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# Clinical Practice Guidelines for Pain Management in Acute Musculoskeletal Injury

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**Purpose:** We aimed to produce comprehensive guidelines and recommendations that can be utilized by orthopaedic practices as well as other specialties to improve the management of acute pain following musculoskeletal injury.

**Methods:** A panel of 15 members with expertise in orthopaedic trauma, pain management, or both was convened to review the literature and develop recommendations on acute musculoskeletal pain management. The methods described by the Grading of Recommendations Assessment, Development, and Evaluation Working Group were applied to each recommendation. The guideline was submitted to the Orthopaedic Trauma Association (OTA) for review and was approved on October 16, 2018.

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Members of the Orthopaedic Trauma Association Musculoskeletal Pain Task Force are listed in Appendix 1.

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**Results:** We present evidence-based best practice recommendations and pain medication recommendations with the hope that they can be utilized by orthopaedic practices as well as other specialties to improve the management of acute pain following musculoskeletal injury. Recommendations are presented regarding pain management, cognitive strategies, physical strategies, strategies for patients on long term opioids at presentation, and system implementation strategies. We recommend the use of multimodal analgesia, prescribing the lowest effective immediate-release opioid for the shortest period possible, and considering regional anesthesia. We also recommend connecting patients to psychosocial interventions as indicated and considering anxiety reduction strategies such as aromatherapy. Finally, we also recommend physical strategies including ice, elevation, and transcutaneous electrical stimulation. Prescribing for patients on long term opioids at presentation should be limited to one prescriber. Both pain and sedation should be assessed regularly for inpatients with short, validated tools. Finally, the group supports querying the relevant regional and state prescription drug monitoring program, development of clinical decision support, opioid education efforts for prescribers and patients, and implementing a department or organization pain medication prescribing strategy or policy.

**Conclusions:** Balancing comfort and patient safety following acute musculoskeletal injury is possible when utilizing a true multimodal approach including cognitive, physical, and pharmaceutical strategies. In this guideline, we attempt to provide practical, evidence-based guidance for clinicians in both the operative and non-operative settings to address acute pain from musculoskeletal injury. We also organized and graded the evidence to both support recommendations and identify gap areas for future research.

**Key Words:** opioid, pain, musculoskeletal, orthopaedic trauma

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## BACKGROUND

Drug overdose deaths have become an epidemic in the United States. In the past 15 years, deaths related to drug overdoses in the United States have tripled, mostly because of the increase in opioid-related deaths.<sup>1,2</sup> In the same period, almost half a million people have died of prescription drug overdoses.<sup>1,2</sup> Opioids, including prescription drugs and heroin, are involved in 61% of drug overdose deaths.<sup>3</sup> The rate of increase in deaths from commonly prescribed opioids has slowed slightly in the past few years, whereas death rates from the synthetic opioids fentanyl and heroin have increased by 72% and 21%, respectively.<sup>3</sup> This epidemic has taken a significant toll on the health of the nation, with emerging findings that opioid-related deaths have

led to a 0.21-year reduction in average life expectancy—contributing to the overall decrease in life expectancy from 2014 to 2015.<sup>4</sup>

The increase in opioid overdose deaths aligns with a proportional increase in opioid prescribing rates. Opioid prescriptions increased substantially from 2006 to 2012<sup>5</sup> with a desired focus on treating patient pain. Family medicine physicians overall provide the most opioids of any specialty; however, orthopaedic surgeons prescribe 7.7% of prescriptions despite representing only 2.5% of physicians.<sup>6</sup> The increase in opioid prescriptions was unfortunately not associated with the anticipated reduction of reported pain among Americans.<sup>7</sup> Without an improvement in patient outcomes, these prescriptions are needlessly associated with a high risk of abuse. Adding to the problem of oversupply for needs, many opioids go unused following orthopaedic surgery,<sup>8,9</sup> creating the possibility of nonmedical usage or diversion. Furthermore, of the patients who receive a first opioid prescription of any duration, 21% progress to receiving more prescriptions episodically and 6% progress to long-term use.<sup>10</sup> Up to half of patients who take opioids for at least 3 months remain on opioids 5 years later and are likely to become lifelong users.<sup>11–13</sup> Therefore, changing prescribing habits has been a high priority.

Because of the increasing recognition of the opioid crisis, several professional societies, health care systems, pharmacies, insurance companies, and governmental organizations have released guidelines and toolkits for the safe prescribing of opioids. Although some of these guidelines address certain aspects of pain from musculoskeletal conditions, many are focused on the management of chronic pain, and unfortunately, few give concrete examples of practical methods and prescribing practices that can be easily implemented when caring for acute musculoskeletal injuries. Thus, we aimed to produce comprehensive guidelines and recommendations that can be used by orthopaedic practices and other specialties to improve the management of acute pain following musculoskeletal injury.

## METHODS

### Panel and Target Audience

This guideline aims to provide evidence-based recommendations for the management of acute musculoskeletal pain. A panel of 15 members with expertise in orthopaedic trauma, pain management, or both was convened to review the literature and develop recommendations on acute musculoskeletal pain management. Chronic pain is outside the scope of this guideline.

### Literature Review

The panel met in person in October 2017 to define the scope of the guideline and identify important topics for inclusion. The topics included cognitive strategies, physical modalities, opioid safety and effectiveness, multimodal pharmaceutical strategies, medical assistance therapy, nonsteroidal anti-inflammatory drugs and fracture healing, nerve/regional/field blocks, pain and sedation assessment strategies, and health care system strategies. One or 2 panel members were assigned to draft recommendations for each topic area. Literature

**TABLE 1.** Best Practice Recommendations\* for Alleviation of Acute Pain After Musculoskeletal Injury

Category	Recommendations
Pain medication strategies	Use MMA. MMA may include NSAIDs, acetaminophen, gabapentinoids, and immediate-release opioids. Prescribe the lowest effective immediate-release opioid dose for the shortest period possible. Do not use extended-release opioids. Consider local or regional block anesthesia as part of the postoperative multimodal regimen.
Cognitive strategies	Discuss alleviation of pain, expected recovery course, and patient experience at all encounters. Connect patients with pain that is greater or more persistent than expected and patients with substantial symptoms of depression, anxiety, or posttraumatic stress or less effective coping strategies (greater catastrophic thinking and lower self-efficacy) to psychosocial interventions and resources. Consider using strategies for optimal mindset such as aromatherapy, music therapy, or approaches based on cognitive behavioral therapy.
Physical strategies	Use immobilization, ice, and elevation appropriately. Consider the use of TENS units. Consider the use of cryotherapy units.
Strategies for patients on long-term opioids at presentation	Use balanced physical, cognitive, and pharmaceutical strategy for alleviation of pain Ensure that there is only 1 prescriber by coordinating with APS (or addiction medicine or psychiatry depending on resources) when inpatient and the patient's prescriber when outpatient.
Pain assessment strategies	Assess pain and sedation regularly for inpatients with short validated tools.
System strategies	Query the state and relevant regional PDMP before prescribing opioids. Develop and support the implementation of clinical decision support for opioid prescribing in the electronic medical record. Support opioid education efforts for prescribers and patients. Implement pain medication prescribing strategy or policy.

\*In conjunction with pain medication recommendations and individualized per treating physician discretion according to patient characteristics, local practice preferences, and state law.

searches were conducted through September 2018. Information about each included article is available in the **Supplemental Digital Content 1** (see **Table**, <http://links.lww.com/JOT/A648>).

### Grading Process

The methods described by the Grading of Recommendations Assessment, Development, and Evaluation Working

**TABLE 2.** Pain Medication Recommended Taper\* Following a Major Musculoskeletal Injury Procedure (eg, Operative Fixation of Long Bone or Complex Joint Fracture, Extensive Soft Tissue Injury or Surgery, etc.)

Status	Opioid	Nonopioid
Inpatient	Oxycodone/acetaminophen 5 mg/325 mg 1 tab po q 4 h PRN moderate pain 5 mg/325 mg 2 tabs po q 6 h PRN severe pain (hold next acetaminophen scheduled dose) Hydromorphone 1 mg IV q 3 h PRN for severe breakthrough pain	Ketorolac 15 mg IV q 6 h × 5 doses, followed by ibuprofen 600 mg po q 8 h Gabapentin 100 mg 1 tab po TID Scheduled acetaminophen 500 mg po q 12 h
Postdischarge		
Week 1 (at discharge)	Oxycodone/acetaminophen 5 mg/325 mg 1 tab po q 4 h PRN Dispense #42 (1 time Rx, no refills)	Ibuprofen 600 mg po q 8 h × 7 d (Rx given) Gabapentin 100 mg 1 tab po TID × 7 days (Rx given) Scheduled acetaminophen 500 mg po q12 h × 7 d (can increase as combined opioid analgesic decreases) NSAIDs PRN as directed Gabapentin if necessary (up to 1800 mg/d)
Week 2	Hydrocodone/acetaminophen 5 mg/325 mg or tramadol 50 mg (only if necessary—3 Rx Max) 1 tab po q 4 h PRN Dispense #42	Scheduled acetaminophen 500 mg po q12 h (can increase as combined opioid analgesic decreases)
Week 3	1 tab po q6 hours PRN Dispense #28	Scheduled acetaminophen 1000 mg po q12 h (can increase as combined opioid analgesic decreases)
Week 4	1 tab po q8 hours PRN Dispense #21	Scheduled acetaminophen 1000 mg po q8 hours (can increase as combined opioid analgesic decreases)
Weeks 5+		NSAIDs PRN as directed Acetaminophen PRN as directed Gabapentin if necessary (then wean)

Dosage and duration can be less if tolerated.

\*In conjunction with other best practice recommendations and individualized per treating physician discretion according to patient characteristics, local practice preferences, and state law.

PRN, pro re nata, “as needed”; TID, ter in die, three times per day.

Group were applied to each recommendation.<sup>14</sup> This method yields a grade for the strength of the recommendation and a grade for the quality of the evidence. The grading of the evidence was based on the study designs, number of studies, sample sizes, and consistency of results among different studies. The panel assigned recommendations as “strong” (practices in which benefits are sure to outweigh potential harms) or “conditional” (the evidence was weaker or if the benefits do not significantly outweigh potential harms).

### Approval of Guideline

Recommendations from each topic area were combined to produce a comprehensive guideline for management of acute musculoskeletal pain. All panel members reviewed and revised the combined guideline. The guideline was submitted to the Orthopaedic Trauma Association for review and was approved on October 16, 2018.

### Best Practice and Pain Management Recommendations

Because of the increasing recognition of the opioid crisis, several professional societies, health care systems, pharmacies, insurance companies, and governmental organizations have released guidelines and toolkits for the safe prescribing of opioids.<sup>3,15–39</sup> Although some of these guidelines address certain aspects of pain from musculoskeletal conditions, many are focused on the management of chronic pain, and few give concrete examples of practical methods

and prescribing practices that can be easily implemented when caring for acute musculoskeletal injuries.

We provide best practice recommendations and pain medication recommendations (Tables 1–4) with the hope that they can be used by orthopaedic practices and other specialties (eg, primary care and emergency medicine) to improve the management of acute pain following musculoskeletal injury. The best practice recommendations for acute pain management following musculoskeletal injury are supplemented with the corresponding in-depth reviews presented in this article. The pain medication recommendations are divided into 3 clinical scenarios—major musculoskeletal injury procedure (eg, operative fixation of long bone or complex joint fracture, extensive soft tissue injury or surgery, etc.), minor musculoskeletal injury procedure (eg, operative fixation of small bone or simple joint fracture, minimal soft tissue dissection or surgery, etc.), and nonoperative musculoskeletal injury (eg, closed management of injury, laceration repair, etc.). The best practice recommendations and the pain management recommendations are meant to be used in conjunction with each other and should be individualized per treating physician discretion according to patient characteristics, local practice preferences, and applicable state laws.

## RECOMMENDATIONS

### Cognitive and Emotional Strategies

- The panel recommends discussing alleviation of pain, expected recovery course, and patient experience at all

**TABLE 3.** Pain Medication Recommended Taper\* Following a Minor Musculoskeletal Injury Procedure (eg, Operative Fixation of Small Bone or Simple Joint Fracture, Minimal Soft Tissue Injury or Surgery, etc.)

Status	Opioid	Nonopioid
Postdischarge		
Week 1	Hydrocodone/acetaminophen 5 mg/325 mg or tramadol 50 mg 1 tab po q 6 h PRN Dispense #28 (1 time Rx, no refills)	Ibuprofen 600 mg po q 8 h × 7 d (Rx given) Gabapentin 100 mg 1 tab po TID × 7 d (Rx given) Scheduled acetaminophen 1000 mg po q12 h (can increase as combined opioid analgesic decreases)
	Hydrocodone/acetaminophen 5 mg/325 mg or tramadol 50 mg (only if necessary—2 Rx Max)	NSAIDs PRN as directed Gabapentin if necessary (up to 1800 mg/d)
Week 2	1 tab po q 8 h PRN Dispense #21	Scheduled acetaminophen 1000 mg po q8 hours (can increase as combined opioid analgesic decreases)
Week 3	1 tab po q12 h PRN Dispense #14	Scheduled acetaminophen 1000 mg po q8 hours (can increase as combined opioid analgesic decreases)
Weeks 4+		NSAIDs PRN as directed Acetaminophen PRN as directed

Dosage and duration can be less if tolerated.

\*In conjunction with other best practice recommendations and individualized per treating physician discretion according to patient characteristics, local practice preferences, and state law.

encounters (strong recommendation, moderate-quality evidence).

- The panel recommends connecting patients with pain that is greater or more persistent than expected and patients with substantial symptoms of depression, anxiety, or posttraumatic stress or less effective coping strategies (greater catastrophic thinking and lower self-efficacy) to psychosocial interventions and resources (strong recommendation, low-quality evidence).
- The panel recommends that clinicians consider using anxiety-reducing strategies to increase self-efficacy and promote peace of mind with patients like aromatherapy, music therapy, or cognitive behavioral therapy (strong recommendation, low-quality evidence).

**Nociception and Pain**

Nociception is the physiology of actual or potential tissue damage. Pain is the unpleasant thoughts, emotions, and behaviors that accompany nociception. There is wide variation in pain intensity for a given nociception.<sup>40</sup> Pain catastrophizing is an ineffective coping strategy characterized by unhelpful preparation for the worst including rumination and

helplessness.<sup>41</sup> Greater catastrophic thinking is consistently associated with greater pain intensity.<sup>42</sup> Increased symptoms of anxiety and depression and greater alcohol use are also associated with higher pain intensity, whereas self-efficacy and fewer symptoms of depression are associated with less pain.<sup>43–45</sup>

Studies of musculoskeletal injuries, including ankle sprains and fractures, have found no association between pain intensity and degree of nociception (injury severity). Variations in pain intensity and magnitude of limitations are accounted for more by measures of psychosocial aspects of illness than by measures of pathophysiology.<sup>44,46–53</sup>

There are also cultural differences in pain intensity and alleviation of pain with medication. Studies document good pain relief using nonopioid medication in patients recovering from fracture surgery in The Netherlands and Vietnam.<sup>54–57</sup> In the United States, however, patients who take more opioids in the hospital after fracture surgery have more pain and less satisfaction with alleviation of pain.<sup>43–45</sup> These findings suggest that psychological factors play a significant role in the intensity of pain for a given nociception.

**TABLE 4.** Pain Medication Recommended Taper\* Following a Nonoperative Musculoskeletal Injury (eg, Closed Management of Injury, Laceration Repair, etc.)

Injury Category	Opioid	Nonopioid
Minor injury (eg, small bone fracture, sprain, laceration, etc.)	Tramadol 50 mg (only if necessary—2 Rx Max) 1 tab po q 6 h PRN Dispense #20, then #10	NSAIDs PRN as directed Scheduled acetaminophen 1000 mg po q8 hours, then PRN as directed
Major injury (eg, large bone fracture, rupture, etc.)	Hydrocodone/acetaminophen 5 mg/325 mg or tramadol 50 mg (only if necessary—2 Rx Max) 1 tab po q 6 h PRN Dispense #20, then #10	NSAIDs PRN as directed Scheduled acetaminophen 1000 mg po q12 h, then PRN as directed

Dosage and duration can be less if tolerated.

\*In conjunction with other best practice recommendations and individualized per treating physician discretion according to patient characteristics, local practice preferences, and state law.

Persistent pain in the absence of infection or implant problems correlates with psychosocial factors.<sup>53,56,58–77</sup> Pain intensity, magnitude of limitations, and continued opioid use are associated with greater symptoms of depression or post-traumatic stress disorder and less effective coping strategies (eg, greater catastrophic thinking).

Chronic pain is defined as pain lasting beyond the usual course of healing or more than 3–6 months, which affects the individual's daily functioning and well-being.<sup>78</sup> Several non-modifiable risk factors have been identified for the development of chronic pain including female sex, age >65 years, intense acute pain, and low socioeconomic status. Several modifiable risk factors have also been identified including greater pain catastrophizing, greater pain-related fear, and greater symptoms of anxiety, depression, and posttraumatic stress disorder. Identifying and addressing psychosocial factors may limit persistent pain.

### Psychosocial Interventions

A notable portion of trauma patients have substantial symptoms of anxiety, depression, and post-traumatic stress disorder months after injury. Giving opioids for pain that is more intense and disabling than expected might represent a misdiagnosis and mistreatment of stress, distress, and less effective coping strategies.

Initial studies of psychosocial interventions to limit psychological distress and improve comfort and ability have had mixed results.<sup>62,79–94</sup> The goals of these interventions are to improve overall mental health and decrease rates and severity of depression, anxiety, and posttraumatic stress disorder. Interventions studied include cognitive behavior therapy, self-management interventions and training, educational information access, peer support, and online social networking. Cognitive behavioral interventions have positive effects on pain relief in some trials.<sup>58,95,96</sup> There is also evidence that web-based cognitive behavioral therapy is effective.<sup>97–99</sup> Meta-analyses of music therapy demonstrate decreased anxiety and better sleep in the setting of chronic medical illness.<sup>100</sup> Music therapy has also demonstrated positive effects on pain relief and opioid dose reduction. Similarly, systematic reviews of aromatherapy have demonstrated anxiolytic effects<sup>101</sup> and pain reduction.<sup>102</sup> Further research on the utility of various interventions can help elucidate the most effective resources for trauma patients.

### Physical Strategies

#### TENS

- The panel recommends the use of transcutaneous electrical stimulation (TENS) as an adjunct to other immediate post-injury or postoperative pain treatments (strong recommendation, low-quality evidence).
- The panel can neither recommend nor discourage a specific TENS device or protocol. Regimens that incorporate sub-optimal frequencies not approaching a “subnoxious or maximal tolerable/painful” setting lack effective pain modulation and should be avoided (conditional recommendation, low-quality evidence).

TENS attempts to modulate pain through delivery of low-voltage electric currents over the skin from a small portable device. The stimulation of large diameter peripheral afferent nerve fibers is believed to reduce pain by activating opioid receptors through an endogenous descending inhibitory pathway.<sup>103</sup> The contraindications to the use of TENS include the presence of a pacemaker or implanted defibrillator, broken skin at the site of application, or significant lymphedema.

There are mixed results on the adjunctive use of TENS to modulate pain, largely due to a relative paucity of high-quality trials and significant interstudy heterogeneity due to the lack of any specific standardized treatment protocols. The panel's literature review was restricted to TENS studies within the last 20 years.

The American Pain Society's 2016 Clinical Practice Guideline for the management of postoperative pain recommends the consideration of TENS as an adjunctive modality with treatments directed near the surgical wound. The review panel found insufficient evidence for specific TENS regimens but emphasized that positive effects were stronger when optimal predefined stimulation parameters were used.<sup>103</sup>

A meta-analysis (21 randomized clinical trials, RCTs) of TENS as an adjunct to reduce postoperative analgesic consumption found that the effectiveness may depend on the current amplitude. The authors only included studies that report a “strong and/or definite subnoxious, and/or maximal nonpainful, and/or maximal tolerable” stimulation with currents >15 mA or a pulse frequency of 1–8 Hz (acupuncture-like TENS; ALTENS) or 25–150 Hz (TENS). The review found TENS (vs. placebo TENS) around the surgical wound significantly reduced postoperative analgesic consumption by 26.5% (range –6% to 51%): subnoxious stimulation reduced opioid consumption by 35.5%, whereas nonspecific trials yielded less effect (4.1% reduction). Overall difference in analgesic consumption favored TENS versus placebo with optimal median frequencies at 2 Hz for ALTENS or 85 Hz for TENS.<sup>104</sup>

The effectiveness of TENS within the orthopaedic literature is limited by nonstandardized clinical trials often without reported or consistent TENS treatment protocols. Adjunctive TENS use within the immediate postoperative period after a total knee arthroplasty (TKA) postulates a trend toward favorable mean weighted reduction in opioid consumption versus placebo TENS or standard care (3 meta-analyses and 1 RTC).<sup>105</sup> One systematic review and meta-analysis found that TENS decreased pain severity at 1, 2, and 6 months after TKA, but this was based on low-quality studies.<sup>105</sup> Interestingly, both TENS and placebo TENS (45-second cutoff) were found to decrease postoperative TKA pain with active extension and fast walking, highlighting a potential placebo effect that subsided by 6 weeks postoperatively versus standard treatment.<sup>106</sup> A prospective double-blind randomized trial on arthroscopic rotator cuff repair found TENS to significantly reduce immediate postoperative opioid use by 25% at both 48 hours and 1 week.<sup>107</sup> These results are moderately consistent with the nonorthopaedic literature where TENS decreased postoperative opioid analgesic requirements (by 53% with mixed frequencies vs. 35% with high-frequency and 32% with low-frequency settings) and

opioid-related side effects when used as an adjunct to patient-controlled analgesia (PCA) after lower abdominal gynecological surgery.<sup>108</sup> In contrast, although TENS was determined useful after thoracic surgical procedures (only when less invasive approaches yield mild to moderate postoperative pain), TENS was ineffective for severe pain with invasive approaches.<sup>109</sup>

A meta-analysis (27 RCTs) of 6 different types of electrical stimulation determined that interferential current, a less common modality, was the only treatment to effectively modulate pain intensity and change pain visual analog scale (VAS) scores (standardized mean difference = 2.06, 95% CI: 1.1–3.19), that the effect of high-frequency TENS was uncertain, and that low-frequency TENS was not effective.<sup>110</sup>

In conclusion, our systematic review indicates that TENS, when applied using strong, subpainful frequencies, is an effective multimodal adjunct to modulate acute orthopaedic injury and postoperative pain. Recent publications demonstrate a substantial degree of interstudy heterogeneity, most notably inconsistent descriptions of both TENS dosing intensities and standardized outcome measures. The long-term tolerance of the same dose TENS parameters and strategies to prolong its effect is largely unknown. Higher-quality clinical trials are necessary to provide stronger evidence in favor of TENS as a consistent treatment for acute pain and perioperative pain modulation.

### Cryotherapy

- The panel recommends the use of cryotherapy for acute musculoskeletal injury and the postsurgical orthopaedic patient as an adjunct to other postoperative pain treatments (conditional recommendation, low-quality evidence).
- The panel cannot recommend a specific cryotherapy delivery modality or protocol (no recommendation, limited evidence).

Cryotherapy is the application of an external cold source in which the desired effect is a drop in tissue temperature. Cold sources that have historically been used include ice bags, cold gel packs, ice massage, cold water submersion, gaseous cryotherapy, and continuous-flow cryotherapy devices with and without pneumatic compression. Basic science studies have shown that the biologic effects of cold therapies are multifactorial. A decrease in tissue temperature results in decreased tissue edema and microvascular permeability,<sup>111,112</sup> reduced delivery of inflammatory mediators,<sup>112–116</sup> reduced blood flow via vasoconstriction,<sup>116–120</sup> overall net decrease in tissue metabolic demand, and subsequent hypoxic injury.<sup>116–118,120</sup> In addition, the decrease in tissue temperature has been shown to increase the threshold of painful stimuli and increase the tolerance to pain.<sup>121</sup>

Multiple studies have looked at the efficacy of cryotherapy in the postoperative orthopaedic patient for various anatomic areas including the knee, hip, shoulder, foot and ankle, wrist, and hand. Among the studies that evaluated cryotherapy versus a noncryotherapy control, 10 randomized controlled trials and 2 meta-analyses have shown a significant benefit for pain control.<sup>105,122–132</sup> Contrary to this, there have been 8 randomized controlled trials that have shown no

benefit to cryotherapy compared with a noncryotherapy control.<sup>133–140</sup> Many studies have also looked at cryotherapy's ability to decrease opioid consumption compared with a non-cryotherapy control. Of these studies, 11 have shown a significant decrease in pain medication consumption<sup>105,123,125–127,129,131–133,138,141</sup> compared with 5 studies showing no difference.<sup>134–136,139,140</sup>

Many randomized controlled trials have compared continuous-flow cryotherapy devices to ice bags or packs. Nine studies have failed to show a difference in pain scores,<sup>142–150</sup> whereas 5 studies have shown improved pain with continuous-flow cryotherapy.<sup>151–155</sup> No studies have shown superior pain control with ice bags or packs compared with continuous cryotherapy.

There are also inconclusive results pertaining to the difference in pain medication consumption when comparing continuous-flow cryotherapy with ice bags or packs. Five studies have demonstrated a decreased need for opioids with continuous cryotherapy,<sup>148,150,151,154,156</sup> one study showed a lower consumption of pain medication with the use of ice packs,<sup>157</sup> and 5 RCTs failed to show a difference between these 2 cryotherapy modalities.<sup>142,145,147,149,158</sup> It is possible that continuous-flow cryotherapy results in a higher patient satisfaction with the cryotherapy treatments<sup>142,148,150</sup> and that there may also be a benefit to continuous-flow cryotherapy at night.<sup>159</sup> It is important to note the methodologic variability within the cryotherapy literature. Variables such as cryotherapy source, temperature, duration, and frequency can vary drastically from treatment groups in the same study, as well as study to study, making the assessment on the magnitude of effect difficult to determine. Because of the current literature's methodological heterogeneity, we are unable to favor 1 method of cryotherapy application, protocol, or both.

Like most therapeutic interventions, cryotherapy can result in complications. Nerve palsies have been reported in the literature, mostly involving more superficial nerves such as the peroneal nerve, lateral femoral cutaneous nerve, ulnar nerve, and supraclavicular nerve. Care must be taken to provide sufficient insulation between the skin and the cryotherapy source, especially in patients with minimal subcutaneous fat. Nerve injuries can range from brief paresthesias to complete axonotmesis.<sup>160,161</sup> Frostbite has also been a concern but, to our knowledge, has not been reported as a result of cryotherapy after an orthopaedic procedure.

Overall, the body of literature provides preliminary support for use of cryotherapy for acute pain management. However, future studies should focus on determining the most efficacious method of application and protocol for cryotherapy.

### Opioid Safety and Effectiveness

- The panel endorses that all opioids used for pain carry a risk of misuse. Opioids are also associated with adverse clinical events. Patient comfort and safety must be carefully balanced when prescribing opioids. Because of the potential for misuse of all opioids, the panel recommends that the prescriber should use the lowest effective dose for the

shortest period possible (strong recommendation, high-quality evidence).

- The panel recommends not prescribing benzodiazepines in conjunction with opioids because of the significant risks of inconsistent sedation and potential for misuse (strong recommendation, high-quality evidence).
- The panel recommends avoiding long-acting opioids in the acute setting (strong recommendation, moderate-quality evidence).
- The panel recommends prescribing precisely. Commonly written prescriptions with ranges of dose and duration can allow tripling of daily dose to levels consistent with adverse events (strong recommendation, low-quality evidence).

Opioids are the most commonly used medications for treatment of most severe pain conditions.<sup>162</sup> All opioids come with some level of safety concern. Regardless of the formulation used, there is always a risk of adverse events, as well as abuse, addiction, or both. The number and severity of adverse events from opioids are related to their potency, half-life, and mode of use.

The number of milligrams in the dosage is not an indication of how strong the medication might be. Potent opioids (eg, fentanyl is 50–100 times as potent as morphine) increase the number and severity of events. Although oxycodone and oxycodone are about equally effective in treating pain, more adverse events are seen with oxycodone because of its higher potency.<sup>163</sup> Oxycodone has 3–7 times the efficacy of morphine, whereas oxycodone is only 1.5 times greater. Currently, immediate-release opioids are prescribed at a significantly higher rate than extended-release options.<sup>164</sup> These extended-release medications result in a 4.6-fold higher abuse rate and a 6.1 times increased diversion potential.<sup>164</sup> The risk of addiction and abuse also has a strong correlation with the length of time the opioids are prescribed. Although some patients may become addicted after long-term therapy, a significantly larger proportion will show behavior of medication misuse and illicit drug use.<sup>165</sup>

The main formulations on the market have vastly different pharmacokinetics. Immediate-release opioids, which cause serum opioid levels to rapidly increase and decrease with a shorter half-life, have a shorter period of pain relief. Long-acting (“continued-release” tablets) may deliver opioids for a longer period, but the amount of opioid absorbed is less per unit of time. This results in less fluctuation in serum drug levels, keeping opioid concentration in the therapeutic range.<sup>166</sup> For the inpatient setting, long-acting opioids may have the same effectiveness as short-acting opioids when used as monotherapy, but given newer multimodal pain management regimens, this is not recommended current practice.<sup>167</sup> Both short-acting and long-acting opioids have been shown to be effective in treating pain and increasing quality of sleep, with the main difference being that the number of pills prescribed will be higher in the short-acting group.<sup>168–170</sup> Other drug formulations have been created to include supposed abuse deterrent properties, but in actuality may have a similar profile in regard to effectiveness and adverse events.<sup>171</sup> Combining opioids with other drugs has been shown to be more effective in managing pain than opioids alone. More

specifically, combining opioids with nonsteroidal anti-inflammatory drugs (NSAIDs) has been shown to be more effective than opioids alone.<sup>172</sup> Benzodiazepines do not have this beneficial synergy. Taking any of these formulations with food does not change the maximum dose of the medication delivered, although when taken after a high fat meal, the time to maximum concentration is delayed.<sup>173</sup>

The literature comparing the difference of the safety and efficacy of opiates for the treatment of pain in acutely injured musculoskeletal patients is scarce. The majority of the literature on safety and efficacy of opioids is in regard to chronic pain from both malignant and nonmalignant conditions. The evidence in these areas is not strong.<sup>162</sup> There is very little in the literature discussing safety and efficacy in the short-term postinjury setting. Hence, the appropriate dose for specific injuries or conditions is not well defined. Standard prescribing habits seem to routinely provide an excess amount of medication. A recent study found that 81% of patients took 20 or fewer pills after knee arthroscopy.<sup>174</sup> A study of opioid use by 250 patients who had undergone elective outpatient upper extremity surgery showed that although all patients were prescribed opioids for 30 days (30 pills), 52% used their prescription for pain control for only 2 days or less. On average, each patient took 11 pills, leaving 19 pills unused. With fewer pills prescribed, there was a 79% reduction of leftover pills in the community, thus decreasing the potential for diversion.<sup>175</sup>

Leaders in musculoskeletal care need to develop specific strategies based on burden of disease. Other non-opioid medications should be used with an intent to obtain balanced patient comfort and safety. Some data have shown that the risk of dependency increases significantly with increasing duration of use.<sup>176</sup> Every effort should be made to minimize prescription length.

The main cause of death in patients using opioids is respiratory depression. This can occur with any opioid regardless of the type or formulation. This deadly complication is dose and concentration dependent with many other variables such as opioid tolerance, body mass index, respiratory disease, obstructive sleep apnea, and concomitant medications. Patients with a history of opioid use are expected to require more opioids for adequate pain relief while experiencing fewer adverse events due to tolerance.<sup>166,177</sup> Common non-life-threatening side effects seen in approximately 10% of patients prescribed immediate-release opioids are pruritus, nausea, vomiting, dizziness, headache, and somnolence.<sup>178,179</sup> Addiction and abuse are complications often seen by psychiatrists or psychologists. Despite early, unsubstantiated claims of improved safety with long-acting opioids,<sup>180</sup> the relative abuse and addiction potential with short-acting or long-acting opioids remains a question. Some evidence suggests that there is no difference in illicit drug use, misuse, or both when comparing long-acting versus short-acting opioids, suggesting that prescribing long-acting opioids will not reduce abuse potential.<sup>181</sup> A contradictory study showed less drug-seeking behavior with extended-release formulations.<sup>182</sup> Benzodiazepines should not be prescribed in conjunction with opioids because the risk of overdose and death increases significantly. There is a 3.9 times risk

of overdose due to respiratory depression when opioids and benzodiazepines are prescribed at the same time.<sup>183</sup>

## Combination Pharmaceutical Strategies

### Multimodal Analgesia

- The panel recommends the use of multimodal analgesia (MMA) as opposed to opioid monotherapy for pain control (strong recommendation, moderate-quality evidence).
- The panel recommends the use of periarticular injections as an adjunct to pain management that improves pain control postoperatively (strong recommendation, moderate-quality evidence).
- The panel cannot recommend specific MMA regimens at this time without further scientific evidence. MMA should be tailored to patients' injuries and medical comorbidities (strong recommendation, very low-quality evidence).

MMA, also referred to as balanced analgesia, is the use of multiple analgesic medications (opioid and nonopioid) and nonpharmacologic interventions designed to affect peripheral and/or central nervous system loci in the pain pathway.<sup>103</sup> Benefits of this treatment paradigm include potentiation of multiple medication effects and greater pain control without relying on any 1 class of medication. MMA therefore mitigates the risk profile of each medication, while allowing for synergistic pain control from different classes of medication. Successful postoperative MMA may include psychotherapy, physical therapy, NSAIDs, acetaminophen, gabapentinoids, regional anesthesia (single shot or peripheral nerve catheters), local injections, and opioids. Recent reviews,<sup>184</sup> meta-analyses,<sup>185</sup> and RCTs<sup>186</sup> have shown that MMA is effective in the perioperative period. There is, however, a paucity of literature in the orthopaedic trauma population, and therefore, literature from other subspecialties and surgical fields was included.

The majority of the orthopaedic literature addresses the arthroplasty population (14 articles). These articles addressed the following 3 main clinical trial questions: (1) comparison of different periarticular injections, (2) oral or "standard" medication regimen versus addition of a peripheral nerve block (covered in later section), and (3) oral or "standard" medication regimen versus MMA.

Four studies compared "standard" medication regimens versus MMA. For example, additions to MMA strategies include gabapentin<sup>187</sup> and duloxetine.<sup>188</sup> Gabapentin seemed to decrease pain scores, but not opioid consumption,<sup>187</sup> whereas duloxetine decreased opioid consumption, but not pain scores.<sup>189</sup>

Finally, 2 studies evaluated the cost-effectiveness of MMA in arthroplasty patients. In both cases, the use of multimodal therapy decreased hospital costs, directly related to medication, and overall hospital costs for patient stay.<sup>190,191</sup>

There is limited literature regarding the use of MMA in other nontrauma orthopaedic subspecialties. Two articles evaluated the use of MMA in foot and ankle surgery where MMA decreased length of stay<sup>192</sup> and decreased pain in the first 24 hours after surgery.<sup>193</sup> In spine surgery, the addition of MMA to a standard PCA regimen, decreased opioid use and improved mobilization.<sup>194</sup> When compared with

intravenous (IV) medication only, MMA decreased VAS scores at all time points following lumbar fusion surgery.<sup>195</sup>

In orthopaedic trauma, addition of periarticular injection to standard pain control for hip hemiarthroplasty improved VAS scores and reduced opioid usage early in the postoperative course.<sup>196</sup> Surgical site injection also improved pain for femoral fracture patients.<sup>197</sup> In the upper extremity, MMA compared with PCA showed additional need for pain rescue in the PCA group and lower patient satisfaction.<sup>198</sup> In a study of emergency department (ED) fracture patients, IV morphine or IV Tylenol + oral oxycodone was equally effective for pain control in the first hour after administration. However, patients in the IV morphine group did have less nausea and site itching.<sup>199</sup>

The use of corticosteroids for postoperative pain has been validated in the literature in other specialties in medicine. As with other medications, there are risks associated with the use of corticosteroids. Systemic side effects often associated with long-term therapy include the following: Cushingoid appearance, hirsutism, exophthalmos, hypertension, arrhythmias, gastritis, osteoporosis, avascular necrosis, dysphoria, and hypokalemia just to name a few. From a postoperative perspective, concerns include a decrease or delay in wound healing potential and infection. There are no data to indicate that short-term use of corticosteroids causes an increase in infection. It is not recommended to use corticosteroids in patients older than 60 years and in immunocompromised patients because some data suggest that there is an increase in healing time.<sup>200</sup> An increase in blood glucose 24 hours after surgery should be expected and has not been associated with an increase in the rate of infection.<sup>201</sup>

Corticosteroids given orally or IV can decrease the use of opioid analgesics by 50%.<sup>202</sup> Benefits of corticosteroids include a decrease in postoperative nausea, decrease in opioid requirements, decrease in the length of hospital stay, and more complete pain relief.<sup>203,204</sup> The smallest dose that is effective should be prescribed. Doses ranging from 15 mg of dexamethasone to 0.1 mg/kg have been shown to be effective with no complications.<sup>201,203,205–207</sup> A meta-analysis of perioperative use corticosteroids concludes that an "intermediate-dose dexamethasone (0.11–0.2 mg/kg) is a safe and effective multimodal pain strategy after surgical procedures. The preoperative administration of the drug provides a greater effect on postoperative pain."<sup>201</sup> Physicians should consider perioperative dosing of corticosteroids in low-risk patients, especially in patients at risk of dependency.

## Managing Acute Pain for Patients on Long-Term Opioids at Presentation

The panel recommends that perioperative analgesia should be managed with a MMA regimen in all opioid-tolerant patients (strong recommendation, moderate-quality evidence).

- The panel recommends coordinating with acute pain service (APS) (or addiction medicine or psychiatry depending on resources) when inpatient and the patient's prescriber when outpatient to ensure that there is only 1 prescriber for patients on medication-assisted therapy (methadone, buprenorphine, or naltrexone), patients using illicit opioids, or patients

misusing prescription opioids (strong recommendation, moderate-quality evidence).

Opioid-tolerant patients present a clinical challenge to effective perioperative pain management. These patients have a medical condition and should be treated with the same respect and dignity as a patient with any other presurgical medical condition. Developed nations have observed a large increase in the number of opioid-tolerant patients over the last decade.<sup>103,208</sup> In the United States, a combination of expanding heroin abuse, pain control metrics, and pharmacologic development of long-acting opioids has resulted in a dramatic increase in the number of opioid-tolerant patients. Managing perioperative pain in the opioid-tolerant patient is both a medical and a social challenge. Opioid-tolerant patients are at an increased risk of receiving inadequate perioperative analgesia.<sup>103</sup> This risk exists as the result of (1) a social stigmatization of opioid prescription and consumption<sup>209</sup>; (2) concerns for drug-seeking behavior<sup>210</sup> or relapse of recovering addicts, or both; and (3) an incomplete understanding of opioid agonist and opioid replacement therapy pharmacokinetics.<sup>211</sup>

Opioid-tolerant patients present with 1 of the following 3 clinical scenarios: (1) scheduled, prescribed opioid (short-acting or long-acting) regimens; (2) prescribed medical assisted therapy (methadone and buprenorphine); and (3) illegal consumption of prescription or nonprescription opioids.<sup>212</sup> Each patient can be further subdivided into those who are actively experiencing acute pain in an emergent setting (secondary to trauma) or whose treatment necessitates elective surgery (nonunion, malunion, infection, and hardware removal). The care of these patients can be difficult, and there is little literature to guide treatment.

At the time of this publication, there are a limited number of observational studies examining acute perioperative pain management in the opioid-tolerant patient. However, care must be taken when managing these patients. In 2 studies on orthopaedic trauma populations, it has been shown that patients on opioids are at a higher risk of receiving prescriptions from multiple prescribers in the postoperative period, which leads to more prescriptions, higher doses, and longer duration of opioid use.<sup>213,214</sup> What follows is a review of available literature and clinical recommendations for perioperative analgesia in the opioid-tolerant patient.

It is critical to identify opioid users immediately after injury or in the preoperative period to avoid uncontrolled acute pain. Physicians should obtain information on type, dose, frequency, and last consumption of all opioids, which will allow conversion to morphine equivalent doses. The opioid-tolerant patient experiences pain, physiologically, differently than the opioid-naïve patient<sup>103,211,215–217</sup> because of the following:

- a. Cross tolerance occurs between different opioids
- b. Increased sensitivity to natural and experimental pain.<sup>103,211,218,219</sup>
  - i. Results in higher-than-expected postoperative pain scores and slower resolution of acute pain in the postoperative period.<sup>211,218</sup>
- c. High-affinity partial  $\mu$ -agonist and antagonist block the effect of standard opioids. When these medications are

used, patients require high opioid doses to displace competitive medications before analgesia takes effect.

The following sections provide brief recommendations for specific populations of opioid-tolerant patients, including those taking chronic short-acting opioid therapy, those using illicit opioids, and those taking methadone, buprenorphine, or naltrexone.

### Chronic Short-Acting Opioid Therapy

Perioperative pain management of patients consuming routine and scheduled oral opioids should include the following:

1. Instructions to continue baseline medication the morning of surgery through the postoperative period.<sup>220</sup>
  - a. If transdermal fentanyl patches are used preoperatively, patients should be converted to an IV morphine equivalent dose. This is because of alterations in fentanyl release during fluid shifts and body temperature changes observed with surgery.<sup>220,221</sup>
2. Titrate short-acting  $\mu$ -agonist to effective pain control.
3. When oral medications cannot be consumed, the 24-hour morphine equivalent dose should be calculated for conversion to IV management until oral medications can be reinstituted.<sup>215</sup>

### Illicit Opioids

Perioperative pain management is further complicated by inaccurate consumption history and variation in strength of illicit drugs:

1. If available, consult addiction medicine, APS, or psychiatry.<sup>103</sup>

### Methadone (Slow-Release Oral Morphine or Opioid Agonist)

Perioperative pain management of patients consuming methadone should include the following<sup>215</sup>:

1. If available, consult addiction medicine, APS, or psychiatry.<sup>103</sup>
2. Continue baseline methadone throughout the perioperative period including the morning of surgery.
3. If unable to take oral medications, convert the 24-hour dose to IV methadone according to the conversion chart and administer in 2–4 divided doses.
  - a. Pharmacokinetics of methadone are influenced by CYP450 and CYP3A4 metabolism and may also vary based on the patient's own metabolism. Consult a pharmacist or APS specialist for conversion to the appropriate morphine equivalent dose.<sup>222</sup>
4. Supplement perioperative pain with short-acting agonist.
5. Close respiratory monitoring due to combined effects.
6. Educate the patient on acute opioid taper.

### Buprenorphine [Partial $\mu$ -Agonist Alone or Mixed With Kappa Antagonist (Naloxone)]

Addiction medicine, APS, or psychiatry (depending on local resources and expertise) should be consulted when managing patients on buprenorphine, which is commonly administered transdermally for chronic pain and sublingually for substitution in opioid abusers.<sup>215,223–225</sup> Owing to the

medication high affinity for Mu receptors and kappa antagonist effect, other agonists may have limited analgesia effect and typically require high doses to achieve affect. For this reason, close respiratory monitoring is required when using short- and long-acting opioids.

Perioperative pain management of patients consuming buprenorphine will vary according to the clinical setting:

1. Elective surgery
  - a. Mild to moderate pain
    - i. Consider management with increased doses of buprenorphine (when low doses are prescribed at baseline)
    - ii. Continue buprenorphine and add short-acting  $\mu$ -agonist
  - b. Moderate to severe pain
    - i. Discontinue 72 hours before surgery and convert to short-acting agonist. 1. Higher-than-expected doses are anticipated for analgesia for 3 to 4 days while buprenorphine is cleared from the body. 2. Reassess analgesia daily and expect to decrease full agonist between days 3 and 43. Manage acute pain with a tapering regimen
    - ii. The patient should be opioid-free for 24 hours before restarting buprenorphine to avoid withdrawal.
2. In acute traumatic presentation
  - a. Conversion to methadone according to conversion tables and titrate dose to effect
  - b. When clinical presentation does not afford conversion and titration, recommend aggressive acute titration to full opioid agonist.
    - i. High doses are required to displace high-affinity buprenorphine from  $\mu$ -receptors
    - ii. Requires continuous cardiopulmonary monitoring

### ***Naltrexone (Opioid Antagonist Often Used to Limit Relapse Following Opioid Dependence Rehabilitation)***

Because of its antagonist mechanism, naltrexone creates a difficult clinical scenario, particularly in the acute traumatic setting. Naltrexone reduces opioid sensitivity by blocking receptors, but also upregulates  $\mu$ -receptors. During initial treatment of postinjury and perioperative pain, a patient may not be sensitive to a short-acting  $\mu$ -agonist and may require many times the normal dose.<sup>226</sup> After 2 weeks, sensitivity to opioids may increase, risking overdose. When the acute pain period is over, and naltrexone is restarted, it carries the risk of inducing withdrawal. Therefore, the recommendation is to consult addiction medicine, APS, or psychiatry.

### **NSAIDs and Fracture Healing**

- The panel recommends for the routine use of NSAIDs as part of a comprehensive analgesic plan for operative and nonoperative fracture care (strong recommendation, low-quality evidence).

One of the major barriers to using non-narcotic analgesics in orthopaedic trauma has been the reluctance to use NSAIDs in the setting of fracture or arthrodesis surgery of any kind. For decades, NSAIDs were avoided because of fears about bone healing. However, a review of the evidence has found the data on the effect of NSAIDs on bone healing

too conflicting to make a clinical recommendation one way or the other.<sup>227–229</sup> Given the proven track record of NSAIDs in alleviating musculoskeletal pain, withholding NSAIDs from our analgesic armamentarium is a significant disadvantage. Under the current circumstances, the basis of this prohibition merits a critical review.

The basic science studies have been conflicting at best. The most rigorous basic science studies are animal models of spinal fusion, whereas fracture healing models yielded mixed results at best.<sup>230</sup> End points for animal studies demonstrated that NSAIDs contributed to reduced mechanical strength (as bone stiffness and load to failure) and delayed time to union.<sup>231,232</sup> Nonetheless, this lack of clarity has reinforced the perception of a deleterious effect. Further animal studies attempted to examine what the possible mechanism of action could be and tried to establish whether there was a lesser impact from COX-2-specific inhibitors compared with indomethacin in the animal setting, again with mixed results.<sup>232,233</sup>

Clinical studies are similarly unclear, but 4 of the clinical studies should be examined critically because they are frequently cited when raising alarm over NSAIDs in fracture healing. Giannoudis et al<sup>234</sup> used a retrospective case-control model to compare femoral shaft fractures that had not healed to a group that healed successfully. The use of NSAIDs was reported to increase the odds of nonunion by 10.7 times (95% CI: 3.55–33.23), but the study was small and underpowered (sample size of 32 patients), NSAID use was severely underrepresented in the control group, and this same sample showed no effect of smoking. Furthermore, by starting with a group of 32 nonunited diaphyseal femur fractures, investigators may well have been preselecting the group most likely to take NSAIDs (for the pain of nonunion). Bhattacharyya et al<sup>235</sup> point out exactly this bias when discussing their finding of higher NSAID use in the subset of humerus fractures that were treated closed and did not heal. To avoid selection bias, Bhattacharyya's group queried Medicare data (1995–2000) from 2 states for patients with a humeral shaft fracture. Starting with nearly 10,000 records, they found 104 patients (1.1%) with a nonunion. They reported that patients who used NSAIDs or opioids within the first 90 days after fracture had relative risks for nonunion of 3.7 (95% CI: 2.4–5.6) or 1.6 (95% CI: 1.1–2.5), respectively.<sup>235</sup> More recently, Jeffcoach and coworkers retrospectively reviewed long bone fractures over a 2-year period at a single trauma center. The patients who had a long bone fracture and received NSAIDs during the inpatient postoperative days (12% of 1901 patients) had an odds ratio for a complication (nonunion, malunion, and infection) of 2.17 (1.15–4.10).<sup>236</sup> In a well-designed, prospective randomized trial on different durations of indomethacin treatment (3 days, 1 week, or 6 weeks) for prophylaxis of heterotopic ossification, Sagi et al<sup>237</sup> showed that at 6 months after surgery, the highest incidence of nonunion of the posterior acetabular wall (67%) occurred in the group with the longest duration (6 weeks) of indomethacin use. Although there were only 13 patients in this group and that raises concerns over adequate power, the rate of nonunion of the posterior wall in all groups was surprisingly high.

Although isolated clinical investigations such as these have been cited as evidence to withhold NSAIDs during fracture treatment, this conclusion is not supported by a critical examination of the existing literature. Two recent comprehensive meta-analyses by Kurmis et al<sup>229</sup> and Marquez-Lara et al<sup>238</sup> have concluded that although some animal studies may raise a concern, there is no high-quality literature support for NSAID inhibition of fracture healing in the clinical setting. Ultimately, these critical evaluations of the existing clinical literature must stand as the cornerstones of our practice guideline recommendations on this issue.

Based on the unknown clinical role of opioids on fracture healing, recent investigations have tried to examine a potential effect of opiate analgesics on fracture healing. Morphine has been demonstrated to inhibit osteocalcin *in vitro*.<sup>239</sup> Chrastil et al<sup>240</sup> used a rat model to examine opioid influence on femur fractures and found that animals treated with opiate analgesia formed callus in greater volume, but that this callus was more disorganized and mechanically weaker than the control animals. Opiate-induced androgen deficiency syndrome describes the naturally occurring reduction in serum testosterone seen clinically with both acute and chronic opioid administration,<sup>241</sup> and Brinker et al<sup>242</sup> have previously demonstrated hypogonadism to be among the metabolic abnormalities identified in patients with nonunion. Chrastil et al<sup>243</sup> attempted to determine whether supplemental testosterone might be used to mitigate the effects of opioids on callus formation and strength, but they found that supplemental testosterone was ineffective for this purpose. This study casts doubt on the theory that the effect of opioids on bone healing is solely mediated by hypogonadism because the opioid-treated animals demonstrated a decrease in serum testosterone, but still had impaired callus formation despite administration of supplemental exogenous testosterone. Overall, any conclusions on the role of opioids in bone healing are very preliminary and have not been corroborated with quality clinical studies, but given its potential impact on clinical practice, the field certainly merits further bench and clinical investigation.

With regard to the effectiveness of NSAIDs for pain control, there are now some head-to-head clinical comparisons available between NSAIDs and opioids for the acute management of musculoskeletal complaints in both the pediatric<sup>244</sup> and adult<sup>245,246</sup> populations. To date, these studies have demonstrated NSAIDs to provide equally effective analgesia.

To summarize, there is simply no conclusive clinical evidence to prohibit the use of NSAIDs in fracture care. Furthermore, risks to the population from oral opioid use, and the prolonged use after resolution of musculoskeletal injury, are well established. NSAIDs also provide effective analgesia in the setting of musculoskeletal pain.<sup>247</sup> Taking all these factors and the existing clinical evidence into account, we recommend the routine use of NSAIDs as part of a comprehensive analgesic plan for operative and nonoperative fracture care.

### Nerve/Regional/Field Blocks

This section is organized around the following 3 periods: (1) during a hospital admission before fracture surgery, (2) intraoperatively and the immediate postoperative period, and

(3) the remote (>3 months) postoperative period. In each of these temporal periods, in relation to fracture surgery, we asked what is the evidence that nerve, or regional, or field blocks improve pain control and decrease use of opioids?

### During a Hospital Admission Before Fracture Surgery

- The panel recommends that regional nerve blocks (femoral nerve or fascia iliaca) should be placed in patients with acute hip fractures at the time of presentation to the ED (strong recommendation, high-quality evidence).

The evidence for this recommendation is confined to hip fracture patients. Multiple studies show that nerve blocks placed in the ED can be accomplished by trained personnel with minimal risks or complications.<sup>248–258</sup> These blocks have consistently been found to be effective in comparison to standard of care (parenteral opioids alone) in decreasing opioid use and improving patient's pain in the preoperative period.<sup>248,251,252,254,256,257</sup> These results have been confirmed in multiple RCTs, and some of these studies are placebo controlled with blinded assessment of the outcome.<sup>252,253,257</sup> Although there is high-quality evidence for these benefits of nerve blocks, instituting routine nerve blocks for hip fracture patients cannot be accomplished by the surgeon in isolation. System-wide changes in practice with involvement of other care providers (emergency medicine and anesthesia) are required.

There are other possible benefits of ED regional nerve blocks for hip fracture patients. One randomized controlled trial (RCT) found that these blocks decrease the incidence of delirium in hip fracture patients who are at an intermediate risk of this condition.<sup>257</sup> Another RCT found a functional postoperative benefit in the hospital (walking distance and stair climbing ability) that lasted until 6 weeks after surgery.<sup>256</sup> There is less strength of evidence for these benefits because they have only been assessed in 1 study each.

The nerve block technique has varied between studies. Some studies have used a 3-in-1 femoral nerve block (FNB), whereas others recommend a fascia iliaca block. Most studies recommend ultrasound guidance for either type of block.<sup>249,255</sup> The fascia iliaca compartment block requires less precision and is probably more easily learned. The location is more remote from the neurovascular bundle and thus nearly eliminates the risk of intraarterial injection. Femoral nerve and fascia iliaca blocks have also been shown to have similar efficacy in TKA patients.<sup>250</sup> Recommended training has been 30 minutes of didactic training, followed by variable periods of practice and supervised clinical performance. This short duration of training, however, may assume preexisting ultrasound skills.<sup>249,252</sup>

Five studies have compared “standard” preoperative MMA to the addition of a nerve block. Addition of an FNB to preoperative oxycontin and celecoxib did not make a difference in TKA patients.<sup>259</sup> YaDeau et al,<sup>260</sup> however, showed lower VAS pain scores with addition of an FNB to standard epidural anesthesia. Divella's group evaluated resting and dynamic VAS scores for 3 days after total hip arthroplasty. Pain control was oxycontin and acetaminophen versus continuous epidural levobupivacaine. Resting VAS scores between the 2 groups were similar for days 1 and 2, but VAS scores

were significantly lower on day 3 for patients in the oxycontin group. Dynamic VAS scores for the oxycontin group were higher on day 1 and lower on day 3.<sup>261</sup> The use of general anesthesia (GA) with preoperative oxycodone and celecoxib versus intrathecal bupivacaine, morphine, and clonidine showed higher pain scores, faster time to first rescue medication need, and longer length of stay in the GA group.<sup>262</sup> Addition of multimodal postoperative pain medication (including oxycodone, tramadol, and ketorolac) compared with parenteral PCA showed less narcotic consumption, lower pain scores, and higher satisfaction and higher physical therapy goal achievement in the MMA group.<sup>263</sup>

The studies reviewed have not reported any complications of blocks, but most admit that the study was not powered to detect rare complications. Clinicians should be aware of the possibility of complications such as inadvertent intravascular injection, infection, intraneural injection, and masking symptoms of compartment syndrome.<sup>251</sup> All studies report a rapid onset of pain relief from these blocks; however, the effect is often not complete, and adjunctive analgesics are often necessary.<sup>252</sup>

### Intraoperatively and the Immediate Postoperative Period

- The panel recommends that clinicians consider local or regional block anesthesia during operative treatment of fractures and as part of the postoperative multimodality pain control regimen (strong recommendation, high-quality evidence).
- The panel recommends that if a block is going to be performed for intraoperative and postoperative pain control, a continuous catheter be considered over a single-shot block to better facilitate postoperative pain control and diminish rebound pain (conditional recommendation; moderate-quality evidence).

The use of peripheral anesthesia via local injections, field blocks, single-shot regional blocks, and indwelling catheter regional blocks have all been shown to decrease pain scores and opioid consumption in the immediate and short-term perioperative period. The bulk of these data comes from the arthroplasty literature with contributing articles from the sports medicine, foot and ankle, and trauma literature.<sup>264</sup> The data outside the orthopaedic literature are even more robust. Problems with these lower extremity blocks include a possible increase in rate of falls and rebound pain that has been reported in some studies.

Five articles have compared various periarticular injections. Early postoperative pain scores and opioid usage were lower with continuous femoral nerve catheter plus sciatic block than with periarticular injection with ropivacaine or liposomal bupivacaine.<sup>265</sup> Ng et al,<sup>266</sup> however, found equivalent outcomes with femoral nerve catheter versus periarticular injection. In addition, periarticular injection alone was not superior to postoperative epidural analgesia for pain control.<sup>267</sup> The addition of periarticular liposomal bupivacaine to a periarticular injection cocktail was more effective than ropivacaine at 6 and 12 hours postoperatively; however, intrathecal morphine was more effective at 6 hours.<sup>268</sup>

Addition of ropivacaine and ketorolac to a periarticular injection cocktail improved postoperative pain control.<sup>269</sup>

In 1 RCT, a significant decrease in opioid consumption and better pain scores was found at 48 hours after hip arthroscopy in patients who received an FNB versus GA. However, the FNB group had a significant increase in the rate of falls compared with the GA group, highlighting one of the risks of this type of anesthesia, which in part accounts for its moderate recommendation.<sup>270</sup>

In another RCT, the benefit of local injection was assessed. A significant decrease in pain scores and opioid consumption was found for 8 hours and trended less over 48 hours in patients receiving a local injection compared with GA alone for femur fractures. The injection (containing ropivacaine, morphine, and epinephrine) was administered at the time of surgical fixation of the fracture. There were no complications attributed to the local injection itself.<sup>197</sup>

Preoperative sciatic or popliteal continuous peripheral nerve block (CPNB) was compared with postoperative PCA in a retrospective study of patients undergoing fixation of talus and calcaneal fractures. Although Numerical Rating Scale pain scores, duration of stay, and side effects were equivalent in the 2 groups over 72 hours, morphine equivalent consumption on postoperative day 1 by the PCA patients was 30-fold that of the CPNB patients.<sup>271</sup>

A single-shot popliteal (SSP) block was compared with an intraoperative ankle block in an RCT of patients undergoing elective forefoot surgery. The length of block time in the popliteal block group was 44% longer than the ankle block group. Although the patient satisfaction and perceived effectiveness with both types of blocks were similar, the popliteal block group showed significantly lower VAS pain scores the night after surgery and throughout the next morning.<sup>272</sup>

In an RCT of patients undergoing open reduction and internal fixation of distal radius fractures, GA patients needed more IV pain medications in the post-anesthesia care unit compared with those who received a single-shot brachial plexus block. In the 12–24 hours after surgery, patients who received the block showed a more aggressive increase in VAS scores and narcotic use consistent with the block wearing off and the patients experiencing rebound pain. Ultimately, the GA group had a statistically significantly higher total narcotic use at 72 hours compared with the block group.<sup>273</sup>

Peripheral anesthesia in the form of a block can be administered either via a single-shot injection or by placing a catheter that has the ability to deliver anesthetic around the nerve in a continuous fashion until the catheter is removed. Rebound pain is the pain a patient experiences when the block wears off and can be quite significant. This is typically because the patient has not been taking other postoperative pain medications because of low pain scores during the duration that the block has been in effect.

Goldstein et al<sup>274</sup> addressed the problem of rebound pain phenomenon and were one of the first groups to write about this effect. They compared an SSP block with GA in an RCT of patients undergoing fixation of ankle fractures. Significantly lower pain scores were reported for the block group at 2, 4, and 8 hours after surgery, but significantly better pain scores were found in the GA group from 8 to 24 hours.

There is some evidence that continuous catheters control pain for a longer duration of time and may help diminish rebound pain by allowing the patient to get farther in the recovery process. In 1 RCT, an SSP block was compared with a CPNB in patients undergoing fixation of unstable ankle fractures. The CPNB catheter was removed at 48 hours. Over the first 72 hours, patients in the CPNB group took significantly fewer oral narcotics and had lower pain scores.<sup>275</sup> Another study of patients undergoing open fixation for calcaneal fractures compared controls (no regional blocks) versus a single-shot block or against a continuous popliteal nerve block. In the 36 hours after surgery, the patients in the continuous block used significantly fewer IV narcotics than did the other 2 groups. However, a limitation of this study was that their postoperative pain protocol changed multiple times during the course of the study.<sup>276</sup>

**Remote (>3 Months) Postoperative Period**

- The panel makes no recommendations for this period because we were unable to find any data to guide us on whether regional or local anesthesia performed before, during, or in the immediate postoperative period has any effect on improving pain scores or decreasing opioid consumption at this time frame (no recommendation, no evidence).

**Pain/Sedation Assessment**

**Inpatient Pain Assessment**

- The panel recommends regular assessment of pain for both inpatients and outpatients to evaluate the need for initiation or continuation of opioid therapy (strong recommendation, low-quality evidence).

Effective January 1, 2018, the Joint Commission required new and revised pain assessment and management standards to improve quality and safety of care.<sup>277</sup> The requirements speak to (1) prioritization of pain assessment and management as an organizational priority, (2) establishment of medical staff in leadership roles to address performance improvement activities related to patient safety, (3) assessment and management of patient pain and minimization of risks associated with treatment with opioids, (4) data collection to monitor performance related to patient safety, and (5) compilation and analysis of data to inform continued performance improvement.

**Inpatient Pain Assessment**

- The panel recommends that sedation assessment be conducted by nursing staff on all inpatients before and after administration of an opioid medication (strong recommendation, low-quality evidence).

In 2012, the Joint Commission issued a warning regarding adverse drug events associated with opioid analgesics, most importantly respiratory depression, among patients in the inpatient hospital setting.<sup>278</sup> The incidence of opioid-induced respiratory depression ranges from 0.1% to 37%.<sup>279</sup> Nurses are typically the first to detect respiratory depression.<sup>280</sup> One cause of opioid-related adverse events, however, is inadequate monitoring of patients administered opioids, occurring in about a third of cases.<sup>278,280</sup> Patient monitoring includes sedation assessments, frequency and quality of respirations, and electronic methods such as pulse oximetry. A survey of nurses belonging to the American Society for Pain Management Nursing<sup>281</sup> indicated that nurses find sedation scales and watching the patient to be more useful than electronic methods. However, although there is no evidence to inform the frequency of monitoring, sedation scale scores should be a major consideration in the decision to administer opioids for pain management. It is important to monitor sedation because it is an indicator of impending opioid-induced respiratory depression; detecting oversedation can prevent a more clinically significant adverse event. The Pasero<sup>282</sup> Opioid-Induced Sedation Scale<sup>283</sup> (Table 5), which has been validated for assessing sedation during opioid administration,<sup>284</sup> is an example of a tool that can be used by nurses to assess patients before and after administration of prescription opioids.

**Naloxone**

- The panel recommends coprescribing of naloxone when factors that increase the risk of overdose are present (strong recommendation, low-quality evidence).

For patients prescribed opioids, risk mitigation strategies are an important consideration. Although limited evidence exists on the outcomes of prescribing naloxone in combination with opioids, distribution via community-based harm reduction programs has demonstrated a decreased risk of death due to opioid overdose.<sup>285–288</sup> Most programs, however, have been conducted with illicit use populations with a focus on harm reduction as opposed to a patient safety focus for patients prescribed opioids for acute or chronic conditions. The *Centers for Disease Control and Prevention Guideline*

**TABLE 5.** Pasero<sup>283</sup> Opioid-Induced Sedation Scale With Intervention

Score	Category	Intervention
5	Sleepy, easy to arouse	Acceptable; no action necessary; may increase opioid dose if needed
1	Awake and alert	Acceptable; no action necessary; may increase opioid dose if needed
2	Slightly drowsy, easily aroused	Acceptable; no action necessary; may increase opioid dose if needed
3	Frequently drowsy, arousable, drifts off to sleep during conversation	Unacceptable; monitor respiratory status and sedation level closely until sedation level is stable at less than 3 and respiratory status is satisfactory; decrease opioid dose 25%–50% or notify prescriber or anesthesiologist for orders; consider administering a nonsedating, opioid-sparing nonopioid, such as acetaminophen or an NSAID, if not contraindicated
4	Somnolent, minimal or no response to verbal or physical stimulation	Unacceptable; stop opioid; consider administering naloxone; notify prescriber or anesthesiologist; monitor respiratory status and sedation level closely until sedation level is stable at less than 3 and respiratory status is satisfactory

for Prescribing Opioids for Chronic Pain<sup>25</sup> recommends co-prescribing or offering naloxone to patients with an increased risk of opioid overdose who are prescribed opioids. These risk factors include history of overdose or substance use disorder, opioid dosages  $\geq 50$  MME/d, or coprescribing with benzodiazepines.

## System Strategies

### Prescription Drug Monitoring Programs

- The panel recommends that all prescribers register to gain access to their state's Prescription Drug Monitoring Program (PDMP) and regularly query the PDMP before prescribing opioids (strong recommendation, low-quality evidence).

PDMPs are databases that track scheduled medications dispensed from pharmacies. The databases were developed to reduce prescription drug misuse and diversion. The conceptual model of PDMPs assumes that increased monitoring of opioid prescriptions is associated with changes in opioid prescribing behavior, opioid diversion and supply, and opioid-related morbidity and mortality.<sup>289</sup> Numerous unintended consequences of PDMPs have been described in the literature and include the following: (1) potential decrease in legitimate prescribing, (2) patient privacy concerns, (3) inability to connect patients with known aberrant use to resources, (4) potential increase in illegal prescription drug activity or users switching to other substances such as heroin, (5) further reduced patient visit time due to time required to check PDMP, and (6) potential decrease in patient satisfaction ratings.<sup>290</sup> Finally, PDMPs vary tremendously from state to state based on (1) the number of schedules included, (2) the frequency of updates, (3) housing entities, (4) accessibility, (5) access requirements, (6) reactive and proactive reporting, (7) associated prescriber education, and (8) interstate data sharing.<sup>290</sup>

Four reviews of PDMPs have been published to date,<sup>289–292</sup> with the most recent one synthesizing articles published through 2015.<sup>289</sup> Worley et al concluded that PDMPs were associated with lower substance abuse treatment admission rates, fewer opioid prescriptions, less diversion, and less “doctor shopping.” The authors acknowledge, however, that results depend on the specific components of each unique PDMP and that evidence is limited.<sup>291</sup> Haegerich et al<sup>292</sup> believe PDMPs to be effective, but that effect sizes from the articles they reviewed were generally very low and may depend on specific PDMP components such as mandatory review or proactive reporting. Gugelmann et al<sup>290</sup> concluded that PDMPs seem to have benefits including reduced per capita supply of opioids and fewer incidents reported to poison control centers; however, there are also studies showing no effect. Finally, Finley et al<sup>289</sup> found no consistent pattern, with efficacy varying by state.

Several articles on PDMP efficacy have been published since 2015, and the results have been mixed as well. The Florida PDMP was associated with a 25% decrease in oxycodone-caused deaths,<sup>293</sup> but a multistate study found that PDMPs were not associated with reduction in overdose deaths and were, in fact, sometimes associated with increased mortality from nonprescription opioid drugs, such as heroin.<sup>294</sup> There

was also evidence of increased ED visits for heroin overdoses in New York, whereas visits for prescription opioid overdose leveled.<sup>295</sup> In contrast, Dowell et al<sup>25</sup> found “relatively large but statistically insignificant reductions” in heroin overdose deaths, indicating that perhaps a decrease in opioids does not lead to an increase in heroin use.

Three studies on PDMP implementation found no association with decreased opioid prescribing,<sup>296–298</sup> whereas 3 others found that PDMP implementation reduced opioid prescriptions<sup>25,299,300</sup> and overdose deaths.<sup>25</sup> Some studies found PDMPs to be effective in specific groups, such as patients with multiple provider episodes (ie, “doctor shopping”) whose prescribers were sent an unsolicited report by the state,<sup>301</sup> Medicare Part D enrollees,<sup>302</sup> and Medicaid patients.<sup>299</sup> Finally, because of the variability in PDMPs by state, 1 study rated the strength of the PDMP and found that a 1% increase in PDMP strength was associated with a 1% decrease in overdose deaths, indicating room for improvement in outcomes for PDMPs of lower strength.<sup>303</sup>

Although the literature remains inconsistent, PDMPs are a promising intervention, especially when the PDMPs are of robust strength. We recommend checking the PDMP before prescribing. Steps must be taken, however, to alleviate the potential consequences of curtailing prescribing based on the results of a PDMP search, particularly the potential for patients to switch to heroin. Therefore, we recommend referring patients to behavioral health and addiction medicine if the PDMP indicates aberrant behaviors. Furthermore, the evidence does demonstrate that PDMPs are not a panacea for preventing prescription opioid misuse, abuse, and diversion.

### Prescriber and Patient Education

- The panel recommends that departments support opioid education efforts for prescribers and patients (strong recommendation, moderate-quality evidence).

Physicians often lack training in pain management and addiction; 59% of physicians report medical school preparation regarding chronic pain treatment as “fair” or “poor,”<sup>304</sup> and median instruction time spent on pain education in US medical schools is 11.1 hours compared with 27.6 hours in Canada.<sup>305</sup> After graduate medical education, only 5 states (CT, IA, MD, SC, and TN) require physicians to obtain periodic continuing medical education (CME) on prescribing, substance use disorders, or pain management.<sup>306</sup>

The effectiveness of educational interventions for physicians is strong. A synthesis of reviews on CME education finds that studies on CME interventions consistently show improvement in both physician performance and patient health outcomes.<sup>307</sup> The most effective CME sessions are interactive, use multiple methods, involve multiple exposures, and are longer.<sup>307</sup> After New Mexico began requiring CME in 2012–2013 about pain and addiction along with required PDMP registration and query, the state saw statistically significantly increased physician knowledge, self-efficacy, and attitudes, as well as a decrease in both statewide morphine milligram equivalents dispensed and drug overdose deaths.<sup>308</sup> Online educational interventions have been moderately effective.<sup>309</sup> Education in conjunction with clinical decision support is also effective at changing naloxone prescribing rates.<sup>310</sup>

Other strategies described in the literature include brief one-on-one physician education,<sup>311,312</sup> development and dissemination of guidelines and policies,<sup>313,314</sup> and Risk Evaluation and Mitigation Strategy.<sup>315</sup> Public health detailing is an approach based on the pharmaceutical sales strategy, by which messages are pushed using brief one-on-one educational visits during the normal workflow. Staten Island saw a reduction in high-dose prescribing and stabilizing of days' supply after implementing this strategy.<sup>311</sup> Similarly, an ED in Australia delivered one-on-one education via a clinical champion and was very effective at improving information given to patients, increasing notifications sent to general practitioners, reducing total dose prescribed, and incorporating nonopioid therapies.<sup>312</sup> This approach is, however, resource intensive and has a limited scope of impact.

Development of department guidelines, policies, or both is another option. Hill et al described an intervention within surgical specialties at an academic medical center, which included dissemination of operation-specific opioid prescribing guidelines. This intervention significantly reduced the number of pills prescribed.<sup>313</sup> When a similar approach was implemented in the ED setting, the number of patients prescribed opioids and number of pills prescribed decreased by 40% and 15%, respectively, with reductions sustained over 2.5 years.<sup>314</sup> Finally, Risk Evaluation and Mitigation Strategies developed by the FDA in 2007 required pharmaceutical manufacturers to take steps to reduce risks associated with the medication. Strategies can include medication guides for patients, clinician education, and physician certification.<sup>316</sup> Both immediate-release and extended-release opioids are now subject to these regulations.<sup>317</sup> Thus, manufacturers are required to fund continuing education regarding opioid prescribing. Overall, the resulting SCOPE of Pain educational program has been shown to increase physician knowledge and reported intention to change practice.<sup>318</sup> The SCOPE of Pain program has also implemented a "train the trainer" approach, which facilitates wide dissemination of information.<sup>315</sup> Physicians are advised to be aware of potential conflicts of interest when attending pharmaceutical company-funded sessions.<sup>319</sup>

Overall, education is a necessary, but insufficient, approach to improving prescribing and patient outcomes. In addition, the literature is mostly limited to opioids for chronic pain management rather than acute or postsurgical pain. Regardless, we recommend supporting opioid education efforts both in graduate medical education and through continuing education.

Literature that focuses on evaluating the effects of patient education is limited, but the few studies conducted support effective patient education. Strategies included educational pamphlets,<sup>320–322</sup> web-based interactive education,<sup>323</sup> and clinician-delivered education.<sup>324,325</sup> All interventions that included knowledge as an outcome demonstrated a significant effect,<sup>320,322,323,325</sup> and many studies observed changes in risky behaviors, such as sharing pills,<sup>320,323</sup> pill storage,<sup>320</sup> saving and disposal of pills,<sup>320,321,323,324</sup> driving,<sup>322</sup> and taking more medication than prescribed.<sup>323</sup>

### Clinical Decision Support

- The panel recommends that prescribers, to the extent possible, develop, support, or both the implementation of clinical

decision support regarding opioid prescribing in the electronic medical record (strong recommendation, low-quality evidence).

We reviewed the literature on the impact of clinical informatics interventions on opioid prescribing. A total of 14 articles were identified that included prescribing outcomes, and the quality of the evidence was low. Most of the studies used study designs that did not have any concurrent control group. This is a significant weakness because of the national attention surrounding the opioid crisis currently in lay press, politics, and medicine. Without concurrent controls, the effects seen after implementation of these interventions could be overestimated if prescribing was already decreasing due to the current climate around opioids. There were, however, 2 randomized controlled trials that demonstrated an effect on some outcomes.<sup>326,327</sup> Most of the 14 studies included patients in the ED<sup>326,328–331</sup> or specifically for patients receiving chronic opioid therapy.<sup>327,332–334</sup> Only 1 study assessed clinical decision support in an orthopaedic surgery population.<sup>335</sup>

There is a gap in the literature surrounding acute pain outside of the emergency department, other than after cesarean section<sup>336</sup> and following hand surgery.<sup>335</sup> This is an important area of research because a short course of opioid treatment for acute pain can often result in chronic opioid therapy.<sup>10</sup>

All these studies were conducted in urban settings or across a wide area including both urban and rural settings. It is critical to study these interventions in rural areas because they are substantially burdened with this epidemic.<sup>337</sup> In addition, prescriber response to these interventions may differ in outlying hospitals and in practices that are not part of an academic hospital where prescribers are consistently exposed to new literature, new techniques, and other clinical innovations. In addition, numerous articles were identified that described clinical decision support regarding opioids but did not report on outcomes of the intervention.

Although these feasibility and implementation articles are important for fully describing interventions, decisions cannot be made regarding continuation, iterative improvement, or adoption of the intervention by another institution without evidence of efficacy. The lack of follow-up outcome articles could represent publication bias, whereby articles in the literature are more likely to have been effective. For example, only 1 study found no effect of the intervention,<sup>331</sup> whereas the rest of the interventions were effective,<sup>328,329,332–334,336,338,339</sup> or mixed (had effect on some outcomes but not all).<sup>326,327,330,335,340</sup> Finally, most studies included outcomes associated with prescriptions (ie, number of prescriptions, number of pills, average dose, number of risky concurrent prescriptions for opioids with benzodiazepines, and number of extended-release prescriptions).<sup>326,328,330,331,335,336,338–340</sup> Others measured outcomes associated with safe prescribing (ie, urine drug screens, treatment agreement, functional assessments, risk assessments, and documented diagnosis).<sup>327,329,332–334</sup> The conceptual framework implicitly presented is that these interventions lead to safer prescribing practices that lead to fewer high-risk prescriptions that in turn ultimately reduce the risk of misuse, abuse, or diversion of prescription opioids. However, no studies measured rates

of overdose, opioid use disorder, or other outcomes to demonstrate this pathway.

Despite the low-quality evidence, we strongly recommend pursuing clinical decision support to the extent possible. Potential approaches include power plans/order sets,<sup>331,335,340</sup> dashboards,<sup>332,338,339</sup> risk assessment and screening,<sup>327,329,333</sup> alerts,<sup>326,328,330</sup> and other decision support.<sup>334,336,339</sup>

Order set interventions could include recommended pain management regimens and dosing based on patient characteristics,<sup>340</sup> prepopulating the dosing at a minimum rather than a range (ie, 1 pill 4× per day rather than 1–2 pills 4–6 times per day),<sup>335</sup> and including nonopioid medication options.<sup>335</sup>

Dashboards are useful for tracking physician adherence to guidelines and protocols. They are particularly useful because they provide actionable information to the prescriber.<sup>341</sup> For example, a prescriber can see what patients are due for a certain screening and conduct the appropriate screening at the patient's next visit. Dashboards can also promote transparency, accountability, and natural competition by which prescribers compare their statistics with those of their partners, leading to improved performance.<sup>342</sup> Dashboards vary in the metrics tracked (eg, urine drug screens, pain agreements, functional status assessment, visits with behavioral health providers, high-dose opioids, and concurrent opioids and benzodiazepines).<sup>332,338</sup> Dashboards also vary regarding the level of integration into workflow. Some are housed on the intranet for prescribers to access on demand,<sup>332</sup> whereas others are "pushed" to prescribers at defined time intervals.<sup>332,338</sup>

Many risk assessment tools are accessible that indicate the risk of opioid abuse, misuse, and diversion. Available tools include the Opioid Risk Tool,<sup>343</sup> the Screener and Opioid Assessment for Patients with Pain,<sup>344</sup> the Drug Abuse Screening Test,<sup>345</sup> the Brief Risk Interview,<sup>346</sup> and the Current Opioid Misuse Measure.<sup>347</sup> In addition, guidelines recommend that providers screen patients before prescribing opioids, although the Centers for Disease Control and Prevention guidelines caution against placing full confidence in the sensitivity and specificity of these screening tools because consequences of underestimation or overestimation of risk can be significant.<sup>348</sup> An electronic risk assessment program called Pain Assessment Interview Network, Clinical Advisory System (PainCAS)<sup>327,333</sup> is completed by the patient before their visit, either at home or on registration at the clinic, and includes the Screener and Opioid Assessment for Patients with Pain and Current Opioid Misuse Measure, both validated instruments. Once completed, administrative staff uploads the report to that patient's electronic medical record. Another electronic assessment is a short 3-item screening for tobacco, alcohol, and drug use that is programmed into the electronic triage tool in the ED.<sup>329</sup> These studies report a significant increase in screening and documentation; however, their use does not seem to alter patient clinical outcomes.

Alerts were originally developed to reduce adverse drug events by alerting the provider to contraindications or allergies associated with medications.<sup>349–351</sup> Since then, alerts have been developed for additional situations, including opioid risk. It is critical when developing alerts to ensure

information is meaningful and does not trigger at unacceptable rates, thus causing "alert fatigue."<sup>352</sup> Alerts may include patient risk factors,<sup>328</sup> suggest nonopioid medications or nonpharmaceutical modalities,<sup>328</sup> inform the prescriber that the patient was referred to pain management,<sup>330</sup> or inform the prescriber that the patient has an existing opioid care plan.<sup>326</sup>

Other examples of decision support implemented in the included articles include "smart set" documentation, a patient-facing tablet decision aid, and comprehensive prescribing tools. "Smart set" documentation standardizes practices by walking prescribers through the appropriate prescribing policies.<sup>334</sup> Similarly, another study described implementation of a large set of decision aids into the electronic medical record as part of Safe and Appropriate Opioid Prescribing Program.<sup>339</sup> Aids included medication menus, medication alerts, preferred and maximum doses, links to guidelines, prompts for alternative treatments and medications, patient treatment agreements, and a link to the PDMP. Finally, 1 article discussed a patient-facing decision aid in which patients used a tablet-based decision tool to learn about postcesarean pain and oxycodone to guide her in making decisions about the number of pills she wanted.<sup>336</sup>

These approaches are promising interventions to improve patient safety and reduce opioid prescribing. Many of these interventions included multiple components in addition to the electronic tool such as pocket cards, educational sessions, prescribing policies, care plans, and patient-facing pain policies.<sup>326,328,335,339,340</sup> Although a multipronged intervention has a greater likelihood of success, it is challenging to identify the unique contribution of the electronic tool in each case.

## CONCLUSIONS

Balancing comfort and patient safety following acute musculoskeletal injury is possible when using a true multimodal approach including cognitive, physical, and pharmaceutical strategies. In this document, we attempt to provide practical, evidence-based guidance for clinicians in both the operative and nonoperative settings to address acute pain from musculoskeletal injury. We also organized and graded the evidence to both support recommendations and identify gap areas for future research.

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