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The Impact of Alternative to Opioids (ALTO) Protocol on Opioid Reduction in the Community Emergency Department – and the Impact of the COVID-19 Pandemic on the ALTO Protocol for Opioid Reduction in the Emergency Department

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I: ABSTRACT

Project 1:

Research Question: In patients visiting the Emergency Department (ED), is an Alternative To Opioid (ALTO) protocol for pain management effective in reducing opioid administration in the ED? Background: The Alternatives to Opioids (ALTO) approach utilizes non-opioid medications for pain management to ultimately diminish opioid utilization in the emergency department (ED). Materials and Methods: This retrospective, single center, cohort study investigates the impact of the ALTO protocol on opioid use, patient satisfaction with pain control, and subsequent ED flow. Patients receiving pain medication in an urban level three trauma center from March to August of 2018 prior to implementation of the ALTO protocol were identified as the pre-protocol control group and patients receiving pain medication between March to August 2019 after implementation of the protocol in the same ED were allocated to the post-protocol group. The primary interest of the study was the effect on opioid use in the ED. The secondary outcomes investigated were door-to-doctor time, the left without being seen (LWOBS) rate, patient satisfaction with pain control, and the average turnaround time. Results: Total opioid administration decreased by 59.6% in the post-protocol group. The LWOBS rate ($p=0.003$) and the average door-to-doctor time ($p<0.001$) were significantly decreased in this group as well. No significant difference in patient satisfaction to pain control ($p=0.192$) or average turnaround time ($p=0.209$) was identified between the groups. Conclusion: ALTO protocol implementation was associated with a significant reduction in opioid administration without impacting patient satisfaction with pain control or ED flow.

Project 2:

The United States (U.S.) experienced the ongoing opioid epidemic in conjunction with the COVID-19 pandemic. Previously, Alternatives to Opioids (ALTO) protocols have been established as an effective approach to promote non-opioid medications as first-line analgesia

in the emergency department (ED). Along with the unprecedented environment the COVID-19 pandemic created over 80% of the states in the U.S. have noted opioid related deaths to have risen during this time. Closure of outpatient resources has also placed new pressure on the ED to provide pain control for patients. Investigation of the pandemics effect on ED opioid reduction through the ALTO approach is novel. This retrospective, single-center, cohort study was completed to compare patients receiving pain medication in the ED from March to August 2020 during the COVID-19 pandemic and patients receiving pain medication in the ED during March to August from one year prior. Alteration in outpatient prescription of opioids and use of opioids in the ED were the primary focus. Additionally, use of each ALTO medication, length of stay in the ED, patient satisfaction with pain control, and the rate of patients who left without being seen (LWBS) were investigated as well. In the pandemic group a significant decrease in the average prescribed Morphine milligram equivalents was noted. (3.16 ± 0.31 versus 7.72 ± 0.31, $p < 0.001$). ED usage of opioids, patient length of stay in the ED, satisfaction of patients, and the rate patients exhibited no significant difference. In the setting of the COVID-19 pandemic, out-patient opioid usage was found to be reduced with the use of an ALTO, multi-modal approach to pain control. No secondary effects on patient satisfaction, opioid use in the Ed, length of stay, or the rate of patients who LWOBS was found.

II: RESEARCH QUESTIONS

Project 1:

In patients visiting the Emergency Department (ED), is an Alternative To Opioid (ALTO) protocol for pain management effective in reducing opioid administration in the ED? Additionally, will implementation of the protocol cause any effects on patient satisfaction with pain control, left without being seen (LWOBS) rates, door to doctor time, or turnaround time in the ED?

Project 2:

In patients visiting the Emergency Department (ED) during the COVID-19 pandemic, does the Alternative to Opioid (ALTO) protocol for pain management remain effective at reducing opioid prescription from the ED? Additionally, will the protocol cause any effects on ED opioid administration, patient satisfaction with pain control, ED length of stay, and the rate of patients leaving without being seen (LWOBS)?

III: INTODUCTION AND SIGNIFICANCE

Up to 78% of patients visiting the emergency department (ED) present with the complaint of pain, making it one of the most common complaints. [1,2] For patients who are experiencing pain, there are a variety of medications that clinicians are able to use for analgesia. Despite the concerns surrounding the associated complications for opioids, data indicates that they are still a frequently used class (259 million prescriptions written in 2012). [3-6] Additionally, the current state of United States opioid epidemic is well known. An estimated 1.9 million Americans reported an opioid use disorder related to prescription medications in 2014. [7] In the U.S. in 2015 an estimated 547,543 ED visits occurred for drug-related poisonings. [8] Two out of every three drug overdose deaths involve an opioid and prescription opioid deaths have increased six-fold since 1999. [9] CDC reports indicate that more than 630,000 people died from a drug overdose in the United States (U.S.) from 1999 to 2016. [10] 2017 data states that for every 100 Americans there were 58.5 opioid prescriptions. [10] For Americans under the age of 50 opioid overdose is the leading cause of mortality, with higher rates than gun violence, motor vehicle accidents, and even HIV at their respective peaks. [11,12] The rise in prescription opioid related deaths has risen in parallel with increasing numbers of prescriptions for opioids and is evidenced by extensive CDC research. [11,12] Opioid prescription rates in the emergency department (ED) have been found to be rising as well. [13] Due to concern about the opioid epidemic many ED-based physician research groups have launched and include the Alternatives to Opioids (ALTO) program and the Opioid-Free ED program. Investigation by these groups continues as they work to effectively reduce ED opioid usage and improve safety for pain control. [1,5,14]

Motov et al 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. [15] LaPietra et al demonstrated 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 ALTO protocol. [16] Since 2016, many EDs have developed similar protocols and a few state level chapters of emergency medicine

formed multi-disciplinary groups to develop robust and more detailed ALTO-first prescribing guidelines. [5,15,17]

The increase in opioid usage and opioid-related deaths continued to climb in the U.S. through the coronavirus disease 2019 (COVID-19) pandemic. Since the pandemic began, more than 40 states have reported an increase in opioid-related deaths. [18] Recent study demonstrated that nonfatal opioid overdoses doubled during the early COVID-19 pandemic, reaffirming the need for aggressive harm-reduction strategies. [19] In the early months of the pandemic more than 40 states reported increases in opioid related deaths. And more recently 107,000 deaths due to drug-related overdose were reported in the U.S. between January 2021 and January 2022. [20] The shelter in place public health ordinance during the COVID pandemic was also found to be associated with an increase in the proportion of opioid overdose that was statistically and clinically significant. [21,22] Systematic reviews have also identified significant increases in opioid related emergency medicine usage and urine drug testing positivity, surrogate measures of the opioid crisis. [23]

COVID-19 infection has been associated with hyperalgesia, wide-spread pain, myalgias, and even referred pain making efficient and effective pain control a significant challenge. [24] The close relationship between the immune system and the perception of pain is well known. Some patients suffering from chronic pain have shown immunosuppression in addition to other sophisticated effects on the immune system as a whole. [25] In patients, the risk of immune suppression and consequentially reinfection with COVID-19 is associated with old age, chronic pain, and the comorbidities of those patients. Opioids have been found to effect the endocrine system and even augment the immune system. [26] Studies have also identified persistent pain as a key manifestation of Long COVID Syndrome. Reviews have uncovered an increased prevalence as high as 19.6% of new-onset chronic pain (≥3 months) in these patients compared to 1.4% of the control population. [27]

There is limited data to demonstrate the impact of the pandemic on the ALTO protocol for acute pain management in ED. With closure of outpatient resources for patients the ED has quickly become a place for patients to seek pain control. With limited data and healthcare

landscape changes this study was devised to examine the impact of the ALTO protocol on opioid use for acute pain in the ED during the COVID-19 pandemic.

Over the course of the pandemic, the ED has quickly become a primary resource for pain management of acute and chronic pain. The effect that the unique challenges of the pandemic had on ALTO protocols is still unclear. There has been limited investigation of ALTO protocols pre-COVID pandemic and during the pandemic with no subsequent studies following the conclusion of the pandemic. Project 1 aims to investigate whether implementation of an ALTO approach to pain management effects the overall opioid administration rate in an urban ED and its effects on various other metrics like door-to-doctor time, patient satisfaction, LWOBS rates, and average turnaround time in the ED. Project 2 aims to investigate the impact of implementing an ALTO protocol in an urban, level three trauma center Emergency Department and its effect on the amount of opioid utilization, patient outcome, percentage of patients that leave without being seen, average door to doctor time, and average turnaround time in the ED. We hypothesize that the ALTO protocol will result in decreased opioid utilization with no change in patient satisfaction, percentage of patients that leave without being seen, average door to doctor time, and average turnaround time in the ED. The challenges of the pandemic, paired with the alterations in frequency of acute and chronic pain have created a need for innovation in the treatment of pain. It is hypothesized that ALTO protocol will still remain effective at reducing the amount of opioids used in the ED and will remain an important strategy for harm reduction with the worsening of the U.S. opioid epidemic.

IV: RESEARCH MATERIALS AND METHODS

Project 1:

This is a retrospective cohort study in an urban community ED in North Texas. The facility is a 574-bed university-affiliated tertiary teaching hospital that serves approximately 50,000 patients in the ED annually. The ED is an urban and level III trauma center within the largest healthcare system in North Texas, the Baylor Scott & White Healthcare system (BSWH). This study was approved by institutional review board in the BSWH (IRB#019-130).

The ALTO training program was initiated in September 2018. At that time there was creation of the protocol, training classes to all physicians, nurses, and pharmacists were provided, and the ED pharmacy was stocked with ALTO medication. The management protocol utilized by the care team is elaborated as Appendix 1. The training that the Emergency Medicine physicians and nurses were given centered around the use of a multi-model non-opioid approach to analgesia. This included education on controlling different types of pain with this approach and included musculoskeletal pain, neuropathic pain, renal colic, headache/migraine, chronic abdominal pain, sickle cell crisis, and dental pain. A 6 month transition period following implementation and training was allotted. Data was then retrospectively collected and compared from 6-month intervals. The pre-protocol group was from March to August 2018 and the post-protocol group was from March to August 2019. This ALTO program was the first to be developed within the BSWH system.

All of the adult patients (age >18 years old) who received pain medications at their ED visit during the study timeframe were included. No other changes in regards to opioid administration were implemented during the timeframe of the study. There were also no significant ED volume reductions during the study period. A report generated via the computer entry system identified opioid use. The EMR system was used to retrieve Patients' demographics, past medical history, and pain medications use in ED. Milligram morphine equivalents (MME) were used to measure opioid administration. The Press-Gany survey was used to measure patient satisfaction scores to pain management. Specifically with focus on the questions of "How well

was your pain controlled?" and "How likely are you to recommend this emergency department?" Press-Ganey surveys were sent randomly to patients who were evaluated, treated, and discharged from the ED. The survey results were collected and analyzed monthly to match the study period. This study only included the medications administered in the ED and not the out-patient prescriptions. A medication dose that contained both an opioid and a non-opioid, such as with acetaminophen/oxycodone, would be considered an opioid.

The primary outcome was the change in ED opioid administration pre- and post-intervention of the ALTO opioid reduction protocol, measured by MME. The secondary outcomes include patient satisfaction to pain control, left without being seen (LWOBS), door-to-doctor time, and turnaround time. The definition of door-to-doctor time is the duration from patient arrival to the ED until they are seen by a physician. The average turnaround time was defined as the duration from patient arrival to final disposition of admission or discharge.

To analyze categorical data a Wilcoxon rank-sum test and Pearson chi-square test were used. These variables were then presented as counts with proportions. A two tailed t-test was selected for analysis of continuous variables. A p-value of < 0.05 was selected for determining significance. The continuous variables were then reported as a mean with standard deviation. Microsoft Excel (Microsoft Excel 2010; Microsoft Corporation, Seattle, WA) was used for entry of statistical testing and analysis was completed with Stata 16.1 (Stata Corp LLC, Texas, USA).

Project 2:

This study was a retrospective, single center, cohort study. Data was retrieved from the electronic medical record (EMR) system at the level III trauma center with annual census of 50,000 patient visits. Institutional Review Board approval was sought (reference number: 344143) and requirement for informed consent was ultimately waived due to the study being retrospective without the requirement of intervention. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used for results reporting. [28]

The ALTO training program was initiated in September 2018. Protocol initiation included the creation of the protocol, provision of training classes to all physicians, nurses, and pharmacists, and stocking of the appropriate ALTO medication in the ED pharmacy. Both physicians and nurses were trained in using a non-opioid, multi-modal approach to pain management. This included guidance for analgesia for different types of pain including musculoskeletal pain, neuropathic pain, renal colic, headache/migraine, chronic abdominal pain, sickle cell crisis, and dental pain (see Appendix 1).

All patients receiving pain medication in ED during the defined study timeframe were included. ED visits by patients during the COVID-19 pandemic (March to August 2020) were distributed into the pandemic group. Patient visits during the same period from the previous year (March to August 2019) were allocated into the control group.

Clinical data was extracted from the health system's EMR (Epic, Verona, WI) with the use of an enterprise data warehouse. The dosages of all opioids were converted to morphine milligram equivalents (MME) for data analysis. The Press Ganey Survey was used to measure pain control and patient satisfaction scores. The primary outcome was the change in ED opioid administration and prescription. Secondary outcomes included patient satisfaction to pain control, ED length of stay, admission rate, and rate of left before treatment complete (LBTC).

Categorical variables are presented as counts with proportions, and continuous variables are presented as means with standard deviations. We used the Wilcoxon rank-sum test and Pearson chi-square test 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 16.1 (Stata Corp LLC, Texas, USA).

V: RESULTS

Project 1:

From the study period, final analysis included a total of 34,251 patients. The pre-intervention group included 16,353 patients and 17,898 patients were included in the post-intervention group. (Table 1A) In the post-implementation group, total opioid administration was lower by 59.6%. The mean MME used per patient was also significantly lower in the post-intervention group (2.69±0.18 versus 1.08±0.15, $p<0.001$). (Figure 1A) There were significant decreases in the percentage of patients that left without being seen ($p=0.003$) and the average door-to-doctor time ($p<0.001$) in the post-intervention group additionally. (Figures 2A & 3A) No statistically significant difference was identified for patient satisfaction ($p=0.192$) or average turnaround time ($p=0.209$). (Figures 4A & 5A)

	2018	2019
Patient number received pain medication (n, %)	16,353	17,898
Age (mean, SD)	46.3 (19.8)	46.7 (19.9)
Sex, female (n, %)	10,631 (65.0)	11,487 (64.2)
Chief complaint (n, %)		
General discomfort	884 (5.4)	1,054 (5.9)
Fever	236 (1.4)	263 (1.5)
HEENT	391 (2.4)	386 (2.2)
Respiratory symptoms	1,560 (9.5)	1,675 (9.4)
CV symptoms	1,847 (11.3)	2,065 (11.5)
GI symptoms	3,283 (20.1)	3,521 (19.7)
Endocrine symptoms	103 (0.6)	536 (3.0)
Reproductive symptoms	155 (1.0)	288 (1.6)
GU symptoms	1,274 (7.8)	878 (4.9)
Hematological symptoms	91 (0.6)	50 (0.3)
Infection	236 (1.4)	334 (1.9)
MSK discomfort	2,125 (13.0)	2,262 (12.6)
Neurological symptoms	1,091 (6.7)	1,184 (6.6)
Skin symptoms	196 (1.2)	214 (1.2)
Trauma	1,626 (9.9)	1,754 (9.8)
Miscellaneous	1,255 (7.7)	1,434 (8.0)
Ordered time (hours) (mean, SD)	1.4 (2.4)	1.2 (1.8)
Departure time (hours) (mean, SD)	4.6 (6.8)	4.4 (3.5)
Care Complete time (hours) (mean, SD)	3.2 (6.1)	3.1 (2.5)
Disposition (n, %)		
Observation	1,386 (8.5)	1,400 (7.8)
Admission to floor	3,585 (21.9)	3,668 (20.5)
Admission to ICU	405 (2.5)	397 (2.2)
Discharge	10,298 (62.3)	11,815 (66.0)
Expire	3 (0.02)	11 (0.1)
Others (ex. Against medical advice, transfer, unknown)	676 (4.1)	607 (3.4)

TABLE 1: Patient characteristics in post-protocol (2019) versus pre-protocol (2018) group

SD: standard deviation; HEENT: head, eyes, ears, nose, and throat; CV: cardiovascular; GI: gastrointestinal; GU: genitourinary; MSK: musculoskeletal

Table 1A

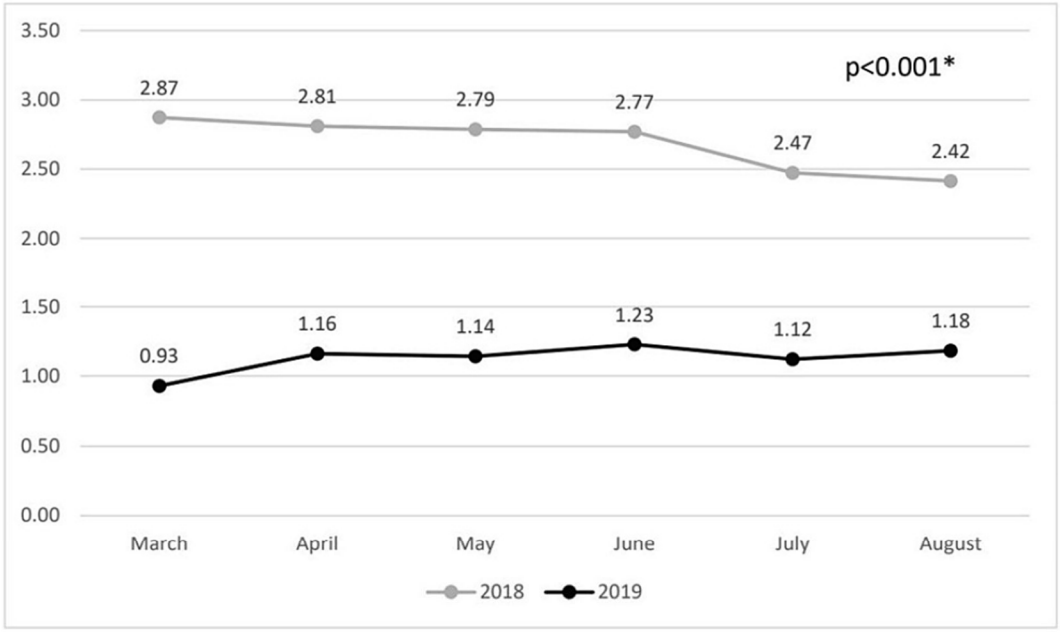


FIGURE 1: Mean morphine milligram equivalents (MME) administered per patient visit at emergency department by month in 2018 and 2019

Figure 1A

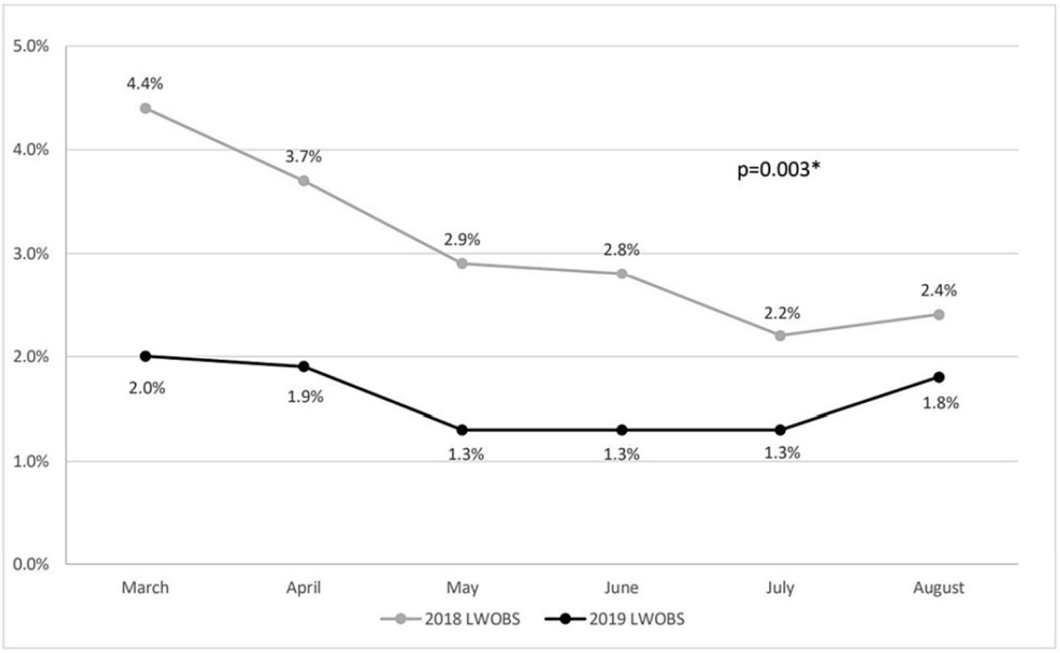


FIGURE 2: Monthly percentage of left without being seen (LWOBS) at emergency department in 2018 and 2019

Figure 2A

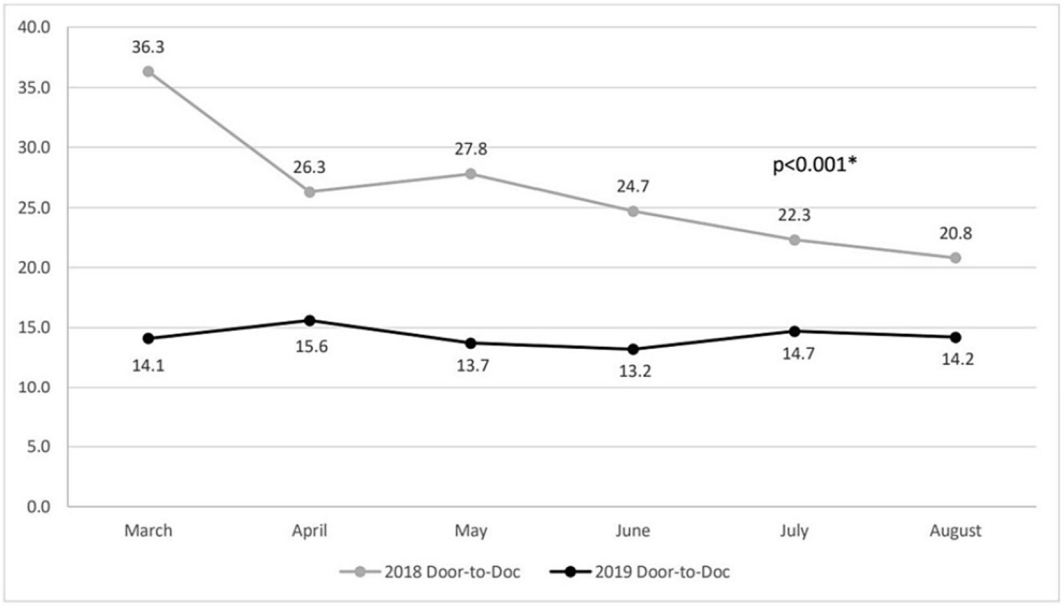


FIGURE 3: Monthly average of door-to-doctor time (unit: minutes) at emergency department in 2018 and 2019

Figure 3A

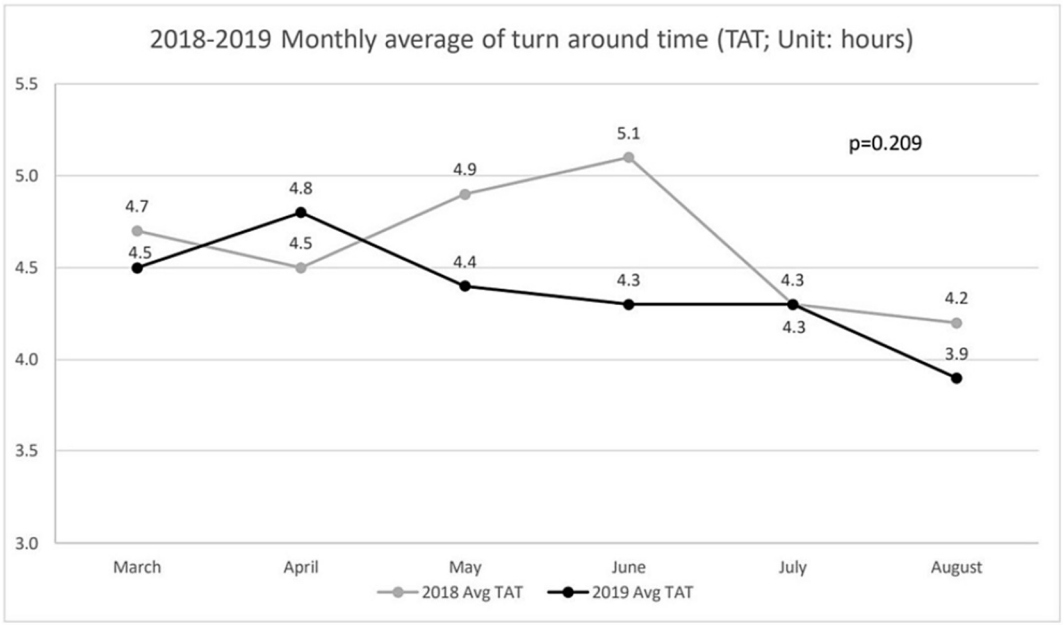


FIGURE 4: Monthly average of turnaround time (TAT) (unit: hours) at emergency department in 2018 and 2019

Figure 4A

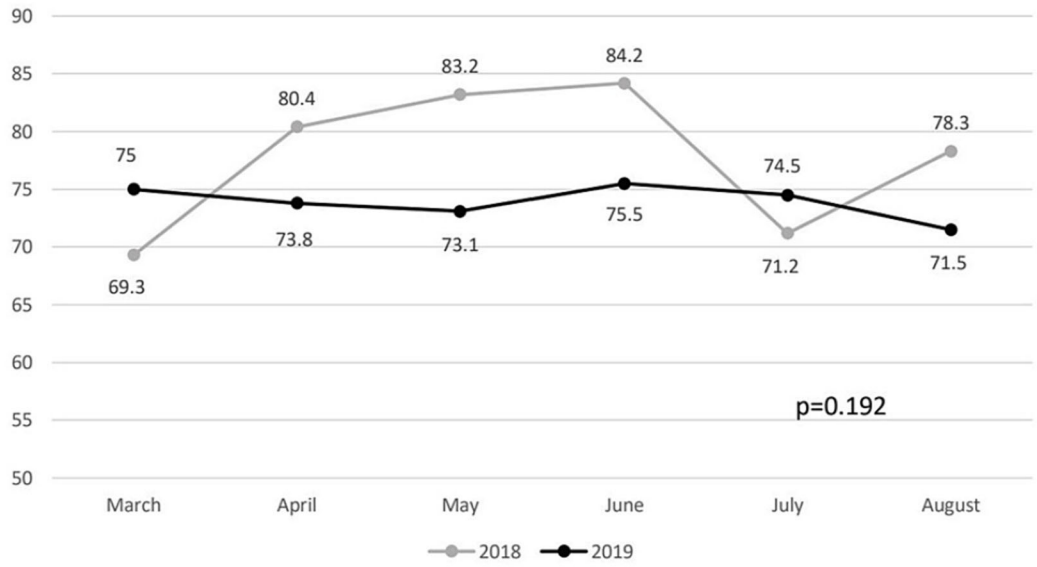


FIGURE 5: Mean patient satisfaction at emergency department in 2018 and 2019

Figure 5A

Project 2:

40,124 visits to the ED were analyzed. 22,949 visits were included in the pre-COVID group and 17,175 visits were allocated to the pandemic group. Baseline characteristics of the analyzed patients can be found in Table 1B. Per discharged patient in the COVID-19 pandemic group a statistically significant decrease in the mean prescribed MME was identified (3.16±0.31 versus 7.72±0.31, $p<0.001$). Opioid administration (1.13±0.04 versus 1.19±0.54, $p=0.389$), patient satisfaction with pain control (78.32±2.74 versus 74.27±0.35, $p=0.173$), ED length of stay in hours (4.12±0.07 versus 4.37±0.12, $p=0.103$), admission rate (34.25±0.97 versus 29.85±0.31, $p=0.001$), and rate of LWOBS (1.83±0.19 versus 1.60±0.14, $p=0.335$) displayed no significant difference between the studied groups.

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

	Control (2019) (N = 22,949)	COVID Pandemic (2020) (N = 17,175)	*p*-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 1B

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)	*p*-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.

Table 2B

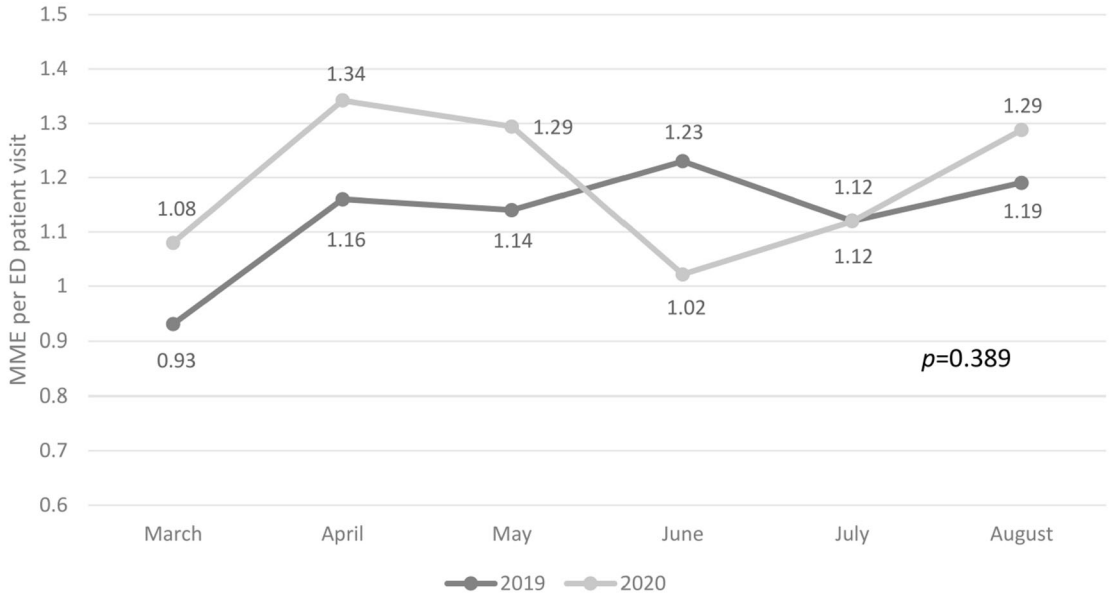


FIGURE 1. Mean morphine milligram equivalents (MME) administered per patient visit at ED by month in COVID-19 pandemic (2020) versus Control group (2019).

Figure 1B

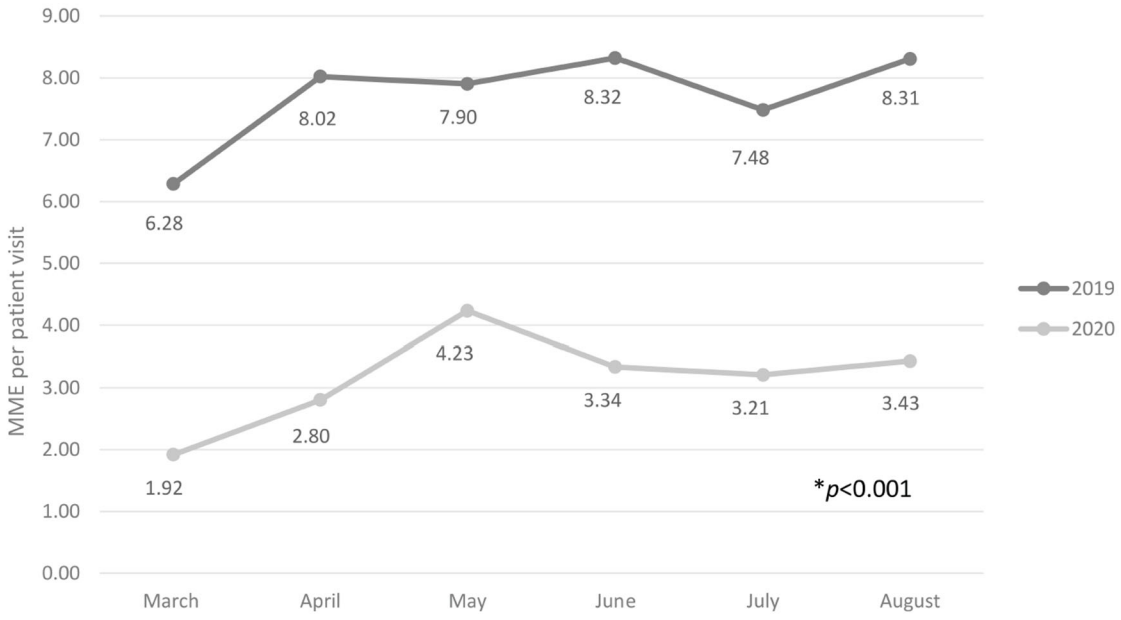


FIGURE 2. Mean morphine milligram equivalents (MME) out-patient prescription per patient visit by month in COVID-19 pandemic (2020) versus Control group (2019). *$p < 0.05$.

Figure 2B

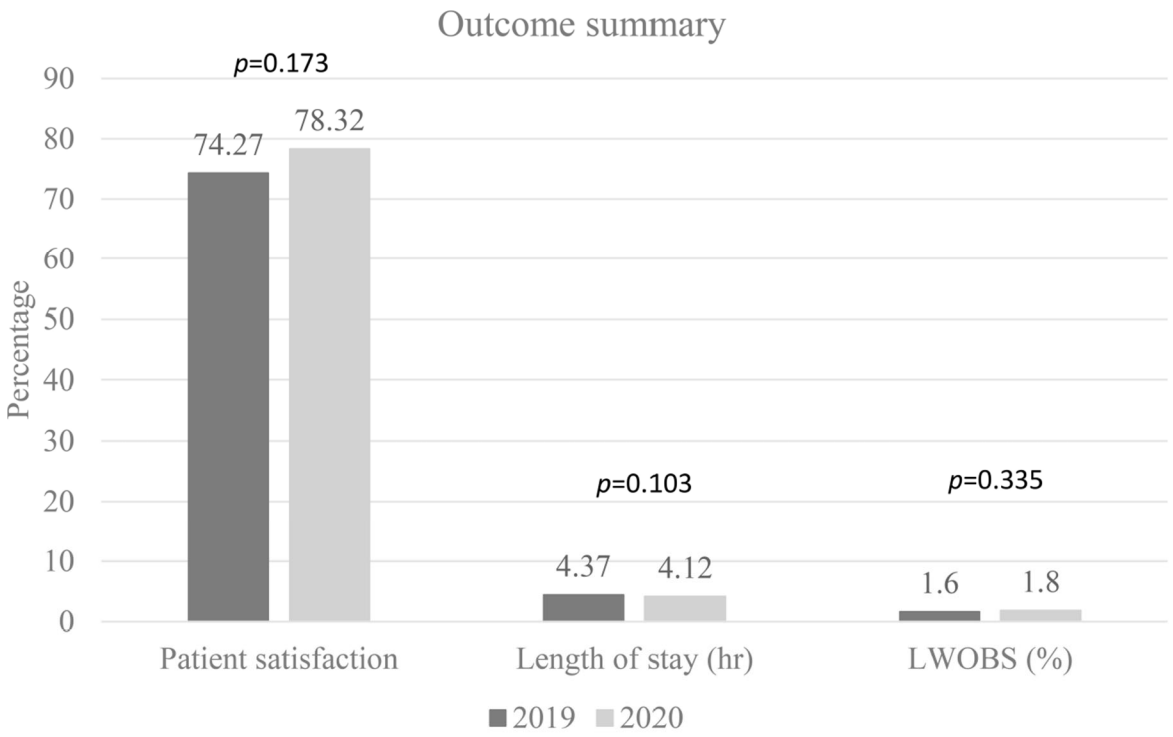


FIGURE 3. Secondary outcome summary in COVID-19 pandemic (2020) versus Control group (2019).

Figure 3B

VI: DISCUSSION

Our initial investigation showed that the amount of opioid administration was lowered by 59.6% in the post-ALTO protocol implementation group in a community ED in North Texas without changes in patient satisfaction to pain management or average turnaround time in the ED. Motov et al. and LaPietra et al. initially demonstrated that implementation of non-opioid pain control strategies could be successful in reducing the administration of opioids. [15,16] Our findings also supported previous literature that the implementation of ALTO protocol could reduce opioid use in the ED setting without decreasing patient satisfaction with pain control. [29,30] A significant decrease in the proportion of LWOBS and the average door-to-doctor time without changes in patient satisfaction or average turnaround time in the ED were also observed. This study aimed to confirm these findings in a community hospital setting while also examining secondary outcomes that had not previously been investigated.

We demonstrated that the ALTO-first approach to analgesia is feasible and effective in a community ED setting, and is in line with previous literature showing significant opioid reduction. [29,30] Patient satisfaction was measured using the Press-Ganey survey, specifically focusing on the questions of “How well was your pain controlled?” and “How likely are you to recommend this emergency department?” Previous investigations have shown that giving opioid or non-opioid pain medications in the ED was not independently associated with Press-Ganey ED satisfaction scores. [30-32] Consistent with previous literature, our results also demonstrated that there was no relation between opioid usage and patient satisfaction. [31,32] The ALTO protocol can be effective for acute pain control and potentially reduce the adverse effects of opioids such as sedation and respiratory depression. [33]

Overcrowding of the emergency department has been a concern in the US, and is linked with lengthened timelines and reduced quality of treatments. This includes delayed analgesic administration, which further contributes to the snowball effect of cumulating wait times. [34] To identify the factors contributing to poor ED flow previous studies have investigated ED length of stay (LOS) or door-to-doctor time. [35,36] Door-to-doctor time has been shown to have a substantial role in the outcomes of patients with serious health conditions (i.e. myocardial infarction, stroke, and sepsis). [37-39] In particular, increased door-to-doctor time was associated with poorer outcomes for these patients. Other factors that can effect ED throughput are the number of laboratory or radiology exams, the need for multiple medications, and number of consultants. [40] However, there is limited evidence regarding the relationship between pain management and ED flow metrics. Anderson et al. demonstrated that the use of opioid in the ED was associated with an increased ED LOS. [41] Our study identified a significant reduction in the average door-to-doctor time after ALTO implementation in ED. Indicating that there may be a novel relationship between ALTO pain management and door-to-doctor time that has yet to be investigated. Opioids are associated with the adverse effects of sedation and respiratory depression. [33] Due to this, patients are commonly observed following the administration of opioids in the ED. If a patient develops any adverse effects, further medical management to address these problems are required. This observation period and possible need for further treatment attribute to longer ED LOS and perpetuate overcrowding, which can lead to increasing the door-to-doctor time for patients presenting following these patients in the ED. Therefore, use of the ALTO protocol can potentially reduce the adverse effects from opioids that would otherwise delay treatment for other critically ill

patients. Although there are a variety of factors that affect ED operational metrics, we believe the ALTO protocol has the potential to improve ED flows and patient care. [29,30,42]

While it could be hypothesized that the use of less potent analgesia could increase the amount of time that patients stay in the ED due to inadequate pain relief, our study found that there was no significant difference in the average turnaround time. It has been shown that turnaround time can significantly affect ED LOS, average daily throughput, and even the number of diversions from the emergency department. [17,43] All of which are critical in the delivery of high quality and efficient care to the greatest number of patients. A significant reduction in the proportion of LWOBS was also identified in this study. Recently, a rise in the number of patients who leave without being seen has been noted due to a variety of factors including ED overcrowding, financial coverage, and longer waiting times. [42] Patients who leave without being seen have been found to be twice as likely to report worsening of their condition or pain within two days of their visit. [44] Previous investigations have also had a difficult time identifying severe adverse events in this population though some have made note of patients experiencing them. At least half of the patients who have LWOBS have been associated with seeking alternative and subsequent care. [45] Optimization of ED flow to prevent overcrowding could lead to lower proportions of patients who LWOBS. This can ultimately result in less patients being readmitted to the ED or seeking alternative care at other locations. [44] Each of these factors have a major impact on the health care system. Implementation of ALTO protocols could have a positive impact on improving ED flow by providing adequate pain relief and decreasing adverse effects from opioids in ED which can subsequently improve the average turnaround time and LWOBS rate. [29,30]

Reduction in the use and prescription of opioids is paramount in addressing the U.S. opioid epidemic head on. This study demonstrated that the ALTO-first approach to analgesia is feasible and effective for opioid reduction in ED with no association in changes to patient satisfaction scores or average turnaround times. This intervention has potential to be implemented across the country as part of a nationwide response to the opioid epidemic. [46]

Though these findings are promising, there were limitations. This study was limited by being single center and retrospective in nature. Potential confounding factors could have influenced the association between intervention and results. This study mainly focused on the trend of opioid reduction, and we attempted to control for as many of the potential confounding factors as possible much like prior studies. [47,48] It is difficult to measure, however, unknown factors including different disease and operational complexity may also have contributed to opioid reduction. It is doubtful that these confounding variables would cause significant differential bias. Future prospective studies are needed to confirm these preliminary findings.

One of the most common surveys that can be used to evaluate patient satisfaction to pain management in ED is the Press-Ganey score. [29] These scores are subjective results that are prone to bias. They also do not account for patients that are admitted, those that leave without being seen, or patients who present to the ED with regularity. This may also exclude patients who leave prior to completing treatment, which would reflect a population of patients that are dissatisfied with their care. Variables other that the ALTO protocol can affect the ED flow metrics like door-to doctor time, ED turnaround time, and LWOBS. It is possible that the results may have been influenced by external factors not addressed in this study. We cannot

identify the relationship between the door-to-doctor time, ED turnaround time, and patient satisfaction which might be skewing the data due to the retrospective study design. In addition, the rate of patients who left without treatment being complete, a potential surrogate measure for patients who are dissatisfied with their care that they are receiving in this study, was not investigated. Additionally the study was also conducted while the "opioid epidemic" was well recognized and prescribing and administration patterns could have secondarily been affected by this during this time. The setting for the study was in an urban level three trauma center, whose patient population may not be generalizable. Repeating the study across differing locations and patient populations could lead to improved generalizability and more robust findings.

As it was hypothesized in our further study, opioid prescriptions during the COVID-19 pandemic displayed a significant reduction thought the ALTO protocol while ED opioid administration, patient satisfaction, and ED flow were unaffected. In the setting of limited outpatient resources this ALTO strategy can potentially reduce opioid use and subsequent complications during the pandemic.

Opioid use and abuse have continued to rise throughout the COVID-19 pandemic. Over 40 states in the U.S. have reported an increase in opioid-related deaths during this time, and recent studies have demonstrated that non-fatal opioid overdoses have doubled as well. [26,49] In addition to concurrent COVID-19 infection other factors associated with the connection between COVID-19 and the increased rates of opioid-related fatalities include social isolation, lack of access to mental health care services or health care services, disruptions in medication for opioid use disorder, and increased homelessness and incarceration rates. [50]

Increasing use of methamphetamines in conjunction with opioids has also complicated the opioid epidemic. [51] The emergence of COVID-19 and the resulting social stressors, economic stressors, and disruptions in health care and social safety nets will likely exacerbate the opioid epidemic. [24] This evolution of the opioid epidemic and the ever rising death toll highlight the necessity for harm reduction strategies like the ALTO protocol.

An opioid-free ED was first described by Motov et al. in 2014 with non-narcotic treatment protocols using a CERTA (Channels/Enzymes/Receptors Targeted Analgesia) multi-modal, physiologic approach for pain management. [15,16] Further studies then demonstrated sufficient pain alleviation in 75% of their patients non-opioid therapies with reduction in opioid usage of 50% following protocol implementation. [16] Protocols have begun to be implemented by other emergency departments and have gained popularity with may state multi-disciplinary groups to develop multi-modal analgesia prescribing guidelines following the studies of 2016. [5, 15, 52] Further, significant reduction in ED opioids have continue to be verified at other locations. [29] Similar to the aforementioned studies the control group (Pre-COVID cohort) of our study had a similar rate of MME usage per patient. Over the years strong data has been collected to support the reduction of narcotic use in the ED thought multi-modal protocols, the COVID-19 pandemic's relationship with these protocols remains novel. Evidenced by our results the ALTO protocol can significantly reduce opioid prescriptions even in the setting of the pandemic. Importantly, ED opioid administration, patient satisfaction, departmental flow remained unaffected. In line with previous studies, the ALTO protocol can be effective in the ED, and especially at the time of discharge with reduction in opioid prescription. [16, 29, 52]

The complexity of COVID-19 infections and their associated myalgias, referred pain, and hyperalgesia continue to gain more evidence as studies continue. [28, 53, 54] Ultimately, making analgesia for COVID-19 and non-COVID-19 patients a challenge in the ED. Additionally, there has been a disproportionate rate of incarceration of those suffering from addiction during the pandemic and decarceration efforts that respond to this will simply move a vulnerable population from high risk environment to high risk environment unless appropriate planning is utilized. [55] As the pandemic causes closures of outpatient facilities new potential pressure has been placed on the ED with requests for opioids. [56] In this study, ED opioid administration during the pandemic did not increase. The rate of opioid dosing remained comparable with the reduced rates of administration demonstrated prior to the pandemic. Additionally, our study found a significant decrease in NSAID prescription during the COVID-19 pandemic period. Early in the course of the pandemic it was hypothesized that through increased expression of ACE2 (the host protein that the SARS-CoV-2 virus attaches to) NSAIDs could worsen the course of infection for affected patients. [57] NSAID prescribing and utilization patterns of physicians may have been influenced by this early hypothesis leading them to turn to other ALTO protocol medications for analgesia. This could have consequently increased Ketamine usage during this period. Ketamine has a variety of uses in the ED and can be extremely versatile without depressing respiratory or cardiovascular physiology. [58, 59] Clarification of the role for Ketamine in patients with COVID-19 infections with require further investigation. [60]

The success of the ALTO-first multimodal approach to pain management is signified by the reduction of ED opioid prescriptions noted in our study. Public health measures have lead to the closure of a variety of outpatient care settings. [61] As a result, outpatient resources for

pain control have been limited by these closures resulting in the ED becoming a more prominent site care establishment. This study highlights the importance of ALTO-first protocols in combating the opioid epidemic during the pandemic with the noted reduction in opioid prescription. The increase in severe adverse opioid related events over the last two decades has matched increasing prescription opioid analgesic usage rates in the US. [62] The 2015 the National Survey on Drug Use and Health proposed that 37.8% of adults (or 91.8 million) in the U.S. used prescription opioids. An estimated 4.7% (or 11.5 million) of those who use prescription pain medications misused them, and 0.8% (or 1.9 million) had a use disorder. [63, 64] From 1990–2014 prevalence of prescription opioid misuse has been uptrending. [65] A concerning evolution of the opioid epidemic is illuminated by this increasing prevalence. [65] Decreasing opioid prescription, as seen in this study, is important in combating this wide-spread problem. Decreasing prescription of opioids is essential for reducing the initial use of these medications. In turn, reducing the further complications including misuse, and abuse. An integral part in reducing nonfatal overdoses, overdose-related deaths, and combating this epidemic may well begin with reducing ED opioid prescriptions and the resulting complications that can arise.

No previous studies have investigated if the ALTO protocol can remain effective in the COVID-19 pandemic. A significant strength of this study lies in the large sample size that was able to be compared between the two groups. As demonstrated by our results, the ALTO protocol in the ED can be a fundamental pain management strategy and aid in combating the opioid epidemic during the COVID-19 pandemic.

The study had several limitations. This was a retrospective, uncontrolled design. The study site also had a previously implemented ALTO-first protocol. The assumption was also made that there were similar ED volumes and patient presentations during the investigated time periods. The differences in the pre-COVID and pandemic groups have potential to be attributed to covariates. There may also be limited generalizability to other populations as this study focused on a single, urban, level three trauma center in North Texas. Furthermore, prescribing patterns during the time may also have been influenced as the study was conducted when the opioid epidemic was publicized and well recognized

VII: FUTURE DIRECTIONS

Our studies highlighted that the ALTO protocol remains effective in reducing opioid use and prescription in the ED even in the face of an unprecedented pandemic. However, there is still much work to be done in combat of the U.S. opioid epidemic. There are several areas that remain to be investigated. It is well known that following the COVID-19 pandemic the healthcare delivery system of the U.S. is forever changed. Further investigation is needed to identify exactly how these changes have affected opioid prescription rates in EDs that now experience overcrowding, prolonged wait times, and boarding rates that have not previously been experienced.

Furthermore, there is ample opportunity to investigate the root cause for alterations in utilization and prescribing patterns in EDs nationwide. Perhaps there is a need for reeducation or improvement on prior ALTO protocols because they no longer fit with the current landscape

of healthcare in EDs. These cannot adequately be addressed without first better understanding the new landscapes current utilization and prescribing patterns.

Within the ALTO protocols themselves there is room for improvement and further innovation. Recent literature has highlighted the effectiveness of peripheral nerve blocks for analgesia. The ALTO protocol can continue to be innovated to match the advancements of neuraxial anesthesia and innovations in medical management for analgesia as well. Further studies can investigate the opioid use reduction secondary to these advancements and potentially further influence the practice of EM physicians nationwide.

The opioid epidemic is also something that cannot be solved with one alteration in medical practice. Though the ED serves as a prime location to help curb the start of a patient's opioid use through limiting prescription and utilization, it alone cannot address the entirety of the problem that the U.S. faces. This instead will require a multifaceted approach. An underutilized facet in EDs nationwide centers around harm reduction strategies for patients that struggle with opioid misuse and abuse as well as safe use education for these patients. Investigation into these arenas can help to illuminate their underutilization as well as their potential effectivity in improving patient safety and outcomes for this patient population.

VIII: CONCLUSIONS

Project 1:

In the setting of a community ED, this study demonstrated that the ALTO-first approach to analgesia is attainable and remains effective. Protocol implementation was associated with a significant reduction in opioid administration without negatively impacting patient satisfaction with pain control or the average turnaround time in the ED. These are preliminary findings and future prospective studies are needed to confirm them.

Project 2:

In summary, the ALTO protocol remains effective and created a significant decrease in opioid prescription during the COVID-19 pandemic. Importantly, ED opioid administration, patient satisfaction, and department flow were not found to be affected. While the pandemic has limited outpatient healthcare delivery, this study highlights that the ALTO-first protocols can have potential benefit for reducing opioid usage and the subsequent complications, and ultimately help to address the opioid epidemic that continues in tandem with the COVID-19 pandemic.

IX: COMPLIANCE

Project 1:

Consent was obtained or waived by all participants in this study. Institutional Review Board issued approval 019130. The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of The Baylor Scott & White (reference number: 019130).

Project 2:

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.

REFERENCES

1. Todd KH, Ducharme J, Choiniere M, et al. Pain in the emergency department: results of the pain and emergency medicine initiative (PEMI) multicenter study. J Pain. 2007;8(6):460-6.

2. Cordell WH, Keene KK, Giles BK, Jones JB, Jones JH, Brizendine EJ. The high prevalence of pain in emergency medical care. Am J Emerg Med. 2002;20(3):165-9.

3. Krebs EE, Gravely A, Nugent S, et al. Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE Randomized Clinical Trial. Jama. 2018;319(9):872-82.

4. Barnett ML, Olenski AR, Jena AB. Opioid-Prescribing Patterns of Emergency Physicians and Risk of Long-Term Use. N Engl J Med. 2017;376(7):663-73.

5. Dowell D HT, Chou R. . Centers for Disease Control and Prevention. Guideline for Prescribing Opioids for Chronic Pain – United States, 2016. Morbidity Mortality Wkly Rep. Recommendations and Reports/ March 18, 2016/ 65(1); 1-49. https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm. 2016.

6. Mazer-Amirshahi M, Mullins PM, Rasooly I, van den Anker J, Pines JM. Rising opioid prescribing in adult U.S. emergency department visits: 2001-2010. Acad Emerg Med. 2014;21(3):236-43.

7. Haffajee RL, Lin LA, Bohnert ASB, Goldstick JE. Characteristics of us Counties with High Opioid Overdose Mortality and Low Capacity to Deliver Medications for Opioid Use Disorder. JAMA Network Open. 2019; 2: e196373.

8. Hedegaard H, Warner M, Minino AM. Drug Overdose Deaths in the United States, 1999-2015. NCHS Data Brief. 2017(273):1-8.

9. Centers for Disease Control and Prevention. 2018 Annual Surveillance Report of Drug-Related Risks and Outcomes—United States. Surveillance Special Report. (2018). Accessed: November 1, 2019: https://www.cdc.gov/drugoverdose/pdf/pubs/2018-cdc-drug-surveillancereport.pdf.

10. Hedegaard H, Miniño AM, Warner M: Drug Overdose Deaths in the United States, 1999-2019 . NCHS Data Brief. 2020, 1-8.

11. Wilson N, Kariisa M, Seth P, Smith Ht, Davis NL: Drug and Opioid-Involved Overdose Deaths – United States, 2017-2018. MMWR Morb Mortal Wkly Rep. 2020, 69:290-297. 10.15585/mmwr.mm6911a4

12. Sutherland TN, Wunsch H, Pinto R, et al.: Association of the 2016 US Centers for Disease Control and Prevention Opioid Prescribing Guideline With Changes in Opioid Dispensing After Surgery. JAMA Netw Open. 2021, 4:2111826. 10.1001/jamanetworkopen.2021.11826

13. Yang BK, Storr CL, Trinkoff AM, Sohn M, Idzik SK, McKinnon M: National opioid prescribing trends in emergency departments by provider type: 2005-2015. Am J Emerg Med. 2019, 37:1439-1445. 10.1016/j.ajem.2018.10.041.

14. Cantrill SV, Brown MD, Carlisle RJ, et al. Clinical policy: critical issues in the prescribing of opioids for adult patients in the emergency department. Annals of emergency medicine. 2012;60(4):499-525.

15. Motov Sea. AAEM White Paper on Acute Pain Management in the Emergency Department. https://www.aaem.org/resources/statements/position/white-paper-on-acute-pain-management-in-the-emergency-department.

16. LaPietra A MS, Rosenberg M. . Alternatives to Opioids for Acute Pain Management in the Emergency Department: Part I. Emergency Medicine Reports. https://wwwahcmediacom/articles/138799-alternatives-to-opioids-for-acute-pain-management-in-the-emergency-department-part-i. 2016.

17. Storrow AB, Zhou C, Gaddis G, et al. Decreasing lab turnaround time improves emergency department throughput and decreases emergency medical services diversion: a simulation model. Acad Emerg Med. 2008;15(11):1130-1135. doi:10.1111/j.1553-2712.2008.00181.x

18. Quality CfBHSa. Results from the 2014 national survey on drug use and health: Detailed tables. 2015. Available at: https://www.samhsa.gov/data/sites/default/files/NSDUHDetTabs2014/ NSDUH-DetTabs2014.pdf (Accessed: 30 August 2021).

19. Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and Opioid-Involved Overdose Deaths - United States, 2013-2017. MMWR. Morbidity and mortality weekly report. 2018; 67: 1419–1427.

20. Daniel Blaney-Koen J. Issue brief: Reports of increases in opioid- and other drug-related overdose and other concerns during COVID pandemic: American Medical Association, 2022.

21. Rosenbaum J, Lucas N, Zandrow G, et al. Impact of a shelter-in-place order during the COVID-19 pandemic on the incidence of opioid overdoses. Am J Emerg Med 2021;41:51-54 doi: 10.1016/j.ajem.2020.12.047 [published Online First: 20201230].

22. Kelley MA, Lucas J, Stewart E, Goldman D, Doctor JN. Opioid-related deaths before and after COVID-19 stay-at-home orders in Los Angeles County. Drug Alcohol Depend 2021;228:109028 doi: 10.1016/j.drugalcdep.2021.109028 [published Online First: 20210902].

23. Simha S, Ahmed Y, Brummett CM, Waljee JF, Englesbe MJ, Bicket MC. Impact of the COVID-19 pandemic on opioid overdose and other adverse events in the USA and Canada: a systematic review. Reg Anesth Pain Med 2023;48(1):37-43 doi: 10.1136/rapm-2022-103591 [published Online First: 20221006].

24. Haley DF, Saitz R. The Opioid Epidemic during the COVID-19 Pandemic. Journal of the American Medical Association. 2020; 324: 1615–1617.

25. Wainwright JJ, Mikre M, Whitley P, Dawson E, Huskey A, Lukowiak A, et al. Analysis of Drug Test Results before and after the us Declaration of a National Emergency Concerning the COVID-19 Outbreak. Journal of the American Medical Association. 2020; 324: 1674–1677.

26. Association AM. Issue brief: Reports of increases in opioidand other drug-related overdose and other concerns during covid pandemic. 2020. Available at: http://www.asapnys.org/wpcontent/uploads/2020/07/Issue-brief_-Reports-ofincreases- in-opioid-related-overdose-and-otherconcerns-during-COVID-pandemic.pdf (Accessed: 30 August 2021).

27. Shanthanna H, Nelson AM, Kissoon N, Narouze S. The COVID-19 pandemic and its consequences for chronic pain: a narrative review. Anaesthesia 2022;77(9):1039-50 doi: 10.1111/anae.15801 [published Online First: 20220718].

28. El-Tallawy SN, Nalamasu R, Pergolizzi JV, Gharibo C. Pain Management during the COVID-19 Pandemic. Pain and Therapy. 2020; 9: 453–466.

29. Duncan RW, Smith KL, Maguire M, Stader DE, 3rd: Alternatives to opioids for pain management in the emergency department decreases opioid usage and maintains patient satisfaction. Am J Emerg Med. 2019, 37:38-44. 10.1016/j.ajem.2018.04.043

30. Stader D, Wald H, Rossi MacKay D, Mannerings A, Valuck R, Kuljis D, Brady MF: Alternatives to opioid protocols in Colorado emergency departments reduce opioid use without changing reported pain. J Am Coll Emerg Physicians Open. 2020, 1:1493-1499. 10.1002/emp2.12263

31. Sharp AL, Shen E, Wu YL, Wong A, Menchine M, Kanter MH, Gould MK: Satisfaction with care after reducing opioids for chronic pain. Am J Manag Care. 2018, 24:196-199.

32. Hallway A. Vu J, Lee J, Palazzolo W, Waljee J, Brummett C, Englesbe M, Howard R: Patient Satisfaction and Pain Control Using an Opioid-Sparing Postoperative Pathway. J Am Coll Surg. 2019, 229:316-322. 10.1016/j.jamcollsurg.2019.04.020

33. Preuss CV, Kalava A, King KC: Prescription of Controlled Substances: Benefits and Risks. StatPearls. StatPearls Publishing, 2022.

34. Pines JM, Hollander JE: Emergency department crowding is associated with poor care for patients with severe pain. Ann Emerg Med. 2008, 51:1-5. 10.1016/j.annemergmed.2007.07.008

35. Gardner RL, Sarkar U, Maselli JH, Gonzales R: Factors associated with longer ED lengths of stay . Am J Emerg Med. 2007, 25:643-650. 10.1016/j.ajem.2006.11.037

36. El Sayed MJ, El-Eid GR, Saliba M, Jabbour R, Hitti EA: Improving Emergency Department Door to Doctor Time and Process Reliability: A Successful Implementation of Lean Methodology. Medicine (Baltimore.2015, 94:1679. 10.1097/md.0000000000001679)

37. Mixon M, Dietrich S, Floren M, Rogoszewski R, Kane L, Nudell N, Spears L: Time to antibiotic administration: Sepsis alerts called in emergency department versus in the field via emergency medical services. Am J Emerg Med. 2021, 44:291-295. 10.1016/j.ajem.2020.04.008

38. Jaffe TA, Goldstein JN, Yun BJ, Etherton M, Leslie-Mazwi T, Schwamm LH, Zachrison KS: Impact of Emergency Department Crowding on Delays in Acute Stroke Care. West J Emerg Med. 2020, 21:892-899.10.5811/westjem.2020.5.45873

39. Pryce A, Unwin M, Kinsman L, McCann D: Delayed flow is a risk to patient safety: A mixed method analysis of emergency department patient flow. Int Emerg Nurs. 2021, 54:100956. 10.1016/j.ienj.2020.100956

40. van der Linden MCC, van Ufford H, van der Linden NN: The impact of a multimodal intervention on emergency department crowding and patient flow. Int J Emerg Med. 2019, 12:21. 10.1186/s12245-019-0238-7

41. Anderson SW, Bhattacharjee S, Patanwala AE: Effect of opioid analgesics on emergency department length of stay among low back pain patients in the United States. Am J Emerg Med. 2020, 38:1802-1806.10.1016/j.ajem.2020.06.002

42. Hitti E, Hadid D, Tamim H, Al Hariri M, El Sayed M: Left without being seen in a hybrid point of service collection model emergency department. Am J Emerg Med. 2020, 38:497-502.10.1016/j.ajem.2019.05.034

43. Nguyen BN, Barta RJ, Stewart CE, Wheelwright M, Heinrich CA: Ketorolac for Patients Undergoing Implant-Based Breast Reconstruction: Impact on Hospital Length of Stay and Postoperative Narcotic Use. Aesthet Surg J. 2020, 40:174-179. 10.1093/asj/sjz179

44. Gorski JK, Arnold TS, Usiak H, Showalter CD: Crowding is the strongest predictor of left without being seen risk in a pediatric emergency department. Am J Emerg Med. 2021, 48:73-78.10.1016/j.ajem.2021.04.005

45. Rathlev NK, Visintainer P, Schmidt J, Hettler J, Albert V, Li H: Patient Characteristics and Clinical Process Predictors of Patients Leaving Without Being Seen from the Emergency Department. West J Emerg Med. 2020, 21:1218-1226. 10.5811/westjem.2020.6.47084

46. Murray M, Stone A, Pearson V, Treisman G: Clinical solutions to chronic pain and the opiate epidemic. Prev Med. 2019, 118:171-175. 10.1016/j.ypmed.2018.10.004

47. Sinatra R. Causes and Consequences of Inadequate Management of Acute Pain. Pain Medicine 2010;11(12):1859-71 doi: 10.1111/j.1526-4637.2010.00983.x.

48. Abdolrazaghnejad A, Banaie M, Tavakoli N, Safdari M, Rajabpour-Sanati A. Pain Management in the Emergency Department: a Review Article on Options and Methods. Adv J Emerg Med 2018;2(4):e45 doi: 10.22114/AJEM.v0i0.93 [published Online First: 20180624].

49. Ochalek TA, Cumpston KL, Wills BK, Gal TS, Moeller FG. Nonfatal Opioid Overdoses at an Urban Emergency Department during the COVID-19 Pandemic. Journal of the American Medical Association. 2020; 324: 1673–1674.

50. Mukherjee TI, El-Bassel N. The perfect storm: COVID-19, mass incarceration and the opioid epidemic. International Journal of Drug Policy. 2020; 83: 102819.

51. O'Donnell J, Gladden RM, Mattson CL, Hunter CT, Davis NL. Vital Signs: Characteristics of Drug Overdose Deaths Involving Opioids and Stimulants - 24 States and the District of Columbia, January-June 2019. MMWR. Morbidity and mortality weekly report. 2020; 69: 1189–1197.

52. Cohen V, Motov S, Rockoff B, Smith A, Fromm C, Bosoy D, et al. Development of an opioid reduction protocol in an emergency department. American Journal of Health-System Pharmacy. 2015; 72: 2080–2086.

53. Yasri S, Wiwanitkit V. Pain Management during the COVID-19 Pandemic. Pain Medicine. 2020; 21: 2008.

54. Song X, Xiong D, Wang Z, Yang D, Zhou L, Li R. Pain Management during the COVID-19 Pandemic in China: Lessons Learned. Pain Medicine. 2020; 21: 1319–1323.

55. Jenkins WD, Bolinski R, Bresett J, Van Ham B, Fletcher S, Walters S, et al. COVID-19 during the Opioid Epidemic – Exacerbation of Stigma and Vulnerabilities. The Journal of Rural Health. 2021; 37: 172–174.

56. Grunvald W, Herrington R, King R, Lamberson M, Mackey S, Maruti S, et al. COVID-19: A new barrier to treatment for opioid use disorder in the emergency department. Journal of the American College of Emergency Physicians Open. 2021; 2: e12403.

57. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? The Lancet Respiratory Medicine. 2020; 8: e21.

58. Weinbroum AA. Perspectives of Ketamine Use in COVID-19 Patients. Journal of Korean Medical Science. 2021; 36: e28.

59. Barrett W, Buxhoeveden M, Dhillon S. Ketamine: a versatile tool for anesthesia and analgesia. Current Opinion in Anaesthesiology. 2020; 33: 633–638.

60. Akinosoglou K, Gogos A, Papageorgiou C, Angelopoulos E, Gogos C. Ketamine in COVID-19 patients: Thinking out of the box. Journal of Medical Virology. 2021; 93: 4069–4070.

61. Khatri UG, Perrone J. Opioid Use Disorder and COVID-19: Crashing of the Crises. Journal of Addiction Medicine. 2020; 14: e6–e7.

62. Coyle DT, Pratt C, Ocran-Appiah J, Secora A, Kornegay C, Staffa J. Opioid analgesic dose and the risk of misuse, overdose, and death: a narrative review. Pharmacoepidemiology and Drug Safety. 2018; 27: 464–472.

63. Han B, Compton WM, Blanco C, Crane E, Lee J, Jones CM. Prescription Opioid Use, Misuse, and Use Disorders in U.S. Adults: 2015 National Survey on Drug Use and Health. Annals of Internal Medicine. 2017; 167: 293–301.

64. Mojtabai R, Amin-Esmaeili M, Nejat E, Olfson M. Misuse of prescribed opioids in the United States. Pharmacoepidemiology and Drug Safety. 2019; 28: 345–353.

65. Jordan AE, Blackburn NA, Des Jarlais DC, Hagan H. Past-year prevalence of prescription opioid misuse among those 11 to 30 years of age in the United States: a systematic review and meta-analysis. Journal of Substance Abuse Treatment. 2017; 77: 31–37.

APPENDIX 1

ALTO Treatment Protocols

MSK/BACK Pain

Note: This includes sprains, strains, or opioid-naïve lower back pain, acute neck, joint and soft tissue pain; rotator cuff tendonitis, arthritis of knee, lateral epicondylitis, greater trochanteric bursitis, biceps tendonitis, etc. Acute on chronic radicular lower back pain (opioid tolerant) can be approached in a similar manner.

- Acetaminophen 1,000 mg PO OR 650 mg PR if unable to tolerate PO
- NSAIDs: Ibuprofen 600 mg PO OR Ketorolac 10 mg IV/15 mg IM
- Muscle relaxant: Cyclobenzaprine 5 mg PO OR Diazepam 5 mg PO OR Tizanidine 2mg PO OR Methocarbamol 500 mg PO
- Trigger-point injection with 1-2 mL of lidocaine 1%
- Gabapentin 300mg PO (if neuropathic pain)
- Lidocaine 5% patch to most painful area; instruct patient to remove after 12 hours
- Dexamethasone 4-10 mg IV
- Ketamine 0.2 mg/kg IVPB over 10 min based on IBW
- Ketamine 0.5 mg/kg intranasal x 1 dose (max = 50 mg)

ALTO – Neuropathic Pain

FIRST LINE TX:

- Acetaminophen 1000 mg PLUS Celebrex 200 mg po x 1 dose OR Ibuprofen 400 mg po x 1 dose

IF UNABLE TO TOLERATE PO THERAPY:

- Acetaminophen 650 mg per rectum x 1 PLUS Ketorolac 10mg IV x 1

ALTERNATIVES:

- Gabapentin 300 mg po x 1 dose
- Topical lidocaine 5% patch transdermal to affected area
- Naproxen 500 mg po x 1 dose

FOR REFRACTORY PAIN:

- Ketamine 0.2 mg/kg IVPB over 10 min based on IBW (max = 30 mg)

OR

- Ketamine 0.5 mg/kg intranasal x 1 dose (max 50 mg)
- Lidocaine 1.5 mg/kg IV IVPB diluted in 50 mL D5W x 1 over 30 minutes (max dose = 200 mg)

ALTO - Renal Colic Protocols

FIRST-LINE THERAPY

Ketorolac 10 mg IV or PO Ibuprofen if pt can tolerate 400-800mg

Acetaminophen 1,000 mg PO vs IV Ofirmev 650 mg – 1 gram over 15 minutes if cannot tolerate PO

1 L 0.9% normal saline bolus

SECOND-LINE IV THERAPY

Lidocaine 1.5 mg/kg IV of 2% cardiac lidocaine in 100 ml normal saline over 10-15 minutes (max 200 mg)

ALTERNATIVES

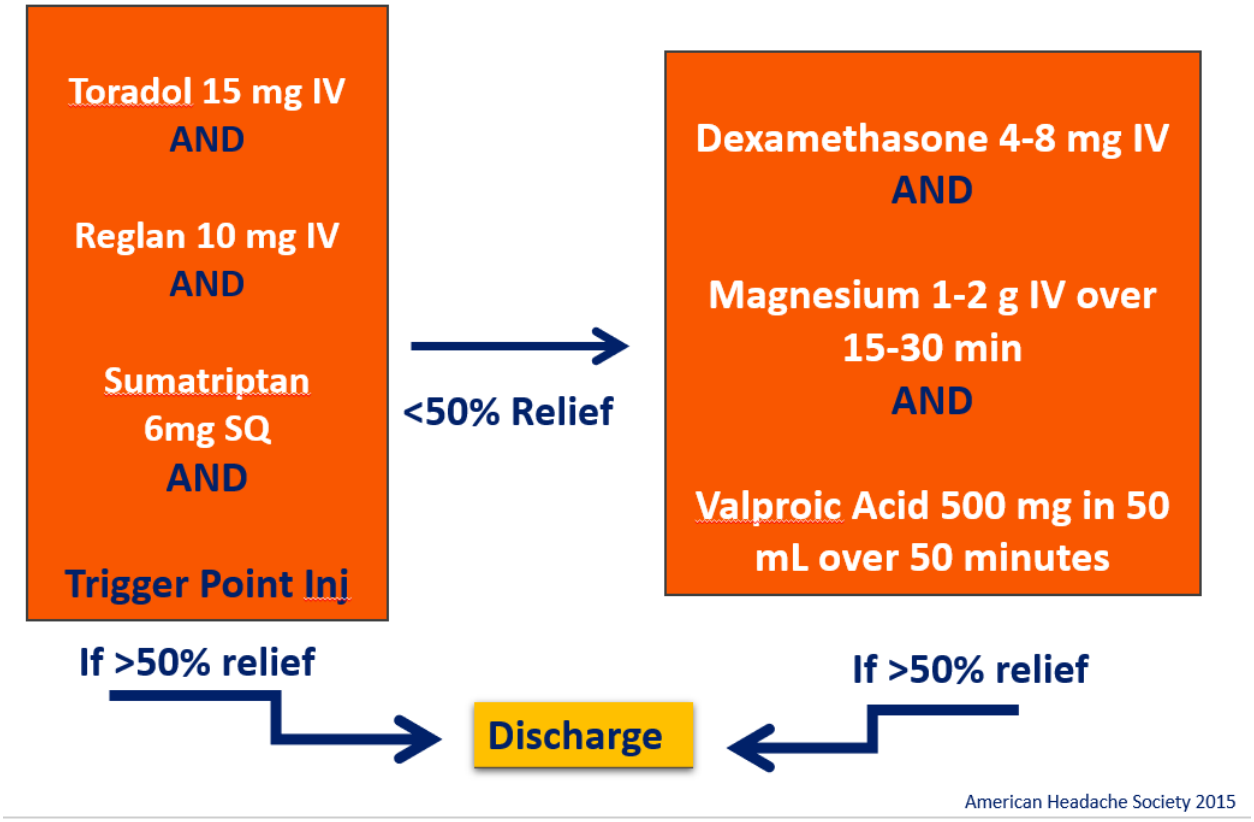
Ketamine 50 mg IN (Intra-Nasal) 0.5 mg/kg (concentration 100 mg/mL); (max 50 mg; max per nare 1 mL)

ALTO – Lidocaine CONTRAINDICATIONS

- Sensitivity or Allergy to Lidocaine
- Pregnancy
- Seizure Disorder

- Hepatic Insufficiency (Tbili > 1.46)
- Renal Insufficiency (CrCl < 30 or ESRD)
- Severe CAD or CHF/Cardiomyopathy w/ EF < 20%
- Hx of AV Block i.e. $2^{nd}/3^{rd}$ Degree AVB; Adams-Stokes; WPW; LGL; AVNRT
- Cardiac Dysrhythmias
- Concurrent treatment with Class I antiarrhythmics or amiodarone use < 3 months
- Acute porphyria
- *Provider Discretion: Cardiac monitoring during and 30 minutes post infusion especially in pts > 65 y/o, RBBB, LBBB known, 1^{st} degree AVB

ALTO - Migraine Algorithm



ALTO – NON-SPECIFIC ABD PAIN

FIRST LINE TX:

- Acetaminophen 1000 mg PLUS Celebrex 200 mg po x 1 dose OR Ibuprofen 400 mg po x 1 dose

IF UNABLE TO TOLERATE PO THERAPY:

- Acetaminophen 650 mg per rectum x 1 PLUS Ketorolac 10mg IV x 1

1ST LINE ALTERNATIVES OR IN ADDITION TO ABOVE THERAPY:

- Dicyclomine 20mg PO or 20mg IM
- GI Cocktail one dose PO
- Naproxen 500mg PO

REFRACTORY PAIN:

- Ketamine 0.2 mg/kg IVPB over 10 min based on IBW (max = 30 mg) OR

  Ketamine 0.5 mg/kg INTRANASAL x 1 dose (max 50 mg)

ALTO - GASTROPARESIS/CHRONIC ABD PAIN

- Toradol 10-15mg IV/IM
- Metoclopramide 10mg IV
- Prochlorperazine 10 mg IV
- Diphenhydramine 25 mg IV
- Dicyclomine 20 mg PO/IM – if cramping component
- Haloperidol 2.5-5 mg IM/IV
- Lidocaine 1.5 mg/kg IVPB over 15 minutes (obtain from pharmacy)
- Ketamine 0.2 mg/kg IVPB over 10 min based on IBW

ALTO – Sickle Cell Crisis Protocol

- PO Ibuprofen-800mg OR IM (Intramuscular) Ketorolac 30mg OR IV Ketorolac 10mg
- IN INTRANASAL Ketamine 0.5 mg/kg (no more than 1ml per nostril, max 50mg) IF difficult IV Access
- IV Ketamine-0.2 mg/kg IVPB over 10 min based on IBW, then reassess, if still pain then + IV drip at 0.1 mg/kg /hr IBW infusion continuous until pain improved
- IV Lidocaine - 1.5 mg/kg IVPB over 15 minutes (obtain from pharmacy)

ALTO – Dental Pain

- Dental Blocks
- Ibuprofen 400mg – 800mg PO
- Acetaminophen 500mg – 1000mg PO
- Dental Referrals/Care Connect

ALTO – Discharge/Outpatient Rx

Neuropathic Pain/Zoster/Peripheral or DM Neuropathy

- Gabapentin 300 mg PO at bedtime
- Amitriptyline 25 mg PO at bedtime
- Pregabalin 75 mg PO 2x/day

Undifferentiated Abdominal Pain

- Dicyclomine 20 mg PO every 6 hour
- Ibuprofen 600 mg PO every 6 hours
- Acetaminophen 1,000 mg PO every 6 hours
- Metoclopramide 10 mg PO every 6 hours
- Prochlorperazine 10 mg PO every 6 hours

Uncomplicated Back Pain

- Acetaminophen 1,000 mg PO every 6 hours

• Ibuprofen 600 mg PO every 6 hours

• Lidocaine 5% transdermal patch every 24 hours (remove after 12 hours)

• Diclofenac 1.3% transdermal patch 2x/day **OR** diclofenac 1% gel 4 g 4x/day as needed

• Cyclobenzaprine 5 mg PO 3x/day or other muscle relaxant: Soma, Robaxin, Tizanidine

• Heat

• Physical therapy

• Exercise program

Fibromyalgia

• Cardiovascular exercise • Strength training • Massage therapy

• Amitriptyline 10 mg PO at bedtime

• Cyclobenzaprine 10 mg PO every 8 hours

• Pregabalin 75 mg PO 2x/day

Headache

FOR ACUTE ATTACKS

- Sumatriptan 100 mg PO
- Acetaminophen/aspirin/caffeine (Excedrin Migraine) PO every 6 hours OR acetaminophen 1,000 mg every 6 hours
- Dihydroergotamine mesylate 2 mg nasal spray
- Naproxen 500-550 mg 2x/day OR ibuprofen 600 mg PO every 6 hours
- Metoclopramide 10 mg PO every 6 hours

FOR PREVENTION

- Propranolol 40 mg PO 2x/day
- Divalproex DR 250 mg PO 2x/day OR extended release 500 mg PO daily
- Topiramate 25 mg PO at bedtime
- Magnesium supplementation 600 mg PO daily

Special Populations

Not all patients are appropriate candidates for each agent suggested in the ALTO treatment protocol. All medications should be administered with thoughtful consideration of patient-specific factors such as age, organ function, comorbidities and other medications being taken.

Geriatric Patients

Great care should be taken when treating elderly patients. Some of the therapies suggested may be inappropriate for use in this vulnerable population, including dicyclomine, haloperidol, diphenhydramine and muscle relaxants. The Beers Criteria list is a well-established resource that should be consulted when making treatment decisions for patients older than 65 years. When possible, consider prescribing topical agents instead of oral or intravenous drugs. Also consider recommending heat, massage and physical therapy on discharge for musculoskeletal pain.

Renal Dysfunction

Not all ALTO agents are safe for patients with renal dysfunction, particularly NSAIDs. In patients who cannot receive systemic NSAIDs, consider prescribing topical agents such as diclofenac gel or patches.

Heart Failure

Not all ALTO agents are recommended for use in patients with heart failure, particularly steroids and NSAIDs. For patients in whom these medications should be avoided, consider prescribing topical alternatives

Pregnant Patients

Pregnant women should be excluded from the ALTO protocol. Many of these agents are contraindicated in pregnancy, including haloperidol, NSAIDs, and valproic acid.

Pediatric Patients

Do not use the ALTO protocol when managing children younger than 15 years or less than 40 kg. Although ALTO principles are applicable to the pediatric population, precautions should be considered and agents must be dosed appropriately.

Exclusions to ALTO

- Rescue Opiate Analgesia:
    - Oxycodone 5 mg po x 1 dose
    - Morphine IR 15 mg po x 1 dose
    - Fentanyl IV x 1 dose

    - Morphine IV x 1 dose

- Provider discretion on when to utilize opiate medications
- Intractable pain from:
    - Advanced stage cancer
    - Trauma/Fractures
    - Diagnosed surgical pathology: i.e. appendicitis, cholecystitis, bowel obstruction, ischemic bowel, etc.