Managing Acute Pain in Patients Taking Medication for Opioid Use Disorder: a Rapid Review

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BACKGROUND: Managing acute pain in patients with opioid use disorder (OUD) on medication (methadone, buprenorphine, or naltrexone) can be complicated by patients' higher baseline pain sensitivity and need for higher opioid doses to achieve pain relief. This review aims to evaluate the benefits and harms of acute pain management strategies for patients taking OUD medications and whether strategies vary by OUD medication type or cause of acute pain.

METHODS: We systematically searched multiple bibliographic sources until April 2020. One reviewer used prespecified criteria to assess articles for inclusion, extract data, rate study quality, and grade our confidence in the body of evidence, all with second reviewer checking.

RESULTS: We identified 12 observational studies—3 with control groups and 9 without. Two of the studies with control groups suggest that continuing buprenorphine and methadone in OUD patients after surgery may reduce the need for additional opioids and that ineffective pain management in patients taking methadone can result in disengagement in care. A third controlled study found that patients taking OUD medications may need higher doses of additional opioids for pain control, but provided insufficient detail to apply results to clinic practice. The only case study examining naltrexone reported that postoperative pain was managed using tramadol. We have low confidence in these findings as no studies directly addressed our question by comparing pain management strategies and few provided adequate descriptions of the dosage, timing, or rationale for clinical decisions.

DISCUSSION: We lack rigorous evidence on acute pain management in patients taking medication for OUD; however, evidence supports the practice of continuing methadone or buprenorphine for most patients during acute pain episodes. Well-described, prospective studies of adjuvant pain management strategies when OUD medications are continued would add to the existing literature base. Studies on nonopioid treatments are also needed for patients taking naltrexone.

Prior presentations*: The full report this work is based on is available on the ESP website at https://www.hsrd.research.va.gov/publications/esp/reports.cfm. The full report was presented during an HSR&D Cyberseminar on August 27, 2019.*

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BACKGROUND

Managing acute pain (such as from surgery or injury) in patients taking medications for opioid use disorder (OUD) can be difficult due to patients' increased pain sensitivity and higher opioid tolerance, as well as clinicians' fear that the use of an opioid during an acute pain episode could trigger an OUD relapse.[1–3] The potential for serious adverse events when methadone and buprenorphine/naloxone (referred to as buprenorphine for brevity) are changed or combined with additional opioids adds to the complexity of acute pain management. Methadone (a full opioid agonist) can cause serious, unpredictable effects such as respiratory depression or overdose when the dose is changed or when other opioids are added.[4, 5] Buprenorphine (a partial opioid agonist) partially activates these receptors and reduces the effect of other opioids. Both medications can cause withdrawal when discontinued.[4, 6] Naltrexone (an opioid antagonist) blocks the effect of other opioids and is often administered in an extended-release injectable format which cannot be withdrawn or reversed in cases of unexpected acute pain.[7, 8]

Guidance from professional societies such as the American Society of Addiction Medicine (ASAM) and the Perioperative Pain and Addiction Interdisciplinary Network (PAIN) suggests possible approaches to managing pain in OUD patients taking medications; however, these approaches are primarily based on expert consensus due to the paucity of available research.[9, 10] For those taking methadone, the 2015 ASAM guidelines comment that higher doses of full opioid agonists in addition to methadone may be needed to manage acute pain and that short-acting opioids may be needed for those undergoing surgery, citing two observational studies.[11, 12] For those taking buprenorphine, ASAM comments that temporarily increasing buprenorphine dosing may

be effective for treating mild acute pain, that in cases of severe acute pain buprenorphine may need to be discontinued and replaced with a high-potency opioid, and that if buprenorphine is discontinued before an elective surgery, it should occur 24–36 h beforehand and be restarted when the need for full-agonist opioids has passed. The authors do not cite any specific studies supporting these statements but do cite 2 observational studies indicating that high doses of opioids in addition to buprenorphine may be needed to overcome the blocking effects of buprenorphine.[13, 14] By contrast, the 2019 guidelines from PAIN which are exclusively focused on buprenorphine comment that it is rarely appropriate to reduce the dose of buprenorphine before surgery and suggest continuing buprenorphine and adding a full-agonist opioid postoperatively if pain is not being effectively managed, then considering reducing buprenorphine dosage if pain persists. The PAIN guideline,[10] which was based on a systematic review,[15] acknowledged that there is weak evidence to support these statements. For those taking naltrexone, the ASAM guideline suggests using nonopioid pain management strategies for acute unexpected pain or discontinuing naltrexone prior to surgery. The authors do not cite any studies supporting these statements.

Given the high prevalence of opioid use worldwide (16 million people worldwide use opioids illicitly;[16] 2 million people in the USA have OUD[17]), and the number of people taking medications for OUD is increasing every year,[18] there is an urgent need to identify evidence-based strategies to manage acute pain in patients taking medications for OUD. In August 2019, the Department of Veterans Affairs Evidence Synthesis Program (VA ESP) conducted a rapid evidence review to inform a VA Health Services Research & Development conference on strategies to improve opioid safety. This manuscript summarizes evidence from that report[19] supplemented by an updated search conducted in April 2020. The primary objective of our review was to assess the available evidence on the benefits and harms of different acute pain management strategies for patients taking medications (methadone, buprenorphine, or naltrexone) for OUD, as well as whether benefits and harms vary by the type of medication or type of acute pain (emergency condition vs planned surgery). Because we identified a lack of rigorous evidence on this topic, our secondary objective was to describe the gaps in literature and provide recommendations for future research.

METHODS

The complete description of our methods can be found on the PROSPERO international prospective register of systematic reviews (http://www.crd.york.ac.uk/PROSPERO/; registration number CRD42019132924).

Search Strategy

An information specialist searched MEDLINE, PsycINFO, CINAHL, and Cochrane Central Register of Controlled Trials (CENTRAL) using terms for OUD, medication-assisted treatment, and acute pain from database inception to April 2019 and updated the search in April 2020 (see ESM Appendix A for complete search strategies). Additional citations were identified from hand-searching reference lists and consultation with content experts. We limited the search to published and indexed articles involving human subjects available in the English language.

Study Selection

Study selection was based on the eligibility criteria described below (Table 1). Titles, abstracts, and full-text articles were reviewed by 1 investigator and checked by another. All disagreements were resolved by consensus.

Quality Assessment and Data Abstraction

For observational studies with control groups, we used Cochrane's ROBINS-I tool[20] to evaluate the potential for bias from participant selection, classification of interventions, departure from intended interventions, measurement of outcomes, confounding, and missing/unreported data. Overall bias ratings range from low, unclear, to high risk of bias. For observational studies without control groups, we adapted the criteria from ROBINS-I as well as the CARE Checklist[21] and focused on the quality of reporting, rather than the potential for bias. Overall quality of reporting ratings ranged from not reported, partly reported, mostly reported, to well reported.

We abstracted data using piloted forms from all studies, including study characteristics, populations, comparators, intervention, and results. All data abstraction and internal validity/quality of reporting ratings were first completed by 1 reviewer and then checked by another. All disagreements were resolved by consensus.

Strength of Evidence and Data Synthesis

We graded the strength of the evidence based on the AHRQ Methods Guide for Comparative Effectiveness Reviews.[22]

Table 1 Eligibility Criteria

Studies were included if they met the following PICOS criteria:	
Population	Nonpregnant adults taking medication for OUD who have acute (sudden onset, time-limited) pain
Intervention	Any pain management approach, including discontinuation or dose change in medication used for OUD, substitution with another opioid, addition of another opioid, or nonopioid or nonpharmacological therapies
Comparator	Any comparator or no comparator
Outcomes	Pain severity, pain-related function, quality of life, patient satisfaction, healthcare utilization, opioid withdrawal symptoms, substance use relapse, opioid overdose, suicidal ideation and suicidal self-directed violence, and other adverse events
Timing	Any
Setting	Any, including primary care, emergency department, dental, perioperative, and palliative care settings
Study design	Any, but may prioritize to accommodate timeline using a best-evidence approach

This approach incorporates 4 key domains: risk of bias (includes study design and aggregate quality), consistency, directness, and precision of the evidence. Strength of evidence is graded for each key outcome measure and ratings range from high to insufficient, reflecting our confidence that the evidence reflects the true effect. Due to limited data and heterogeneity, we synthesized the evidence qualitatively. We focused our discussion on the studies that provided the best available evidence (i.e., observational studies with control groups), and discussed lower-tier evidence (i.e., observational studies without control groups) only when it addressed gaps in higher-tier evidence.

RESULTS

Our search identified 324 unique articles, of which 12 articles[11, 13, 14, 23–31] met our inclusion criteria (Fig. 1). All studies were retrospective (3 studies with a control group and 9 without): 4 studies examined patients with OUD taking buprenorphine,[14, 24, 28, 30] 5 examined those taking methadone,[11, 25–27, 31] 1 examined a patient taking naltrexone,[29] and 2 examined a mixed group of medications.[13, 23] Four studies examined those with emergency conditions,[14, 24–26] 7 examined those undergoing planned surgery,[13, 23, 27–31] and 1 examined a mixed group of emergency and surgical patients.[11] Study size ranged from 1 to 134 participants, and studies were conducted in hospitals/tertiary care centers, specialized pain centers, and outpatient addiction treatment clinics. Follow-up ranged from 1 day to over 2 years. Detailed data abstraction is available in ESM Appendix B and highlighted findings appear in Tables 2 and 3. Detailed quality assessment and quality of reporting ratings are available in ESM Appendix C and overall ratings appear in Tables 2 and 3.

Studies with Comparison Groups

Overall, the best available evidence comes from 3 observational studies with comparison groups (Table 2). None of these studies directly compared different pain management strategies; instead, they provide indirect evidence by comparing the same or similar pain management strategies in different populations. One study found that continuing the use of both methadone and buprenorphine in patients after surgery may reduce total doses of opioids and a second found that discontinuing methadone can lead to disengagement from care. A third study confirms that patients taking medication for OUD are opioid-tolerant and may need higher doses of opioid agonists for effective pain control; however, because the study did not report whether medications for OUD were continued or discontinued, it is hard to know in what circumstances high doses of opioids should be prescribed. Our confidence in the findings of these studies is low as studies provided only indirect evidence to address our review question, lacked detailed descriptions of pain management strategies, rarely used validated outcome measurements, and did not look at long-term harms of pain management strategies such as relapse or overdose.

The first observational study with a control group[13] compared surgical patients (orthopedic, abdominal, orofacial, thoracic, and other) taking methadone to those taking buprenorphine 1 day after surgery. The study found similar pain management strategies (high doses of morphine-equivalent opioids in the intraoperative period) and outcomes (use of patient-controlled analgesia [PCA], pain severity, and adverse events like nausea, vomiting, and sedation) in both groups. However, only half of the patients taking buprenorphine and three-quarters of patients taking methadone received their dose of OUD medication the day after surgery. Those taking buprenorphine who missed their dose used more PCA for longer than those that did not, and similar trends were found in patients taking methadone. The authors of the study did not know why some patients missed their dose.

The second observational study with a control group[23] compared patients undergoing hip or knee joint replacement surgery who were taking medication for OUD (methadone or buprenorphine/naloxone) to non-OUD patients. Patients taking medication for OUD received 8 times the dose of opioids at discharge as non-OUD patients. Both groups had similar pain, functionality, and quality of life outcomes at 6 weeks and 1 year. It was unclear whether OUD medications were continued or discontinued in these patients, as the authors of the study only reported overall doses of morphine-equivalent doses. It was also unclear whether these high opioid doses were titrated down over time.

The third study with a control group[11] compared patients with OUD taking methadone with acute pain from surgery or injury (type of surgery or injury not reported) to patients not taking methadone (presumably without OUD but the study does not specify). This study found that when similar doses of opioids were used to manage pain, patients taking methadone had similar number of pain reports but higher rates of behavioral problems and were more likely to discharge against medical advice. Due to limitations in how data on patients' pain was collected, the authors of the study could not determine why patients discharged against medical advice and the study did not report any follow-up information on these patients (for example, whether they continued OUD treatment in outpatient settings). Previous research has indicated that those with substance use disorders (SUDs) are up to 3 times as likely to discharge against medical advice as those without SUDs, with untreated withdrawal, uncontrolled pain, perception of stigma, and hospital restrictions as potential contributors.[32] It is plausible then that patients taking methadone in this study experienced uncontrolled pain or withdrawal symptoms which resulted in them discharging against medical advice; however, other factors (including perceived stigma and hospital restrictions) may have also played a role.

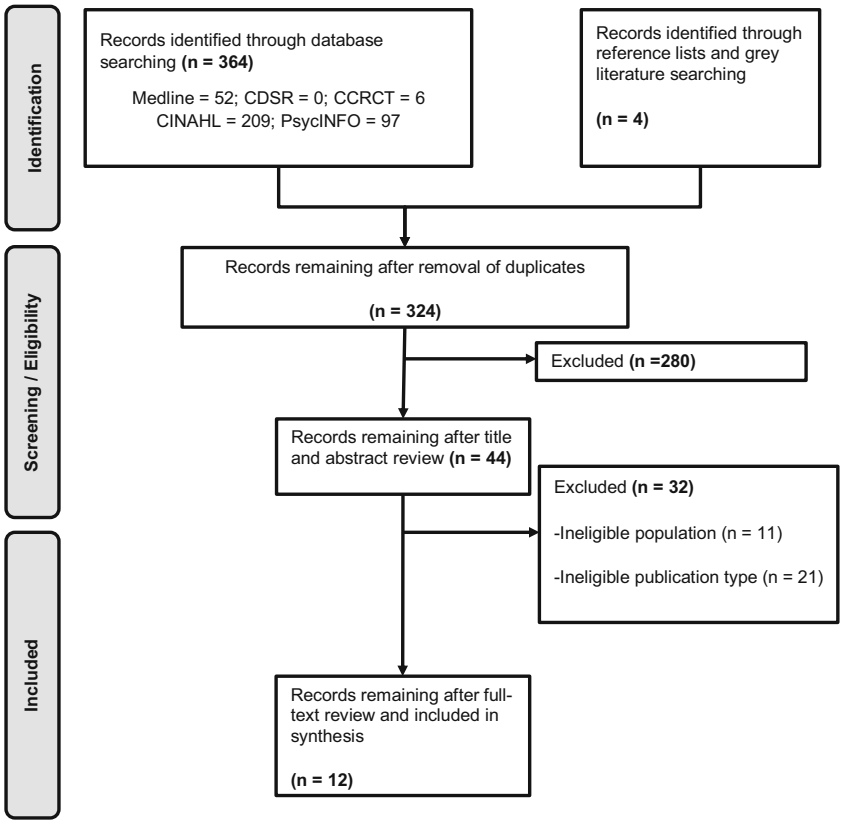

Figure 1 Literature flowchart.

Studies Without Comparison Groups

Additional evidence from 9 observational studies that lacked control groups[14, 24–31] (Table 3) address some gaps in evidence, as they looked at additional causes of acute pain (especially emergency conditions), examined naltrexone, and provided more detailed descriptions of the timing, dosage, and sequence of acute pain management strategies. The most notable finding among these studies is that tramadol adequately managed pain in a patient on extended-release naltrexone undergoing a planned surgery.[29] However, because all these studies examined small numbers of patients, rarely used measurement tools to assess outcomes, and are by design at high risk of both selection and reporting bias, they do not provide a strong foundation on which to guide clinical decision-making.

Differences by Patient and Intervention Characteristics

It was not possible to determine whether benefits and harms of acute pain management strategies vary by patient characteristics or type of acute pain due to insufficient descriptions of patient populations (especially those with emergency conditions) as well the acute pain management strategies, including adjuvant analgesics.

DISCUSSION

This rapid evidence review synthesizes the available evidence on the benefits and harms of strategies for managing acute pain in patients taking medications for OUD. Given that there are increasing numbers of patients taking medications for OUD, it is critical to identify effective ways to manage acute pain in these patients. Unfortunately, we identified limited research on this topic, with the best available evidence suggesting that continuing buprenorphine or methadone for patients undergoing major surgery may reduce overall opioid doses,[13] that discontinuing methadone can lead to disengagement from care,[11] and that high doses of opioids may be required to control pain for some (although it is unclear which) patients. Our overall confidence in the findings is low as the 3 best-conducted studies provided only indirect evidence comparing the same or similar pain management strategy in different populations and had substantial methodological limitations, most notably failing to report if OUD medications were continued in one study, rarely using validated outcome measurements, and not reporting on long-term, patient-important outcomes such as OUD relapse.

Our findings on buprenorphine align with a recent systematic review by Goel and colleagues on managing perioperative pain in patients on buprenorphine that informed the 2019 PAIN guidelines,[15] although our review identified an additional case study[24] that reported buprenorphine needed to be

Table 2 Findings from Studies with Control Groups

Author, year	Study design Study size Duration Comparison	Population	Acute pain management strategies	Key findings	Quality assessment (high, unclear, or low risk of bias) and major limitations
MacIntyre, 2013[13]	Retrospective cohort *N* = 51 24 h after surgery Methadone vs buprenorphine groups as well as those who did and did not miss their medications for OUD dose after surgery	Surgical patients (33% orthopedic, 27% abdominal, 16% orofacial, 13% thoracic, and 10% other) on medications for OUD (57% methadone; 43% buprenorphine) who required IV PCA	•Use of medications for OUD: 64% of the buprenorphine group received medications for OUD (mean 13.7 mg) and 79% of the methadone group received medications for OUD (mean 78.9 mg) the day of surgery. Only 50% of the buprenorphine and 76% of the methadone groups received medications for OUD the day after surgery. •Use of opioids: Similar high doses of morphine-equivalent doses given in the postoperative period (mean 200 mg/day for the buprenorphine group vs 221 mg/day for the methadone group); < 1/4 of patients received tramadol. •Use of adjuvant analgesics: Patients received regular paracetamol and varying doses of nonsteroidal anti-inflammatory drug or continuous ketamine infusion; 1/4 of patients received ketamine, 1/8 received clonidine, and 1 patient received remifentanil.	•The methadone and the buprenorphine groups, and those that did and did not receive their medications for OUD dose the day after surgery, were similar in terms of pain, functionality, and adverse events (nausea, vomiting, sedation) the day after surgery. •Buprenorphine patients who were not given their usual medications for OUD dose the day after surgery used significantly more PCA for longer periods of time, and similar trends were seen in PCA amount in methadone patients.	•High risk of bias •Differences between groups at baseline in terms of substance use (alcohol, cannabis, and benzodiazepines) that were not controlled for •Some patients had medications for OUD discontinued and it is unclear why.
Hansen, 2016[23]	Retrospective cohort *N* = 51 27.2 months Those taking OUD medications for OUD vs those not taking OUD medications	17 knee or hip replacement surgical patients on medications for OUD (methadone or buprenorphine/naloxone) were matched to 34 controls not on medications for OUD	•Use of medications for OUD: the medications for OUD group was taking methadone or buprenorphine/naloxone at baseline (median 870 mg/day), but it is not clear whether medications for OUD were continued or discontinued during surgery. •Use of opioids: Medications for the OUD group received 8 times the morphine-equivalent dose of oral opioids at discharge compared to the non-OUD group (mean 793 mg/day vs 109 mg/day). This is a decrease from baseline for the medications for the OUD group and an increase from baseline for the non-OUD group. •Use of adjuvant analgesics: Similar pain management approaches in both groups including regional block and preoperative anesthesia adjunct medications	•Similar pain, functionality, and quality of life at 6 weeks and 1 year, except the medications for the OUD group had worse knee range of motion at 1 year.	•High risk of bias •Unclear if medications for OUD were continued for all, some, or no patients. •No information on which opioids were prescribed at discharge •Different medications for OUD medications grouped together and no subgroup analysis
Hines, 2008[11]	Retrospective cohort *N* = 134 7 days Methadone vs no methadone groups	67 with acute or surgical condition taking methadone were matched to 67 controls not taking methadone	•Use of medications for OUD: Patients taking methadone received an average of 82.4 mg methadone at admission; a total of 12% of patients had methadone increased; 16% experienced withdrawal	•Patients taking methadone had the same number of pain reports per day as controls. •Patients taking methadone spent a higher median number	•High risk of bias •Pain assessments based on how often the word "pain" appears in a patient's ward notes •Unclear why some patients had methadone dose increased

(*continued on next page*)

Table 2. (continued)

Author, year	Study design Study size Duration Comparison	Population	Acute pain management strategies	Key findings	Quality assessment (high, unclear, or low risk of bias) and major limitations
			symptoms (of which 18% had methadone dose increased). •Use of opioids: Median morphine-equivalent dose of opioids similar in methadone and nonmethadone groups (5.07 vs 6.67 mg/day, respectively). •Use of adjuvant analgesics: Some patients in both the methadone and nonmethadone groups received a nonopioid analgesic (42% vs 40%, respectively) and very few received nondrug pain relief (8% vs 5%). The methadone group received a higher median dosage of benzodiazepines than the nonmethadone group (5 vs 2.67 mg/day, respectively).	of days in the hospital, although this difference was not significant when obstetric cases were excluded. •Methadone patients were more likely to have behavioral problems, to discharge themselves against medical advice, and to transfer to another hospital. Methadone patients also had longer hospital stays overall compared to nonmethadone patients.	•The authors do not report the source of acute pain or types of surgery.

IV = intravenous; medications for OUD = medication-assisted treatment; PCA = patient-controlled analgesia

discontinued in a patient with injuries from a motorcycle accident in order to achieve adequate pain control with full-agonist opioids. Although this study was not included in the review by Goel and colleagues, it aligns with the 2019 PAIN guidelines and ASAM guidelines that buprenorphine may need to be discontinued in cases of severe acute pain. Similarly, our findings on methadone align with a recent systematic review by Taveros and colleagues.[33] In addition to confirming the results of these reviews, our review adds to the evidence base by looking for studies evaluating naltrexone. Unfortunately, we only identified a single case study, which found that tramadol can be used to manage acute pain in patients taking naltrexone.[29]

There were limitations of both our rapid review methods as well as limitations of the primary studies we identified. Our rapid review literature search required that a study include the term "acute pain," which may have missed studies in which it is assumed that the patient is in acute pain but is not described that way (such as management of pain in the "perioperative" period). Additionally, our use of first reviewer inclusion and data abstraction with second reviewer checking may have resulted in missing eligible studies or study data. However, given our results align with two recent systematic reviews on this topic, we believe we identified most of the important data. Additionally, there were significant limitations in both the design and reporting of primary studies that limit our confidence in the findings. First, there were no prospectively designed studies, so evidence is limited to information that researchers collected from data sources not originally designed to address these questions. This was especially problematic in assessments of pain—some studies assessed pain through a scale, but others just noted how often a patient mentioned the word pain or gave a physicians' overall impression of a patient's pain. Second, most studies did not thoroughly describe their pain management approach—for example, 2 studies with control groups[11, 23] lacked detailed information on whether OUD medication was continued, whether the dosage stayed the same, increased, or decreased, and why those decisions were made.

There are several important gaps in the available literature that should be addressed by future research:

1. There is a need for well-described, prospective studies (such as randomized controlled trials [RCTs] or cohort studies). We did not identify any studies that adequately described a specific pain management strategy and its effects on patient outcomes. Prospective studies with deliberate reporting of intervention elements (such dosage and timing of OUD, dosage and timing of opioid or nonopioid analgesics, and a rationale for why any changes are made) can be more informative than retrospective studies where intervention reporting is often less complete. Randomizing patients into different groups (i.e., an RCT) would provide the most rigorous, defensible answers to what pain management approaches are safe and effective; however, even a well-described, controlled cohort study that adjusts for differences in patient groups at baseline would be a useful step forward.
2. There is a need for studies evaluating approaches to acute pain management when methadone and buprenorphine are continued. Given the best evidence suggests continuing methadone and buprenorphine

Table 3 Findings from Studies Without Control Groups

Author, year	Study design Study size Duration	Population	Acute pain management strategies and key findings	Quality of reporting (total, mostly, partly, none) and major limitations
Barelli, 2019[31]	Case study *N* = 1 2 days	50-year-old man currently receiving current methadone maintenance treatment and scheduled for a parotidectomy	Desflurane, IV fentanyl, and ketamine during surgery. Tramadol infused 30 min before end of surgery. Ketamine and tramadol infusion after extubating. Ketamine discontinued after 2 h—methadone restarted after 6 h. Tramadol discontinued after 1 day postoperative—acetaminophen and ketorolac 2 days postoperative.	•Partly reported •Unclear whether patient received medications for comorbidities and how that may have affected treatment
Book, 2007[28]	Case study *N* = 1 11 days	32-year-old woman who underwent surgical removal of breast implants	Patient received buprenorphine/naloxone for postoperative pain. Patient was able to taper dose to baseline dose by day 11.	•Partly reported •Limited information on patient characteristics and limited outcome data
Harrington, 2010[24]	Case study *N* = 1 6 days	30-year-old man with multisystem injuries from a motorcycle accident on buprenorphine	Initial treatment with full-agonist opiates could not be down-titrated without increasing pain. Buprenorphine was eventually removed, which helped to stabilize pain, improved mental status, and reduced agitation.	•Partly reported •Limited information on OUD history and treatment approach, unclear how pain was measured
Israel, 2013[29]	Intervention series *N* = 2 2 days–3 weeks	27-year-old man who underwent mastectomy for gynecomastia and a 37-year-old woman who underwent bilateral mastectomies	First patient received naltrexone for opioid dependence. Received tramadol for postoperative pain, then resumed naltrexone 2 weeks later. The second patient received fentanyl patch, ketorolac, and fentanyl pump to control postoperative pain, then switched to fentanyl patch, and oxycodone plus acetaminophen. Discharged with acetaminophen and oxycodone.	•Partly reported •Limited information on patient characteristics and outcomes
Kornfeld, 2010[27]	Case series *N* = 5 2–9 days	Patients taking sublingual buprenorphine for chronic musculoskeletal pain for > 1 year before major surgery	Pain management with opioids, bupivacaine, and/or ketamine in the intraoperative and postoperative period led to generally good pain control.	•Partly reported •Only a portion of patients in the study had OUD and it is unclear which ones they were.
McCormick, 2013[14]	Case study *N* = 1 2 months	50-year-old man with acute thigh pain due to McArdle's disease taking buprenorphine/naloxone	Treatment with buprenorphine/naloxone required higher than expected doses of hydrocodone for pain relief.	•Partly reported •Not clear if/when buprenorphine was discontinued or how pain was managed during the resultant fasciotomies to relieve compartment pressure
Sartain, 2002[25]	Case study *N* = 1 34 days	25-year-old man on methadone treatment then slow-release morphine prior to a major trauma	Administration of PCA morphine, naproxen, MS contin, and ketamine did not help in alleviating initial pain or subsequent pain from surgeries. Morphine and ketamine were stopped and methadone was added, which resulted in pain relief.	•Partly reported •Limited information on duration of treatment or cause of chronic pain condition
Tucker, 1990[26]	Case study *N* = 1 7 days	52-year-old man in a methadone maintenance program with abdominal pain who eventually underwent surgery on his appendix	Patient received morphine, then switched to acetaminophen with codeine and methadone until his discharge at 7 days.	•Partly reported •Unclear how pain was measured
Rodgman, 2012[30]	Case study *N* = 1 8 months	29-year-old woman who received a bilateral ventricular assist device for congenital cardiomyopathy	Fentanyl drip, IV hydromorphone, and IV morphine as needed, oral oxycodone/acetaminophen postoperative—buprenorphine was reinduced a week later. Opiates were held at midnight and buprenorphine/naloxone was administered. Buprenorphine/naloxone, gabapentin, and medications for graft maintenance at discharge (day 19).	•Mostly reported •Limited information on comorbidities, dosages of pain medications used, and outcomes after discharge

OUD = opioid use disorder; PCA = patient-controlled analgesia; IV = intravenous

during episode of acute pain, future research should compare protocols that vary the timing (e.g., dividing doses) and/or doses (e.g., increasing the dose) and evaluate adjunctive opioid and nonopioid pain treatments. Slow-release oral morphine is being used for OUD treatment in some settings as an alternative to methadone and buprenorphine.[34] The use of slow-release oral morphine in acute pain management for patients with OUD is another strategy that could be explored.

3. There is a need for studies on acute pain management in patients taking naltrexone. We only identified a single case study on the management of acute pain in a patient taking naltrexone. Research on management of acute pain in these patients is urgently needed.

4. Studies should use validated measurements and measure long-term, patient-important outcomes. Of the best available evidence, only 1 study[23] used validated tools to measure quality of life or functionality. All other studies provided limited information on how outcomes were measured, with many commenting that outcomes were retrospectively collected from medical records. We identified no studies that rigorously evaluated patient satisfaction, healthcare utilization (other than length of hospitalization), opioid withdrawal symptoms, substance use relapse, opioid overdose, or suicide ideation or suicidal self-directed violence. Furthermore, with few exceptions, studies ended when patients were discharged, so it is impossible to determine what the long-term effects of pain management strategies were on patients' health, especially the impact of administering opioids on patients' likelihood of relapse or overdose.

This review confirmed that there is a lack of rigorous evidence on the management of acute pain in patients taking methadone, buprenorphine, or naltrexone, although the best available evidence suggests that continuing methadone and buprenorphine during episodes of acute pain is preferable to discontinuing these medications. More research is needed that evaluates patient outcomes following well-characterized acute pain management interventions including OUD medication dose and schedule adjustments and use of adjunctive nonopioid pain management strategies.

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Compliance with Ethical Standards:

Conflict of Interest: *The authors declare no conflicts of interest.*

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