

## Opioid-sensitized patients and acute pain in the ED: A Systematic Review

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## Introduction

Emergency Departments (ED) commonly service patients presenting with acute pain of diverse etiologies. EDs also regularly see patients who are known opioid users and perceived as exhibiting drug-seeking behaviors. Therein exists a challenging tension between adequate pain management and opioid stewardship.<sup>13</sup> Evidence-based guidelines are needed to standardize pain treatment protocols when servicing this complex patient demographic

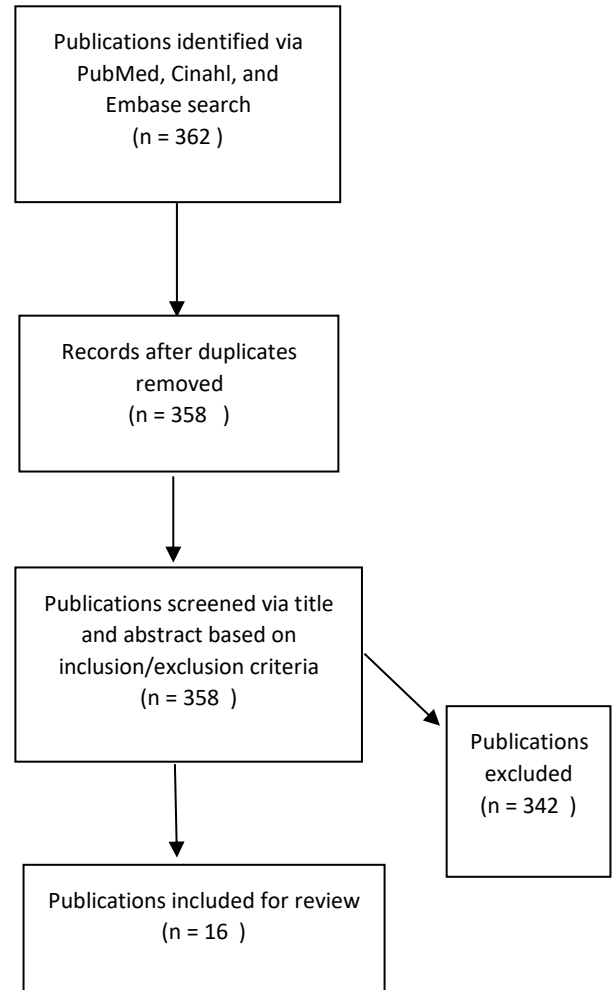
## Objectives

This systematic review endeavored to identify existing clinical guidelines used in Emergency Departments for treating acute pain in opioid-sensitized patients. In the absence of such guidelines, various clinical insights and recommendations deemed relevant will be considered for analysis. We also aim to destigmatize opioid use by identifying standardized acute pain management algorithms that are inclusive of opioid-sensitized patients.

Our intent is not to address opioid overdose management in the context of emergency medicine, nor is it to examine chronic opioid use or opioid prescription guidelines. Our scope does not include social determinants of ED use by opioid users nor strategies to reduce the volume of opioid users in the ED, although we recognize that these are extremely important considerations that must be addressed at a public health and policy level.

## Methods

In June 2018, PubMed, Cinahl, and Embase were queried for three concepts: acute pain, opioid-using patients, and emergency department services. We built our search in PubMed, using a combination of MeSH terms and keywords, then translating this into search syntax appropriate for both Cinahl and Embase (see tables 1 – 3). This retrieved 326 articles, 6 of which were duplicates. After screening titles and abstracts for inclusion and exclusion criteria, 16 publications were identified: 7 RCTs and cohort clinical studies, 3 systematic reviews, 2 US government white paper reports, 2 conference abstracts, 1 clinical case study, and 1 qualitative study (see table 4).



Inclusion criteria included treatment of acute pain or acute exacerbations of chronic pain, alternatives to opioids in pain management in the ED, and patient perspectives on acute pain management and opioid analgesia in the ED. Articles, literature reviews, RCTs, cohort studies, case studies, and conference abstracts were all eligible for inclusion. Exclusion criteria included chronic pain management, opioid prescribing guidelines, initiation of chronic opioid dependence from short-term opioid prescriptions for acute pain, and pediatric pain management (see table 5).

Search concept	MeSH terms / Keywords
Acute Pain	"Acute Pain"[Mesh] OR (acute[tiab] AND pain*[tiab])
Opioid-using patients	"Substance-Related Disorders"[Mesh] OR ((drug*[tiab] OR opioid*[tiab] OR narcotic*[tiab]) AND (use*[tiab] OR abus*[tiab] OR misuse[tiab] OR dependen*[tiab])) OR addict*[tiab]
Emergency Department	"Emergency Service, Hospital"[Mesh] OR "Emergency Medicine"[Mesh]) OR emergency[tiab]

Table 1: PubMed search query

(((MH "Emergency Service") OR (MH "Emergency Medicine")) OR TI emergency OR AB emergency) AND ((MH "Substance Use Disorders+") OR (MH "Substance dependence") OR TI ((drug* OR substance OR opioid* OR narcotic*) N1 (use* OR abus* OR misuse OR dependen*)) OR AB((drug* OR substance OR opioid* OR narcotic*) N1 (use* OR abus* OR misuse OR dependen*)) OR TI addict* OR AB addict*) AND (TI acute N2 pain OR AB acute N2 pain)
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Table 2: Cinahl search query

'acute pain':ti,ab,kw AND ('substance use':ti,ab,kw,jt OR 'drug dependence':ti,ab,kw,jt) AND ('emergency medicine':ti,ab,kw,au OR 'emergency ward':ti,ab,kw,au OR 'emergency health service':ti,ab,kw,au OR 'emergency treatment':ti,ab,kw,au OR 'emergency':ti,ab,kw,au)
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Table 3: Embase search query

Inclusion criteria	Exclusion Criteria
Treatment of acute pain and acute exacerbations of chronic pain in the ED	Chronic pain management, including opioid prescription guidelines
Alternatives to opioids in pain management in the ED	Initiation of chronic opioid dependence from ED services
Patient perspectives on acute pain management in the ED	Pediatric Pain management
Published within the last 5 years	

Table 5: Inclusion and Exclusion Criteria

## Results

No singular practice guideline existed in the literature for treating pain that is inclusive of this complex patient demographic. In lieu of this, themes present in the literature were noted and cross-referenced with each other, such that a mosaic of recommendations was extrapolated from the literature.

The following themes have been highlighted for analysis as they offer partial solutions in the context of our clinical question: *questioning opioid efficacy, non-opioid pain management, providing patient-centered care, and appropriate clinician training.*

### **Questioning opioid efficacy**

Several authors indicate a paucity of high quality, double-blind RCT's providing supporting evidence for opioid efficacy.<sup>1,4,15</sup> The literature also highlights a clinical bias towards using opioids for pain management.<sup>1,3,4,10,15</sup> Berthelot et al examine the legitimacy of the belief that opioids provide the best therapeutic benefits for patients; they frame this bias around morphine's placement at the top analgesic step of the WHO ladder of pain management:

“The scarcity of high-quality studies (randomized, double-blinded, and controlled versus placebo or another analgesic such as acetaminophen) on the efficacy of step III analgesics is stunning, given the long history of widespread use and abuse of these drugs.”<sup>1</sup>

Several other sources likewise highlight that there is a clinician dependency on opioids in acute pain management.<sup>1,3,4,10,15</sup> Two publications discuss the pro-opioid push from pharmaceutical companies in the late 1990s, in which pain emerged as a “fifth vital sign” and aggressive opioid therapy was championed as the solution for pain management.<sup>10,15</sup> The literature asks us to think critically about opioid efficacy. As we shall see below, the literature also offers a growing body of evidence that supports non-opioid analgesia in acute pain management.

### **Non-opioid pain management**

Multiple publications indicated specific clinical contexts in which non-opioid parenteral analgesic agents were at least as effective as opioids for acute pain.<sup>1,3,4,9-12,15</sup> A variety of sources

likewise acknowledge that opioids are not effective monotherapy for pain control and that a multimodal approach to pain management with non-opioid agents is generally preferred. <sup>1,3-5,9,10,12,15</sup>

Acetaminophen was found in some clinical contexts to be as effective as opioid analgesia in cases such as sciatica, low back pain, acute limb pain, and renal colic.<sup>1</sup> Parenteral ketamine administered in low, sub-dissociative doses (low dose ketamine, or LDK) was supported in the evidence as an alternative to opioids for acute pain management in the ED setting. <sup>9, 10,11</sup> That said, clinicians may be less comfortable administering LDK than opioids, and it requires greater nursing resources and monitoring, which are potential barriers to its widespread uptake.<sup>11</sup> Parenteral Lidocaine has also been identified in the literature as a possible analgesic agent in the ED, and it has a growing body evidence citing efficacy in managing pain secondary to cancer, stroke, neuropathies, and nephrolithiasis, and MSK pain.<sup>12</sup> Acupuncture also is a possibility. Both the FDA and the National Academies of Sciences, Engineering, and Medicine (NASEM) have recommended acupuncture as a first line non-pharmacologic therapy in managing pain within the current opioid crisis.<sup>4</sup>

The trial “Opioid-Free Shift” in an ED in Brooklyn, New York in 2014, saw 12 patients stratified to receive either oral or parenteral non-opioid analgesics (predominantly NSAIDs) based on their subject pain rating; only 1 patient (with renal colic) required rescue therapy with morphine.<sup>3</sup> Patient satisfaction with pain management was 83% at 30 minutes and 86.7% at 60 minutes.<sup>3</sup>

This evidence collectively suggests that a wide variety of pain treatment options are available for use in the ED (see Table 6), and it could be possible to develop evidence-informed algorithms recommending analgesic agents for specific etiologies of acute pain: “Management of acute pain in the ED should be patient-centered and pain-syndrome targeted, and should utilize combinations of nonpharmacological and pharmacological analgesic modalities.”<sup>10</sup>

Limitations exist. Just one publication discusses cost-effectiveness of different treatment options.<sup>4</sup> None of the publications come from Canada. Importantly, only two of these publications discussed the efficacy or usefulness of their non-opioid suggestions in opioid-sensitized patients, for example, patients enrolled in a methadone program.<sup>4,11</sup>

Modality	Reference	Year, country	Efficacy as Opioid Adjunct	Efficacy as Monotherapy	Noted side effects, adverse events	Cost-effectiveness
Acetaminophen	Berthelot	2015, France	Yes	Yes	Yes	No
Low-dose Ketamine	Motov	2018, USA	Yes	Yes	Yes	No
	Pourmand	2017, USA	Yes	Yes	Yes	No
	Motov	206, USA	Yes	Yes	Yes	No
IV lidocaine	Sin	2018, USA	Yes	Yes	Yes	No
	Fitzpatrick	2016, USA	Yes	Yes	Yes	No
	Cohen	2015, USA	No	Yes	No	No
Acupuncture	Fan	2017, USA	Yes	Yes	Yes	Yes

Table 6: Summary of publications advocating for non-opioid analgesia

### Providing patient-centered care

The need for judicious pain relief for patients experiencing acute pain in the ED permeated the literature.<sup>3,9,10,12-16</sup> This advocacy for compassionate care is not made in naïveté: rather, it rises from the context of opioid stewardship. Cohen et al describe this as the tension between beneficence, or rapidly resolving pain, and maleficence, or using opioids and increasing the risk of opioid dependence or adverse events.<sup>3</sup> From Sohi et al:

“Effective pain control is desirable on humanitarian grounds, as well as for its potential to improve patients’ recovery, rehabilitation, and outcome. Acute pain can also increase heart rate and blood pressure, suppress immune function and reduce pulmonary function, leading to an increased risk of dangerous complications.”<sup>14</sup>

Sin et al state that “acute pain is one of the most adverse stimuli a patient could experience,” and note that “it has been well documented that acute pain is often inappropriately treated and assessed.”<sup>12</sup> Motov et al recommend in their white paper on treatment of acute pain in the ED that

“EM clinicians and associates who work in an ED should acknowledge and assess a patient’s pain in an empathetic manner by expressing an understanding of the patient’s suffering and a willingness to alleviate pain using a multimodal analgesic approach.”<sup>10</sup>

Two sources (of note: from Iran and France, not North America) recommend aggressive treatment of acute pain with opioids in opioid-sensitized patients.<sup>2,14</sup> Consideration of possible opioid withdrawal while patient’s are receiving ED services was discussed by two publications.<sup>14,15</sup> These publications serve largely to illuminate the challenge of providing compassionate care to opioid-sensitized patients, without imparting useful or practical clinical guidelines for clinicians to refer to while providing care to this patient population.

Important also is the manner in which the physician involves the patient in their own treatment. Multiple sources identify the need to provide patient counselling, including shared decision making and discussing risk of opioid dependence.<sup>6,10,13,14,15</sup> Smith et al published a qualitative study on patient perspectives regarding pain management received in an American ED.<sup>13</sup> They completed 23 patient interviews, and conclude that “patients identified a deficit of communication around opioid risk and pain management options in the ED,” and that “many ED patients desire to be more involved in conversations relating to their pain management options, and they want to know more about the risks associated with opioids.”<sup>13</sup> Adjunctive to this, several sources identify the ED physician’s clinical responsibility to recognize patient risk factors for current or potential opioid dependence.<sup>3,10,13,15</sup>

This patient-centered evidence is valuable and should be heeded and considered in future guidelines to be developed for acute pain management in the ED setting. While harder to quantify into an algorithm than analgesic pathways, and more challenging to teach to physicians, it is equally important in adequate acute pain management for complex patient populations in the ED setting.



## **Clinician Education**

The need for proper clinician training and education is a salient point raised by several authors, especially since many contemporary mid-career clinicians “were trained to liberally prescribe opioids for a variety of acute pain syndromes.”<sup>3,6,13,15</sup> The development of a sustainable curriculum on substance use disorders for emergency medicine residents at Cooper University Hospital in the United States provides an educational model for early education of clinicians.<sup>6</sup> Developed with guidance by two medical toxicologists with addiction medicine training alongside frontline social workers, this curriculum consists of formal didactic lectures, weekly EM residence conferences, and clinical exposures in multiple settings beyond the ED, including inpatient detoxification care and outreach clinics.<sup>6</sup> This may be the way of the future.

## **Conclusion**

No single, comprehensive clinical algorithm or best practice guidelines exists for managing acute pain in patient populations for whom pain management is challenged by their concurrent opioid use, either in Canada or internationally. A mosaic of collective recommendations were extrapolated from the literature, however it is important to acknowledge that no publications were Canadian or involved Canadian studies or data in their own analysis.

There is much room for development and standardization of acute pain management in the ED setting—both generally and also with respect to the key patient population identified in our research question. Growing clinical and academic interest in seeking efficacious non-opioid analgesia for acute pain presentations in the ED will likely continue to gain momentum in our current era of global opioid public health crisis. Based on their pharmacologic and biochemical action, there seems to be most

promise in the following non-opioid analgesia modalities: low dose IV ketamine, IV lidocaine, acupuncture, as well as oral and parenteral acetaminophen and NSAIDs. Compassionate, patient-centered care is of utmost importance as clinical encounters require provision of analgesic agents. Timely clinician education must be implemented to support evidence-based, interdisciplinary, and effective care.

Reference	Year, country	Publication type	Research objective	Questioning opioid efficacy	Non-opioid pain management	Patient-centered care	Clinician education
Berthelot	2015, France	Literature Review focusing on RCTs & meta-analyses	To determine if the designation of “strong” opioids by the WHO analgesic ladder is misinforming clinical practice	Yes	Yes	No	No* but gaps in clinician knowledge noted
Bounes	2013, France	Prospective, multicenter observational cohort study	To assess impact of acute pain exposure on long-term opioid maintenance therapy retention in a cohort of patients under methadone or buprenorphine followed up during 12 mos	No	No	Yes	No
Cohen	2015, USA	Case report	Results of a study of an opioid-sparing protocol for acute pain management in the ED of Maimonides Medical Center in NYC in Sept 2014.	Yes	Yes	Yes	No
Fan	2017, USA	White paper	Assessing acupuncture as a non-pharmacologic agent in solving the opioid epidemic	Yes	Yes	Yes	Yes
Fitzpatrick	2016, USA	Case series	To evaluate IV lidocaine’s safety and efficacy as an analgesic agent isn’t he treatment of a variety of painful conditions presenting to the ED	No	Yes	No	No

Gruber	2017, USA	Conference abstract	Reporting the development of a sustainable curriculum on substance use disorders for EM residents at Cooper University Hospital	No	No	Yes	Yes
Logan	2017, USA	Descriptive, retrospective cohort study	To determine the prevalence of indicators of potential ED opioid misuse and inappropriate prescription practices by ED providers in a large, commercially insured, adult population.	No	No	Yes	No
Motov	2016, USA	Literature review of RCTs, Meta-Analysis, systematic reviews, and observational studies evaluating ketamine analgesia	To determine if there is a role for IV subdissociative-dose ketamine administered as an adjunct to opioids or as a single agent for acute pain management in the ED	No	Yes	Yes	No
Motov	2018, USA	White paper	To determine safe and judicious analgesia recommendations in the ED	No	Yes	Yes	Yes
Pourmand	2017, USA	Literature review	To determine and present evidence supporting the use of low dose ketamine for pain management in the ED	No	Yes	No	Yes
Sin	2018, USA	Case study	Describe the use of IV lidocaine for opioid-refractory acute pain secondary to traumatic ankle injury	No	Yes	No	No
Smith	2016, USA	Qualitative study	To inform the development of interventions that could improve patient engagement around the risks and benefits of alternative approaches to pain management in the ED via	No	No	Yes	No

			perspectives and experiences of patients treated for pain in this setting				
Solhi	2016, Iran	RCT	To compare effectiveness and side-effects of morphine and meripidine for acute pain management in opioid-dependent patients in the ED	No	Yes	Yes	No
Strayer	2017, USA	Lit review	To consider best treatment options for patients presenting to EDs with exacerbations of chronic pain or painful conditions associated with opioid misuse, and to provide proper phraseology in validating patient experience	No	Yes	Yes	Yes
Zosel	2017, USA	Conference abstract	To determine opioid administration in the ED to patients presenting with acutely painful conditions and chronic pain before and after implementation of an opioid prescribing guideline	No	No	Yes	No

Table 7: Literature summary and prevalence of thematic analysis

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