dosages were converted to morphine milligram equivalents (MME) for data analysis. Secondary outcomes included changes in ALTO medication use, patient satisfaction with pain control, ED length of stay, and rate of left without being seen (LWBS). The mean prescribed MME per discharged patient visit was significantly lower in the COVID-19 pandemic group (3.16 ± 0.31 versus 7.72 ± 0.31 , $p < 0.001$). There was no significant difference in ED opioid administration, patient satisfaction with pain control, ED length of stay, and rate of LWBS between both groups. In conclusion, during the COVID-19 pandemic, the ALTO protocol can reduce out-patient opioid usage without changing opioid administration in the ED.

Keywords

Pain management; Alternatives to opioid; Emergency department; COVID-19

1. Introduction

1.1 Background and motivation

The United States (US) is in the midst of both an opioid epidemic and the COVID-19 pandemic [1]. Pain remains one of the most frequent emergency department (ED) complaints in the US [2]. An estimated 1.9 million Americans reported an opioid use disorder related to prescription medications in 2014 [3]. According to the Centers for Disease Control and Prevention, opioid overdose killed 47,600 people in 2017 [4]. The increase in opioid usage and opioid-related deaths continues to climb as the COVID-19 pandemic persists [5, 6]. Since the COVID-19 pandemic began, more than 40 states have reported a rise in opioid-related deaths [7]. One recent study demonstrated that nonfatal opioid overdoses doubled during the early months of the COVID-19 pandemic [8]. Thus, it is important to develop an aggressive harm-reduction strategy to

reduce opioid usage during COVID-19 pandemic.

1.2 Challenges

Pain management during the COVID-19 pandemic can be challenging, especially with growing evidence that COVID-19 infection is associated with myalgias, referred pain, and widespread hyperalgesia [9–12]. Pain and the immune response appear to be closely linked. Chronic pain exerts complex effects on the immune system, including immunosuppression in some individuals [13]. The association of comorbidities, old age, and chronic pain increases the risk of immune suppression and subsequent COVID-19 infection [14]. Opioids themselves can have serious adverse effects, including endocrine changes and immune suppression [15]. Since resources are more limited for patients suffering from acute or chronic pain during the pandemic, pain management has been

a challenge in ED [10, 11].

1.3 Objectives and significance

The Alternatives to Opioids (ALTO) approach is a strategy of utilizing non-opioid options as the first-line pain therapy to decrease opioid use in ED [16]. Motov *et al.* [17] first described an opioid-free ED in 2014 with multi-modal non-narcotic treatment protocols for pain management [17, 18]. Since 2016, many EDs have developed more detailed ALTO-first prescribing guidelines [17, 19, 20]. Prior to the COVID-19 pandemic, the ALTO protocol has been well-established in the US and has shown promising results for opioid reduction [16]. Since there is a potentially increasing need for pain management due to limited outpatient resources during COVID-19 pandemic, it is unclear whether the COVID-19 has affected the effectiveness of the ALTO protocol in reducing opioid administration in the ED. Given that EDs offer an opportune setting to initiate acute pain management, it is hypothesized that the ALTO protocol can still reduce the usage of opioids in the ED despite the increasing need for pain control during the pandemic.

1.4 Contribution and novelty

To the authors' knowledge, this is the first study to clarify the effectiveness of the ALTO protocol during the COVID-19 pandemic. During the COVID-19 pandemic, many outpatient care settings have been closed or restricted due to public health measures to curb the virus' spread [21]. These closures have limited outpatient resources for pain control, causing the ED to become a prominent site for patients to seek care during this time. Thus, the ALTO protocol has become the essential pain management strategy in combating the opioid epidemic within the COVID-19 pandemic. This study aims to investigate the impact of COVID-19 on the ALTO protocol for opioid reduction in the ED during the pandemic.

2. Materials and methods

2.1 Design and setting

This retrospective, single center, cohort study was conducted using data retrieved from the electronic medical record (EMR) system at an urban and level III trauma center with an annual ED volume of 50,000 patients. The Institutional Review Board approved this study (reference number: 344143) and waived the requirement for informed consent because of the retrospective and non-interventional nature. This study was ethically approved by Baylor Scott & White Research Institute. The results are reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [22].

2.2 Intervention

The ALTO training program was initiated in the study hospital ED in September 2018, including the creation of the protocol, provision of training classes to all physicians, nurses, and pharmacists, and stocking of ALTO medications in the ED pharmacy. Emergency Medicine physicians and nurses were

trained to use a multi-model non-opioid treatment approach to pain management for controlling different types of pain, including musculoskeletal pain, neuropathic pain, renal colic, headache/migraine, chronic abdominal pain, sickle cell crises, and dental pain (see the Supplementary material). The standardized order set was built and split up by indication to facilitate efficient use of the protocol. All opioid dosages were converted to morphine milligram equivalents (MME) for data analysis [16]. Based on the preliminary results in 2020, it was observed that the mean MME use per patient was significantly lower in the post-protocol phase (2.69 ± 0.18 vs. 1.08 ± 0.15 , $p < 0.001$) [23]. This result demonstrated that the implementation of the ALTO protocol was associated with a significant reduction of opioid administration, similar to prior literature [16].

2.3 Selection of participants

All patients in the ED receiving pain medications, including opioids and non-opioids, were included during the study time-frame. Patient medication use was identified via electronic report generated by the computer order entry system. ED patient visits during the COVID-19 pandemic (March to August 2020) and patients during the same period from the prior year (March to August 2019) were divided into the COVID-19 pandemic group and control group, respectively.

2.4 Data collection and outcome measures

Clinical data were extracted from the health system's EMR (Epic, Verona, WI) with the use of an enterprise data warehouse. Pain control and patient satisfaction scores were measured using the Press Ganey survey. The primary outcome was the change in ED opioid administration and out-patient opioid prescriptions between the pre-COVID-19 and COVID-19 periods. Secondary outcomes included dosage changes in ALTO medication use (see the Supplementary material), patient satisfaction with pain control, ED length of stay, and rate of left without being seen (LWBS). Patient satisfaction scores were measured using the Press Ganey survey, which is one of the most widely used surveys to measure and compare patient feedback in the US [24].

2.5 Statistical analysis

Categorical variables are presented as counts with proportions, and continuous variables are presented as means with standard deviation. Wilcoxon rank-sum test and Pearson chi-square test were used for categorical data comparisons between groups. Continuous variables were compared by paired *t*-test. A two-tailed *p*-value < 0.05 was considered significant. All statistical tests were calculated using Stata Statistical Software version 16.1. (StataCorp LLC, Texas, USA).

2.6 Sample size calculation

The sample size was estimated for the primary outcome assuming the difference between groups was 10% based on prior results [16]. Paired *t*-test for two groups comparison was used with 2-tail comparisons and 20% of attrition rate. Using a type I error of 5% and a type II error of 20%, a total of 3928 patients

TABLE 1. Patient characteristics in COVID pandemic (2020) versus Control (2019) group.

	Control (2019) (N = 22,949)	COVID Pandemic (2020) (N = 17,175)	<i>p</i> -value
Patient number received pain medication (n, %)	10,631 (65.0)	11,487 (64.2)	0.109
Age (mean, SD)	44.3 (0.3)	51.4 (0.5)	<0.001*
Male gender (%)	7458 (32.5)	6939 (40.4)	<0.001*
Patient satisfaction (mean, SD)	74.3 (0.9)	78.3 (6.7)	0.192
Arrived by ambulance % (mean, SD)	17.9 (0.8)	19.7 (1.9)	0.061
Door-to-provider (mean, SD; Unit: mins)	8.5 (0.6)	11.8 (1.8)	0.002*
Admission % (mean, SD)	29.8 (0.8)	34.3 (2.4)	0.001*

*SD, Standard deviation. * $p < 0.05$.*

TABLE 2. Mean morphine milligram equivalents administered per patient visit and ALTO medication use in COVID pandemic (2020) versus Control (2019) group.

	Control (2019)	COVID Pandemic (2020)	<i>p</i> -value
Morphine equivalent per patient visit (mean, SD)	1.13 (0.04)	1.19 (0.54)	0.389
ALTO medication per visit (mean, SD)	27.35 (1.24)	28.26 (0.82)	0.554
-Acetaminophen	9.10 (0.82)	12.47 (0.72)	0.011
-NSAIDs	16.64 (0.48)	11.77 (0.26)	<0.01
-Ketamine	1.61 (0.11)	4.02 (0.39)	<0.01
Morphine equivalent per discharged patient visit (mean, SD)	7.72 (0.31)	3.16 (0.31)	<0.01

ALTO, alternatives to opioid; ED, emergency department; SD, standard deviation; NSAIDs, non-steroidal anti-inflammatory drugs.

are required with 1964 patients in each group.

3. Results

During the study period, a total of 40,124 visits to the ED involving pain management were analyzed. (22,949 in the control group and 17,175 in the COVID-19 pandemic group). Baseline characteristics are shown in Table 1. The mean prescribed MME per discharged patient visit was significantly lower in the COVID-19 pandemic group (3.16 ± 0.31 versus 7.72 ± 0.31 , $p < 0.01$) without a significant difference in ED opioid administration (Table 2, Figs. 1,2). In Table 2, the doses of non-steroidal anti-inflammatory drugs (NSAIDs) ordered per ED patient visit were significantly lower (11.77 ± 0.26 versus 16.64 ± 0.48 , $p < 0.01$), while the doses of Ketamine were significantly higher (4.02 ± 0.39 versus 1.61 ± 0.11 , $p < 0.01$) in the pandemic group. There was no significant difference in patient satisfaction with pain control (78.32 ± 2.74 versus 74.27 ± 0.35 , $p = 0.173$), hours of ED length of stay (4.12 ± 0.07 versus 4.37 ± 0.12 , $p = 0.103$), and rate of LWBS ($1.83\% \pm 0.19\%$ versus $1.60\% \pm 0.14\%$, $p = 0.335$) in the COVID-19 pandemic group vs the pre-COVID-19 group (Fig. 3).

The datasets used and/or analyzed during the current study

are available from the corresponding author upon reasonable request.

4. Discussion

As it was hypothesized, it was demonstrated that the ALTO protocol significantly reduced opioid prescriptions during the COVID-19 pandemic without changes in ED opioid administration, patient satisfaction, or ED flow. While there are more limited outpatient resources for patients suffering from acute or chronic pain during the pandemic, this ALTO strategy can potentially reduce opioid use and subsequent complications.

Since the COVID-19 pandemic began, opioid use and abuse have continued to rise. In the US, over 40 states have reported an increase in opioid-related deaths [7], and recent studies have demonstrated that non-fatal opioid overdoses have doubled during the pandemic as well [8]. The connection between COVID-19 and increased rates of opioid-related fatalities includes social isolation, disruptions in medication for opioid use disorder, lack of access to mental health care services or health care services, increased homelessness and incarceration, and concurrent COVID-19 infection [25]. The opioid epidemic has also been complicated by the increasing use of methamphetamines in combination with opioids [26]. It is likely that

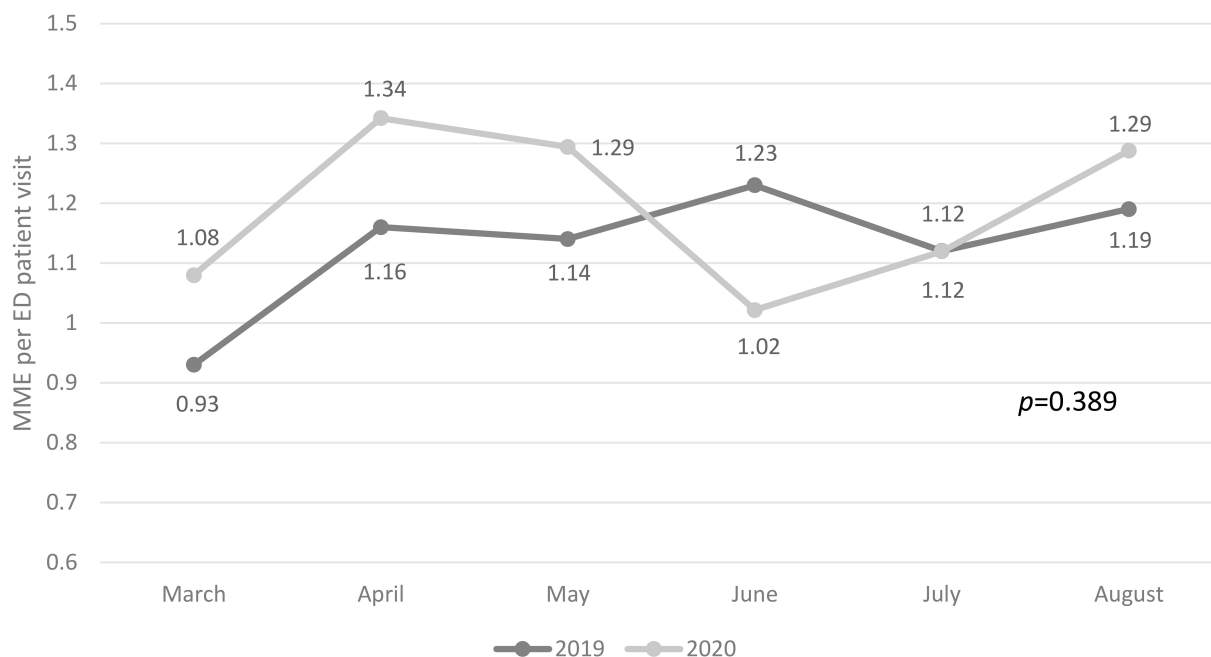


FIGURE 1. Mean morphine milligram equivalents (MME) administered per patient visit at ED by month in COVID-19 pandemic (2020) versus Control group (2019).

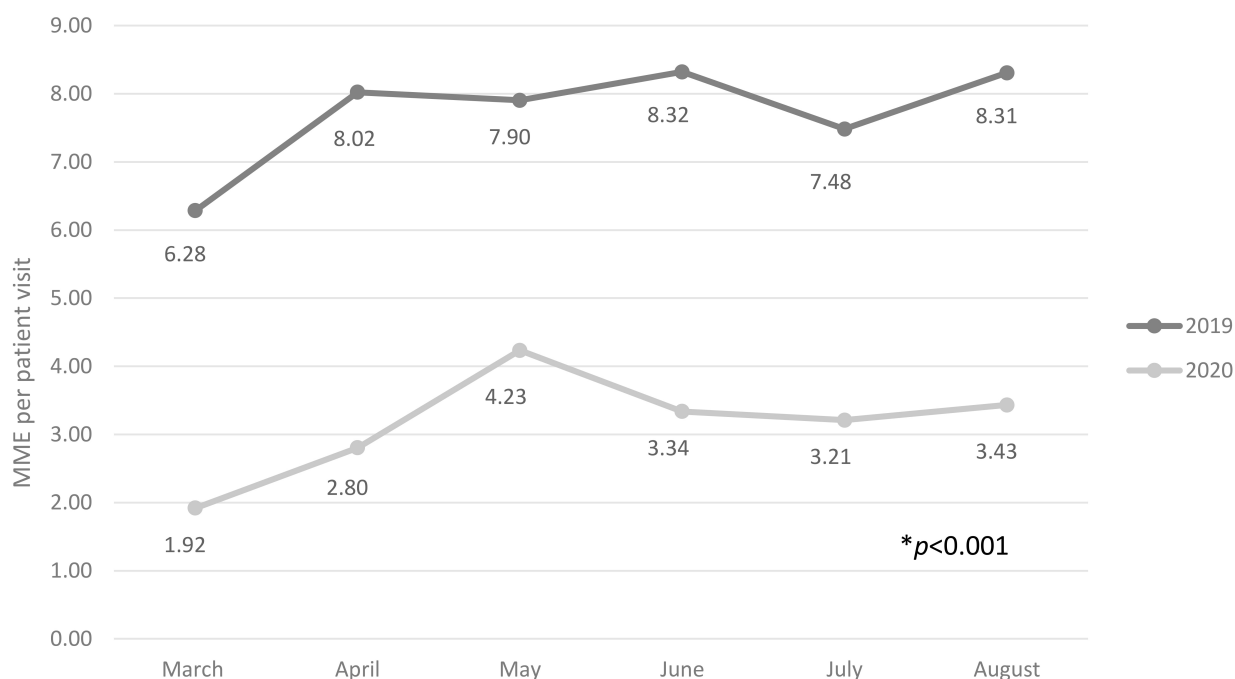


FIGURE 2. Mean morphine milligram equivalents (MME) out-patient prescription per patient visit by month in COVID-19 pandemic (2020) versus Control group (2019). $*p < 0.05$.

the emergence of COVID-19 and the subsequent disruptions in health care and social safety nets combined with social and economic stressors will exacerbate the opioid epidemic [5]. This rising death toll and the evolution of the opioid epidemic illuminate the necessity for harm reduction strategies like the ALTO protocol.

Motov *et al.* [17] first described an opioid-free ED in 2014 with multi-modal non-narcotic treatment protocols using a CERTA (Channels/Enzymes/Receptors Targeted Analgesia) physiologic approach for pain management [17, 18]. LaPietra

et al. [18] demonstrated that up to 75% of patients achieved adequate pain relief with non-narcotic therapies and a reported decrease in opioid utilization by almost 50% since the implementation of the ALTO protocol. Since 2016, other EDs have developed similar protocols, and a few state-level chapters of emergency medicine formed multi-disciplinary groups to develop more robust and detailed ALTO-first prescribing guidelines [17, 19, 20]. Duncan *et al.* [16] found that opioid administration was significantly reduced upon implementing an ALTO-first approach to pain control in ED. The amount

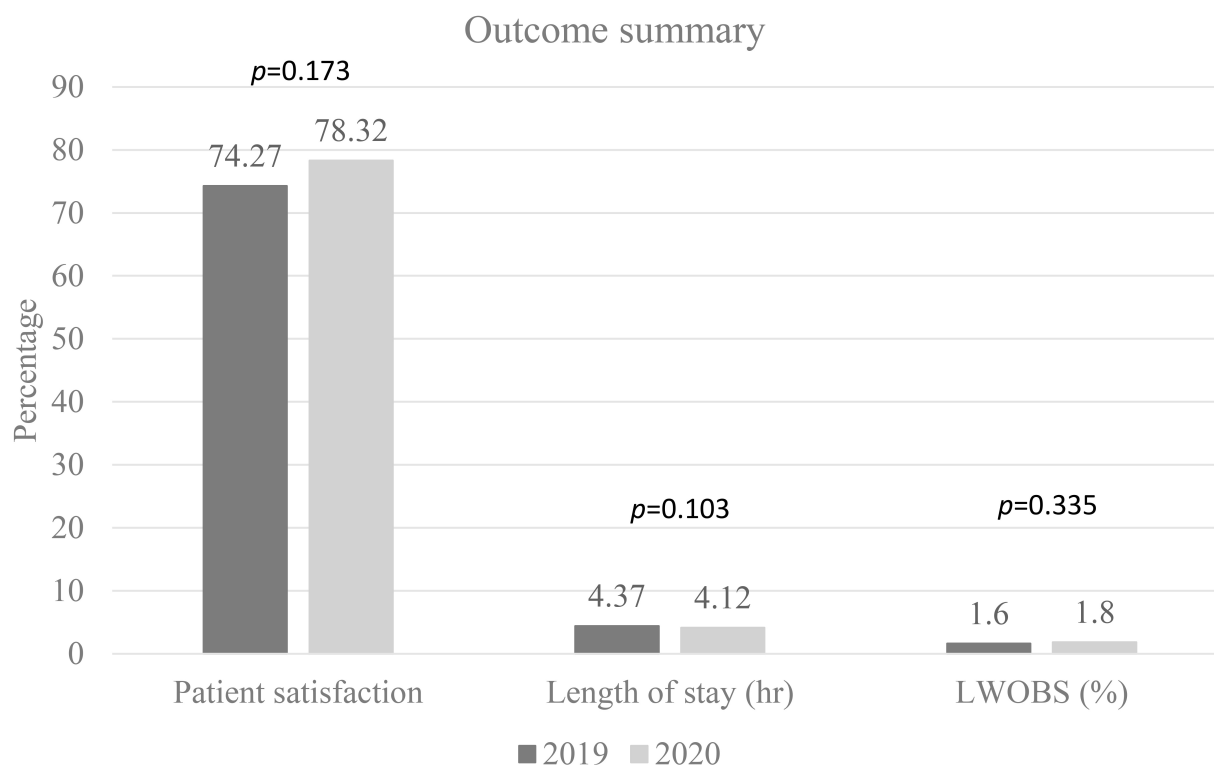


FIGURE 3. Secondary outcome summary in COVID-19 pandemic (2020) versus Control group (2019).

of mean MME used per patient was reduced from 1.45 ± 0.88 to 1.13 ± 0.69 [16]. In the pre-COVID-19 cohort at the study facility, a similar mean MME used per patient (1.08 ± 0.15) while following the ALTO protocol was demonstrated. However, it is still unclear if the ALTO protocol can reduce opioid usage during the COVID-19 pandemic. These results provide further evidence that the ALTO protocol can significantly reduce opioid prescriptions during the COVID-19 pandemic without adverse effects on ED opioid administration, patient satisfaction, or ED flow. Similar to prior studies, the ALTO protocol can be effective on opioid reduction, especially out-patient opioid prescriptions [16, 20, 27].

Since the COVID-19 pandemic began, pain management for both COVID-19 and non-COVID-19 patients in the ED has been more challenging. There is growing evidence that COVID-19 infections are commonly associated with myalgias, referred pain, and widespread hyperalgesia [9–11]. During the pandemic, people with opioid use disorders have been disproportionately incarcerated. Without adequate planning, decarceration efforts in response to COVID-19 may move this vulnerable population from one risk environment to another [28]. Since there are more limited out-patient resources for patients suffering from acute or chronic pain during the pandemic, there is a potential increase in opioid requests for pain control in ED [29]. In this study, by using the ALTO protocol, ED opioid administration during the pandemic did not increase. The rate of opioid administration was still comparable with the reduced rates of administration when using an ALTO-first multimodal treatment approach. However, this study found a significant decrease in NSAID use for pain management during the COVID-19 pandemic. This decrease in administration could be attributed to an early hypothesis that

NSAIDs could worsen the course of COVID-19 infections due to their effect of increasing the expression of ACE2, which is the protein that the SARS-CoV-2 virus uses to attach to host target cells [30]. This early hypothesis may have influenced physicians to utilize fewer NSAIDs and instead turn to other ALTO medications for pain management. Consequently, this could have contributed to the observed significant increase in Ketamine administration during this period. In the ED, Ketamine is a unique and common medication that enables well-controlled sedation, analgesia, attenuates depression and mitigates suicidal thoughts, without depressing respiratory or cardiovascular physiology [31, 32]. Given its suggested role in the treatment of certain mental health disorders and its anti-inflammatory effect, future study is needed to clarify the role of Ketamine in COVID-19 patients presenting with specific neuropsychiatric symptoms [33].

The reduction of ED opioid prescriptions signifies the success of the ALTO-first multimodal approach to pain management. During the COVID-19 pandemic, many outpatient care settings have been closed or restricted due to public health measures to curb the virus's spread [21]. These closures have limited outpatient resources for pain control, causing the ED to become a more prominent site for patients to establish their care during this time. In conjunction with the reduction in ED opioid prescriptions, this study indicates the importance of ALTO-first protocols in combating the opioid epidemic during the pandemic. Over the past two decades, the rise in severe adverse events has paralleled increased prescription opioid analgesic use in the US [34]. The 2015 the National Survey on Drug Use and Health estimates suggested that 91.8 million (37.8%) U.S. adults used prescription opioids. Of those, 11.5 million (4.7%) misused them, and 1.9 million

(0.8%) had a use disorder [35, 36]. One study showed a trend of an increasing prevalence of prescription opioid misuse from 1990–2014 [37]. This trend of an increasing prevalence is alarming for the evolution of the opioid epidemic over the years [37]. The observed decrease in opioid prescription in this study is important in combating this crisis head-on. Decreased opioid prescriptions are vital to reducing the initial use of opioids by patients, thus reducing the further complications including opioid decency, misuse, and abuse. Reducing ED opioid prescriptions and those subsequent complications is vital in reducing nonfatal opioid overdoses, opioid overdose-related deaths, and combating the opioid epidemic in the US.

To the authors' knowledge, this is the first study to clarify the effectiveness of the ALTO protocol during COVID-19 pandemic. The strength of this study is that it is based on a large sample size comparison between pre-COVID-19 and COVID-19 populations. These results demonstrate that the ALTO protocol can be an essential pain management strategy in combating the opioid epidemic during the COVID-19 pandemic.

There are several limitations of this study. First, it was a retrospective, uncontrolled design with a previously implemented ALTO-first protocol, caring for a heterogeneous population in both disease and operational complexity. Second, it was assumed there were similar ED volumes and patient presentations during the time periods of the two groups. However, there are potential covariates that could contribute to the differences observed in the pre-COVID-19 and pandemic group results. Third, the analyses were conducted based on data collected from a single center in North Texas; it may not be applied to other populations due to limited generalizability. The study was conducted when the opioid epidemic was well recognized and may have further influenced prescribing patterns.

5. Conclusions

In summary, this study demonstrated that the ALTO protocol significantly reduced opioid prescription during the COVID-19 pandemic without changes in ED opioid administration. While there are limited outpatient resources for patients suffering from acute or chronic pain, an ALTO strategy can potentially be an effective strategy to reduce opioid usage and subsequent complications, and therein combat the opioid epidemic within the COVID-19 pandemic.

AUTHOR CONTRIBUTIONS

EHC, TB and RKC designed the study; EHC, CFTT, and AJ acquired and processed the raw data; EHC and CFTT analyzed the data; EHC, AS, MH and JW interpreted the data; EHC and AJ drafted the manuscript; MH, CP, RKC and DH provided critical revision of the manuscript; EHC and CFTT provided statistical expertise; EHC and DH supervised the study and provided administrative or funding support. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Baylor Scott & White Research Institute Institutional Review Board approved this study (reference number: 344143) and waived the requirement for informed consent because of the retrospective and non-interventional nature.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at <https://oss.signavitae.com/mre-signavitae/article/1470319345936547840/attachment/Supplementary%20material.docx>.

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