Treating acute pain without overusing opioids

Evidence-based pain management approaches

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Alosa Health

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The Harvard Medical School designates this enduring material for a maximum of 1.25 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Activity Overview:

The primary goal of this educational program is to address the need for safe, effective pain relief among older adults across a range of settings. Achieving functional goals while avoiding harm from side effects, addiction, or potential overdose is challenging in this patient population due to such issues as altered pharmacodynamics/pharmacokinetics with age; polypharmacy; potential cognitive deficits; and heightened risk of falls and organ-specific vulnerabilities.

The educational program has several components, which include:

- Written evidence report (print monograph)
- Summary document of top 4-5 key messages
- “Academic detailing” educational sessions in physicians’ offices with trained outreach educators (pharmacists, nurses, physicians) who present the material interactively
- Reference cards for easy access to key materials
- Patient education information (brochure/tear off sheets)

This program works to synthesize the current clinical information on this topic into accessible, non-commercial, evidence-based educational material, which is taught interactively to providers by specially trained clinical educators.

Target Audience:

The educational program is designed for primary care physicians practicing internal medicine, primary care, family practice, and geriatrics, and other health care professionals who deliver primary care.

Learning Objectives:

Upon completing this activity, participants will be able to:

- Optimize the use of non-opioid alternatives before considering opioids to manage different types of acute pain conditions.
- Explain the evidence supporting the efficacy and risks of different treatment options for acute pain conditions.

- Follow recommended principles for responsibly prescribing opioids for acute pain if opioids are necessary.
- Establish realistic expectations for patients about the analgesic efficacies of different acute pain treatment options to reduce their concerns and limit demands for opioid analgesics.
- Use a multimodal strategy for managing acute pain that combines non-pharmacologic and non-opioid pharmacologic options.
- Prescribe naloxone for at-risk patients and/or partners/family members.

Disclosure Policy:

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Media used:

Printed educational material.

Instructions for Participation and Credit:

There are no fees to participate in this activity. To receive credit, participants must (1) read the statements on target audience, learning objectives, and disclosures, (2) study the educational activity, and (3) complete the post−test and activity evaluation. To receive *AMA PRA Category 1 Credit*™, participants must receive a minimum score of 70% on the post−test.

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Why focus on acute pain?

In the past decade, much popular and professional attention has been paid to the management of chronic non-cancer pain and, in particular, the range of problematic issues related to treating chronic pain with opioid analgesics.[1-4] The management of acute pain, in contrast, has, until recently, "flown under the radar" of professional scrutiny.[5] It is now becoming clear, however, that many of the problems and risks associated with managing chronic pain with opioids are also at play in when managing acute pain with opioids. For example, a number of studies demonstrate increased risk of new persistent opioid use in opioid-naïve patients after having been prescribed opioids for acute pain.[6-9] Although the risk of opioid misuse in patients prescribed opioids for acute post-surgical or post-procedural pain is relatively small (absolute risk roughly 0.6% per year),[10] the volume of such procedures[11] translates into large numbers of patients who may develop iatrogenic dependence, abuse, or overdose every year.

A related issue with opioid prescription for acute pain is the risk of diversion or inappropriate use from leftover pills. Approximately 40-50% of those who abuse opioids initially obtain the drugs from family members or friends with pills remaining from legitimate prescriptions.[12] Many studies have found excessive levels of routine opioid prescriptions for a range of surgical procedures or emergency department visits for painful conditions.[13,14] One study of 1,416 patients in a 6-month period found that surgeons prescribed a mean of 24 pills (standardized to 5 mg oxycodone) after a procedure, but patients reported using a mean of only 8.1 pills (utilization rate 34%).[15] A comparison of opioid prescribing by dentists in the U.S. vs. the United Kingdom (U.K.) found that 22.3% of U.S. dental prescriptions were for opioids vs. 0.6% in the U.K. (difference 21.7%; 95% CI: 13.8%-32.1%).[16]

Renewed attention on acute pain management is also warranted because both under-treatment and over-treatment of acute pain can set the stage for the development of chronic pain.[17] A 2019 trial of prophylactic treatment to reduce post-operative persistent pain, for example, randomized 200 women having surgery for breast cancer to perioperative pregabalin plus usual operative anesthesia vs. placebo plus usual anesthesia.[18] Pregabalin was given as 75 mg twice daily, starting one hour before surgery and for a week post-operatively. Three months later, the incidence of neuropathic pain was 14% in the pregabalin group vs. 32% in the placebo group ($P=0.002$), and the incidence of post-mastectomy pain syndrome was 11% vs. 29% ($P<0.001$).[18] The 7-day period of pregabalin treatment covered the postoperative hyperexcitability and excitatory neuroplasticity of dorsal horn neurons that is known to persist for 5-6 days after surgery. The authors suggest that the reduction in post-surgical chronic pain resulted both from the direct effects of the pregabalin, as well as from the reduced need for opioid analgesics in the intervention group, which "reduced the probability of opioid-induced hyperalgesia."[18]

Older patients are at increased risk of acute pain due to higher rates of degenerative conditions such as osteoarthritis, and higher rates of surgery or other invasive procedures.[19] In those aged ≥65 years, acute pain leads to about 4 million U.S. emergency department (ED) visits each year.[20]

Assessing and treating pain in older patients is often complicated, however, by age-related physiologic changes, physical accessibility to treatment, psychosocial concerns, frailty, poor memory, coexisting illnesses, polypharmacy, and communication problems related to cognitive impairment. Clinical decision-making must take into account all of these considerations, each of which can increase the risk for adverse outcomes. Managing acute pain with opioids is particularly problematic in older adults, not only because of the risks of misuse, abuse, addiction, and overdose, but because older adults may be more sensitive to

adverse events (e.g., constipation and falls) and reduced hepatic or kidney function can lead to higher-than-expected blood levels of analgesic.

This evidence document outlines the principles of effective acute pain management in older adults, with special emphasis on ways to limit the use of opioids to those times or conditions for which the known risks of opioid therapy are outweighed by their benefits. It also reviews evidence for three pain syndromes common in older adults: acute low back pain, post-operative pain, and acute musculoskeletal pain. Finally, it offers recommendations on the management of acute pain in patients who use opioids on a long-term basis, either for chronic pain or as part of medication-based treatment for opioid use disorder (OUD).

Defining acute and chronic pain

Acute pain is defined as having an abrupt onset and is typically due to an obvious cause, such as an injury or surgical procedure. It generally has a short duration and usually lasts less than four weeks, improving with time.[21] Acute pain is one of the most common presenting complaints in ambulatory care.[22]

In contrast, chronic pain is defined as lasting more than three months or past the time of normal tissue healing. It can result from an underlying medical disease or condition, injury, medical treatment, inflammation, or an unknown cause.[23] (Chronic pain is addressed in a separate Alosa Health module, which is available at AlosaHealth.org/Opioids.)

Although pain is expected after injury or surgery, the patient pain experience can vary markedly. The intensity of pain can be influenced by psychological distress (depression/anxiety), heightened concern or anxiety about an illness, and ineffective coping strategies regarding the ability to control pain and function despite it.[24] It may also be shaped by personality, culture, attitudes, and beliefs. For example, injured soldiers who had positive expectations of pain (e.g., evacuation and safe recuperation) requested less analgesic medication than civilians with comparable injuries who had more negative associations with pain (e.g., loss of wages and social hardship).[21]

Assessing acute pain

Acute pain intensity can be assessed with unidimensional tools such as the Visual Analog Scale and Numeric Rating Scale (0-10 scales with higher numbers indicating worse pain) and the Wong-Baker FACES Pain Rating Scale (faces depicting increasing levels of pain).

While useful for a quick assessment, these scales alone may not appropriately identify patients with pain-related suffering driven by functional limitations, worry, or other factors, and may not detect some patients with clinically significant pain.[25]

Although developed for patients with chronic pain, the Brief Pain Inventory (BPI) is also applicable to patients with acute pain. Completed by the patient, the BPI captures ways that pain impacts function and quality of life, although, like most multidimensional questionnaires, it requires more time (about 10 minutes) and concentration to complete, which may limit its utility in some elderly patients.[26] See Appendix I for a sample of the BPI.

Assessing pain in patients with cognitive impairment

Cognitive impairment and/or language deficits can be major barriers to adequate pain assessment and treatment in the elderly.[27] Patients with severe dementia may be unable to report or describe pain, or request analgesia. Asking the patient to point to the body part that hurts can be useful in cognitively impaired older adults. Pain maps have been used among adults of all ages with both acute and chronic pain and have been effectively used with cognitively impaired elderly patients in long-term care facilities.[28]

Pain assessment can also be hampered by delirium, which can produce symptoms overlapping with manifestations of pain in older patients. In some cases, poorly controlled pain may even *precipitate* delirium or behavioral changes in patients with cognitive impairment and increase symptoms such as fast or loud speech, irritability, anger, or lethargy.[27] In a prospective observational study of 333 patients who had elective non-cardiac surgical procedures, higher preoperative pain scores at rest were associated with an increased risk of delirium over the first three days after surgery (OR for moderate pain 2.2; 95% CI: 1.2-4, and OR for severe pain 3.7; 95% CI: 1.5-9).[29]

When self-report is not possible, careful observation of pain behaviors may help identify treatable causes of pain in older adults with cognitive impairment. For example, the Pain Assessment Checklist for Seniors with Severe Dementia (PACSLAC) is a checklist of six pain behavioral categories:[27]

- facial expressions (grimacing, closed eyes, rapid blinking)
- verbalization (moaning, calling out, verbal abusiveness)
- body movement (guarding, fidgeting, gait changes)
- changes in interpersonal interaction (combativeness)
- changes in activity patterns or routines (cessation of common routines)
- changes in mental status (confusion, irritability)

Both the revised Iowa pain thermometer and the FACES pain rating scales may also be useful, and both have been validated in older adult populations.[30]

BOTTOM LINE: Assessing acute pain in the elderly can be challenging and requires the use of validated instruments, caregiver reports, and a thorough history and examination.

Managing acute pain

A central tenet of pain management, whether acute or chronic, is that the goal of treatment is not necessarily zero pain, but a tolerable level of pain that allows the patient maximum physical and emotional functioning with the lowest risk of side effects, progression to chronic pain, or misuse or abuse.[31] This requires an adroit balancing of patient-related factors (e.g., comorbidities, medical history, risk of abuse) and drug-related factors (e.g., potency, mechanism of action, expected side effects). A commonly-recommended way to achieve this balance is with multimodal analgesia, in which several therapeutic approaches are used, each acting at different sites of the pain pathway, which can reduce dependence on a single medication and may reduce or eliminate the need for opioids and associated risks/side effects.[32]

Multimodal analgesia (e.g., using drugs from two or more classes, or a drug plus a non-drug treatment) can produce synergistic effects, reduce side effects, or both. One example of multimodal analgesia is the

use of both a non-steroidal anti-inflammatory drug (NSAID) and acetaminophen, plus physical approaches (e.g., cold, compression, or elevation) to manage postoperative pain. Demonstrated benefits of multimodal analgesia include earlier ambulation, earlier oral intake, and earlier hospital discharge for postoperative patients, as well as higher levels of participation in activities necessary for recovery (e.g., physical therapy).[32]

Managing patient expectations

Patients in pain are understandably worried that the pain will persist or get worse with time. Physicians can reduce such fears and set realistic expectations for treatment effectiveness and healing with clear, compassionate communication couched in terms that patients can easily understand. It can be helpful, for example, to tell patients that most forms of acute nociceptive pain (e.g., nonspecific low back pain) are self-limited, subside within weeks, and do not require invasive interventions. (In a systematic review of 15 prospective cohort studies, 82% of people who stopped work due to acute low back pain returned to work within one month.[33] See Low Back Pain section beginning on page 12 for more information on relevant studies.) An example of appropriate expectation-setting language is: “Some pain is normal. You should be able to walk and do light activity, but may be sore for a few days. This will gradually get better.”[34]

A systematic review of 14 controlled trials of patient education interventions for low back pain showed that structured messaging by providers can reassure patients with acute pain more than usual care/control education both in the short and long term.[35] Messaging was significantly more reassuring to patients when delivered by physicians than other primary care practitioners, and such communication reduced the frequency of primary care visits.

Specific examples of effective messaging specific to patients with low back pain include:

- “Based on the history and exam, you have a good prognosis.”
- “The acute pain you are experiencing is not the result of serious injury and is likely to resolve without need for x-rays or invasive treatments.”
- “Avoid bed-rest…daily exercise is helpful.”

Non-pharmacological treatments for acute pain

When possible, non-pharmacologic methods should be used, alone or in combination with analgesics, to manage acute pain.[36] The degree to which this is possible depends on the severity, type, and origin of the pain, but many non-pharmacological approaches can be very effective and their use avoids the potential side effects and risks associated with pharmacological interventions.

Physical methods of pain management can be helpful in all phases of care, including immediately after tissue trauma (e.g., rest, application of cold, compression, elevation) and later in the healing period (e.g., exercises to regain strength and range of motion).

Non-pharmacologic methods can include:[36]

- application of cold (generally within first 24 hours) or heat
- compression
- elevation
- immobilization
- relaxation exercises

- distraction/guided imagery
- acupuncture
- massage
- electroanalgesia (e.g., transcutaneous electrical nerve stimulation)
- physical therapy
- yoga

Physical therapy may be useful for a range of musculoskeletal issues and can be helpful in recovering from acute pain-producing traumas initially treated with other methods. A 2018 study reported that patients with low back pain who first consulted a physical therapist were less likely to receive an opioid prescription compared to those who first saw their primary care physician.[37]

Exercise therapy can take many forms, including walking, swimming or in-water exercise, weight training, or use of aerobic or strength-training equipment. According to a review by the Centers for Disease Control and Prevention (CDC), exercise therapy may improve low back pain, neck pain, hip and knee osteoarthritis pain, fibromyalgia, and migraine.[38]

Non-opioid pharmacologic treatments for acute pain

Acetaminophen and NSAIDs

In general, mild-to-moderate acute pain responds well to oral non-opioids (e.g., acetaminophen, NSAIDs, and topical agents). NSAIDs, such as aspirin and other salicylic acid derivatives, and acetaminophen are used to manage acute pain from injury, arthritis, dental procedures, swelling, or surgical procedures. Although many patients perceive them to be weaker analgesics than opioids, evidence supports the notion that pain relief from acetaminophen and NSAIDs is equal to and sometimes superior to that of opioids.[39] Acetaminophen and NSAIDs do not produce tolerance, physical dependence, or addiction and they do not induce respiratory depression or constipation. Acetaminophen and NSAIDs are often added to an opioid regimen for their opioid-sparing effect. Because non-opioids relieve pain via different mechanisms than opioids, combination therapy can provide improved relief with fewer side effects.

The choice of medication may be driven by patient risk factors for drug-related adverse effects (e.g., NSAIDs increase the rate of gastrointestinal, renal, and cardiovascular events). If acetaminophen or NSAIDs are contraindicated or have not sufficiently eased the patient's pain or improved function despite maximal or combination therapy, other drug classes are sometimes used, e.g., anticonvulsants or opioids.

Non-opioid analgesics are not without risk, particularly in older patients. Potential adverse effects of NSAIDs include gastrointestinal problems (e.g., stomach upset, ulcers, perforation, bleeding, liver dysfunction), bleeding (i.e., antiplatelet effects), kidney dysfunction, hypersensitivity reactions, and cardiovascular concerns, particularly in the elderly.[40] The threshold dose for acetaminophen liver toxicity has not been established. The Food and Drug Administration (FDA) recommends that the total adult daily dose not exceed 4,000 mg in patients without liver disease,[41] although a lower ceiling of 3,000-3,250 mg per day is sometimes recommended for older adults.[42,43]

The FDA currently sets a maximum limit of 325 mg of acetaminophen in prescription combination products (e.g., hydrocodone and acetaminophen) in an attempt to limit liver damage and other potential ill effects of these products.[32]

Topical capsaicin and salicylates can both be effective for short term pain relief and generally have fewer side effects than oral analgesics, but their long-term efficacy is not well studied.[44,45] Topical aspirin, for example, can help reduce pain from acute herpes zoster infection.[46] Topical NSAIDs and lidocaine may also be effective for short-term relief of superficial pain with minimal side effects. Topical agents can be simple and effective for reducing pain associated with wound dressing changes, debridement of leg ulcers, and other sources of superficial pain.[46]

Anticonvulsants

Anticonvulsants, such as gabapentin, pregabalin, oxcarbazepine, and carbamazepine, are often prescribed for both chronic and acute neuropathic pain (e.g., post-herpetic neuralgia and diabetic neuropathy), although evidence for efficacy in acute pain conditions is weak.[47] A 2017 trial, for example, randomized 209 patients with sciatica pain to pregabalin 150 mg/day titrated to a maximum of 600 mg/day vs. placebo for 8 weeks.[48] There was, however, no significant difference in pain between groups at 8 weeks (mean leg pain intensity on a 0-10 scale 3.7 with pregabalin vs. 3.1 with placebo; P=0.19).

Potential side effects of anticonvulsants include sedation, dizziness, and peripheral edema. Gabapentanoids have been associated with an increased risk of respiratory depression when combined with opioids,[49] and some epidemiological studies have shown an increased risk for opioid-related death with co-prescription of opioids and gabapentanoids (OR 1.99; 95% CI: 1.61-2.47) compared to patients who did not have co-prescription.[50] Pregabalin and gabapentin also have abuse potential in the general population (although probably significantly less than opioids) because some users report euphoric effects, and abrupt cessation at high doses (e.g., greater than 1800 mg/day of gabapentin) may precipitate withdrawal symptoms.[47]

Cannabis

With medical cannabis now legal in 33 states and recreational use legal in 10 states and the District of Columbia (as of April 2019),[51] there has been increased interest among patients for the use of cannabis or cannabis derivatives (e.g., cannabidiol [CBD]) for pain relief. The cannabinoid (CB) 1 and CB2 receptors have been shown to mediate the analgesic effects of cannabinoids,[52] and some evidence suggests a potential benefit for chronic pain. A 2017 National Academies of Science report, for example, concluded that “conclusive or substantial evidence” supports a beneficial role for cannabis or cannabinoids for treating chronic pain,[53] and a 2018 Cochrane review of the existing literature evaluating cannabinoids (cannabis, CBD, or combinations) suggested that these agents are moderately effective for neuropathic pain with adverse effects that are less than, or comparable to, existing non-opioid analgesics.[54]

The evidence that cannabinoids can relieve acute pain, however, is extremely limited and mixed. A small double-blind, cross-over study in 18 females and experimentally-induced mild acute pain found no significant analgesic effect of oral cannabis extract.[55] Another randomized, double-blind study with 15 healthy volunteers using smoked cannabis found no analgesic effect with low doses of cannabis, a modest effect with moderate doses, and enhanced pain responses with high doses.[56] The authors of a 2017 review on cannabis and pain concluded that cannabis may have a narrow therapeutic window as a pharmacotherapy for pain but that much more research is needed to inform physician recommendations to patients regarding the analgesic efficacy of cannabis.[57]

Opioids for acute pain

Reasons for caution

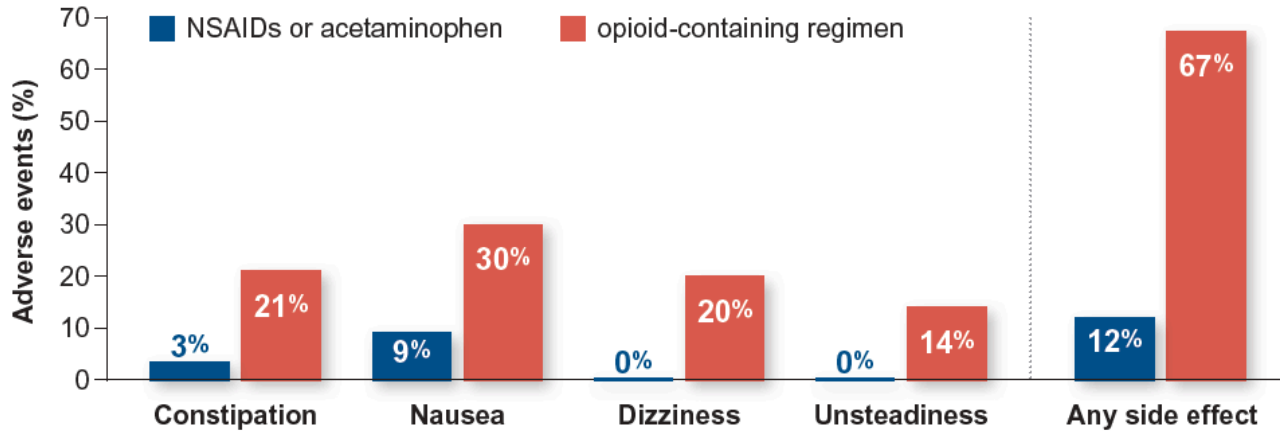
Opioids are commonly prescribed for pain, with approximately 20% of patients presenting with non-cancer acute or chronic pain receiving an opioid in any given year,[58] and nearly two thirds (64%) of the public reporting being prescribed an opioid for pain at some point in their lives.[59] However, opioids are not as safe and effective as once thought, and high-dose prescriptions or prolonged use not only increase the risk of misuse, addiction, or overdose, they may actually *increase* pain and pain sensitivity.[60,61]

Recent evidence suggests that non-opioid pain regimens may be as effective for moderate to severe pain as opioids.[62,63] A randomized trial of 416 patients with acute extremity pain found no clinically important differences in pain reduction at two hours after single-dose treatment with ibuprofen and acetaminophen vs. three different combinations of opioid and acetaminophen analgesics (Figure 1).[62]

Physical dependence can readily occur after use of opioids for just a few days. In addition, side effects of opioid use include constipation, confusion/gait instability, respiratory depression, pruritus, erectile dysfunction, and fractures, all of which may be more problematic in older patients and occur at higher rates than with non-opioid analgesics.

A cross-sectional study compared common side effects experienced during the first week of treatment with opioid analgesics vs. non-opioid analgesics in patients over age 65 with acute musculoskeletal pain. The intensity of six common opioid-related side effects were significantly higher with opioids (Figure 1).[20] (A limitation of this study is that it could not assess severe but less common adverse events associated with NSAIDs and acetaminophen, including gastrointestinal bleeding, acute kidney injury, and hepatotoxicity.)

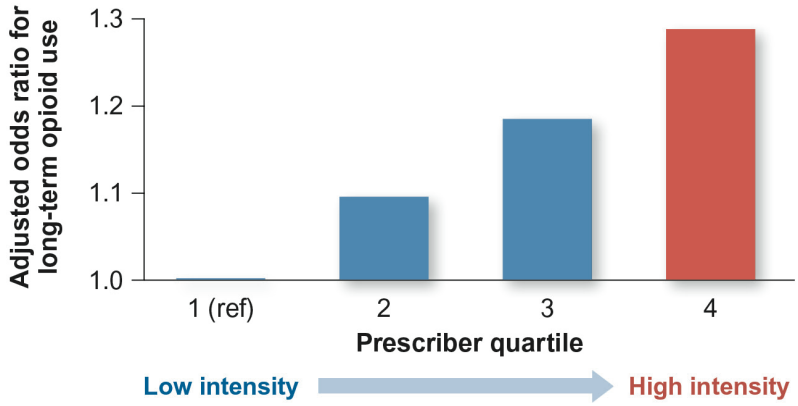
Figure 1: Comparison of adverse events associated with opioids vs. non-opioid analgesics in older patients[20]



In a retrospective study of 12,840 elderly patients with arthritis, opioid use was associated with an increased risk relative to non-opioids for cardiovascular events (HR 1.77; 95% CI: 1.39-2.24), fracture (HR 4.47; 95% CI: 3.12-6.41), events requiring hospitalization (HR 1.68; 95% CI: 1.37-2.07), and all-cause mortality (HR 1.87; 95% CI: 1.39-2.53).[64]

High-intensity prescribing of opioids (high doses or high numbers of pills prescribed) for acute pain may be associated with greater likelihood of long-term opioid use.[13,65] In a retrospective analysis of a national sample of opioid-naïve Medicare beneficiaries who received emergency treatment from 2008 through 2011, initial exposure to an opioid was a strong predictor of subsequent long-term use (Figure 2).

Figure 2: Opioid prescribing rates and odds ratios for long-term opioid use[13]



The risk of prolonged opioid use is particularly high after arthroscopic joint procedures. In a 2019 case-control study of 104,154 opioid-naïve adults, 8,686 (8.3%) developed new prolonged opioid use (continued opioid use between 91 and 180 days after shoulder arthroscopy).[66] Subgroups at higher risk for long-term use included women (OR 1.3; 95% CI: 1.2-1.3), those with a history of alcohol dependence or abuse (OR 1.6; 95% CI: 1.3-1.9), those with a mood disorder (OR 1.3; 95% CI: 1.2-14), and those with an anxiety disorder (OR 1.2; 95% CI: 1.1-1.3).

State policies addressing opioid prescribers

As of October 2018, 33 states have enacted laws regulating the prescription of opioids for acute or chronic pain, including restrictions on prescription durations for opioid-naïve patients for 5-10 days. Most states now limit prescriptions to ≤7days.[67,68] As of this writing, no data exist about whether, or to what extent, such laws reduce opioid-related morbidity and mortality, or whether they are associated with unintended outcomes.[69]

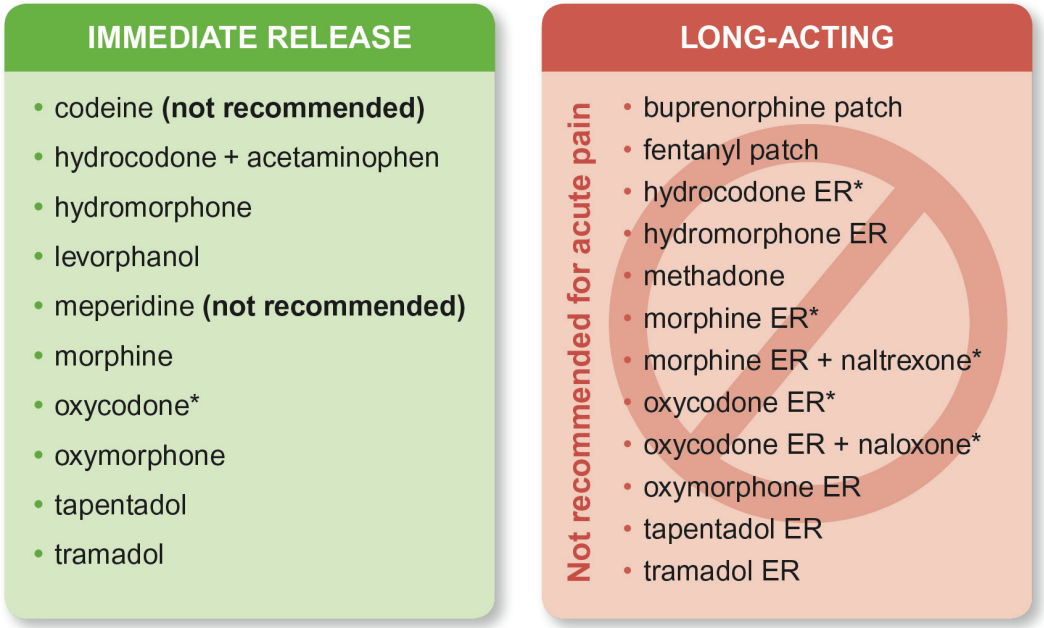
Another way states are attempting to reduce opioid-related harms is by requiring clinicians to check their state's Prescription Drug Monitoring Program (PDMP) prior to any new opioid prescription. As of January, 2018, 41 states have some kind of PDMP mandate, although requirements for when the PDMP must be checked and for which controlled substances varies by state.[70] A 2019 study of PDMP data from Kentucky, Ohio, and West Virginia found that rates of overall opioid prescribing, having multiple providers write opioids, and overlapping opioid prescriptions all declined after mandatory PDMP laws were enacted.[71]

Opioid choices for acute pain

If an opioid is deemed necessary to treat moderate-to-severe acute pain, the following general principles are recommended:

- Avoid extended-release and long-acting opioids such as methadone, fentanyl patches, and extended release/long-acting (ER/LA) versions of opioids such as oxycodone or oxymorphone.
- Avoid co-prescribing opioids with other drugs known to depress central nervous system function (e.g., benzodiazepines)
- Limit the dose and quantity of opioids to address the expected duration and severity of pain (usually less than three days).
- Combine opioids with other treatments (e.g., non-pharmacologic options, NSAIDs, or acetaminophen).
- Closely monitor patients with impaired hepatic or kidney function if they are prescribed opioids

Figure 3: Immediate release vs. long-acting opioids for acute pain



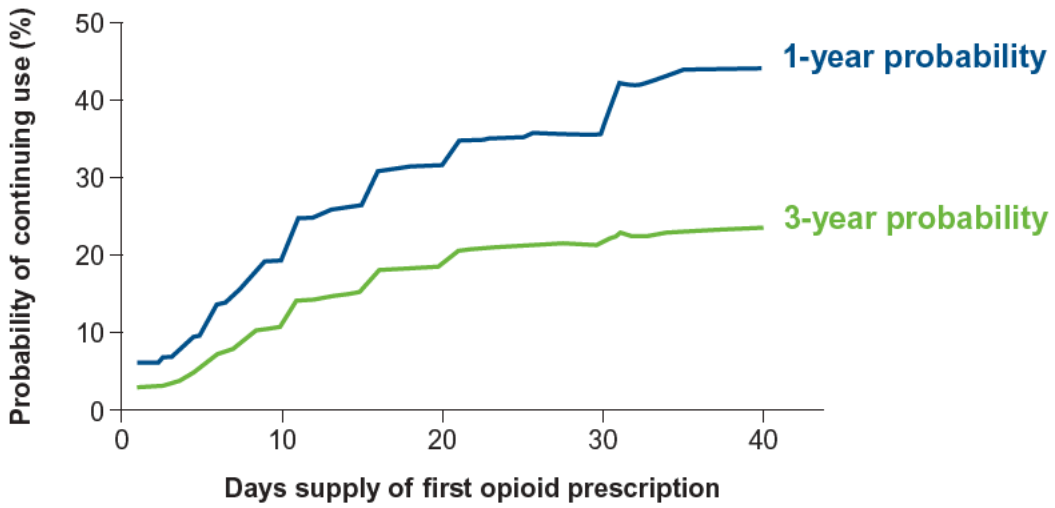
* available in “abuse-deterrent” formulations

Immediate-release agents are strongly preferred because of the higher risk of overdose associated with ER/LA agents. A cohort study of 840,000 opioid-naïve patients over a 10-year span found that unintentional overdose was five times more likely in patients prescribed ER/LA agents compared to immediate-release opioids.[72]

Little high-quality evidence exists to support the choice of any one opioid over another for acute pain. However, some opioids are associated with more adverse events. For example, codeine is not preferred due to differential metabolism to the active ingredient, morphine. It is associated with a risk of both under-treatment in usual doses (due to CYP2D6 mutations) and overtreatment (in ultra-rapid metabolizers of CYP2D6).[73]

Meperidine is associated with an increased risk of post-operative delirium[74] due to its long half-life and its active metabolite, normeperidine, which is a central nervous system stimulant.[75]

Figure 4: One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of days' supply in the initial opioid prescriptions[65]



The amount of opioid prescribed should relate to the level of pain expected from the injury or procedure. Injuries or procedures involving bones and joints tend to be more painful than those involving soft tissues.[15] Table 1 illustrates the wide range of expected pain and associated recommended opioid doses for some common surgeries or procedures based on patients surveys, though the number of tablets may vary among patients and the number of tablets may be reduced as more non-opioid analgesics are employed.

Table 1: Opioid dose recommendations for post-procedural pain[76]

Procedure	Number of oxycodone 5 mg tablets (or equivalent)
Dental extraction	0
Thyroidectomy	5
Breast biopsy or lumpectomy	5
Lumpectomy plus sentinel lymph node biopsy	5
Hernia repair (minor or major)	10
Sleeve gastrectomy	10
Prostatectomy	10
Open cholecystectomy	15
Cesarean delivery	15
Hysterectomy (all types)	15
Cardiac surgery via median sternotomy	15
Open small bowel resection	20
Simple mastectomy with or without sentinel lymph node biopsy	20
Total hip arthroplasty	30
Total knee arthroplasty	50

Tamper-resistant/abuse-deterrent opioids

One strategy to mitigate the risk of opioid abuse has been the development of "abuse-deterrent" formulations of opioids that make it more difficult to alter for non-oral consumption (e.g., injecting, snorting, or smoking).[77] However, these opioids are more aptly called "tamper-resistant" formulations instead of "abuse-deterrent" because they are no less addictive than regular opioids when taken by mouth. Tamper-resistant formulations often contain a higher opioid dose than immediate-release preparations. Furthermore, most are extended release and also considerably more expensive than generic, off-patent opioids.[77] As of this writing, only one immediate-release opioid is available in a tamper-resistant formulation (RoxyBond).[77]

Patient education

Before prescribing an opioid for acute pain, clinicians should discuss with patients the risks and benefits of such therapy. Here are some suggestions:

- Frame expectations that complete pain relief is unlikely and not necessarily desired.
- Focus on improved function, rather than pain relief, as the primary goal of treatment.
- Review potential serious adverse effects including respiratory depression, constipation, and development of OUD.
- Review common effects such as nausea, vomiting, drowsiness, confusion, tolerance, physical dependence, and withdrawal symptoms when stopping opioids.
- Discuss effects that opioids might have on one's ability to operate a vehicle, particularly when opioids are initiated, when dosages are increased, or when other central nervous system depressants, such as benzodiazepines or alcohol, are used concurrently
- Discuss risks to household members and other individuals if opioids are intentionally or unintentionally shared with others from whom they are not prescribed.
- Consider whether cognitive limitations might interfere with management of opioid therapy, and if so, determine whether a caregiver can responsibly co-manage the therapy

In addition, patients should be educated about the safe storage and disposal of opioid medications. Safe use means following clinician instructions about dosing, avoiding potentially dangerous drug interactions (e.g., alcohol), and assuring full understanding of how the medication should be consumed or applied. Remind patients that pain medications are sought after by many people, and, therefore, opioids should be stored in a locked cabinet or a place that is not obvious or easily accessed by others if a locked unit is not available.

Proper disposal methods should be explained:[78]

- Follow any specific disposal instructions on the prescription drug labeling or patient information that accompanies the medication.
- Return medications to a pharmacy, health center, or other organization with a take-back program.
- If medication return is not possible or feasible, flush opioids down the toilet, mix with an undesirable substance (e.g., dirt, used coffee grounds or kitty litter) and put it in the trash, or use special drug deactivation pouches that your health care provider may recommend.

BOTTOM LINE: Except with severe pain (e.g., after many forms of surgery), physicians should maximize non-opioid therapies prior to initiating treatment with opioids for acute pain. When

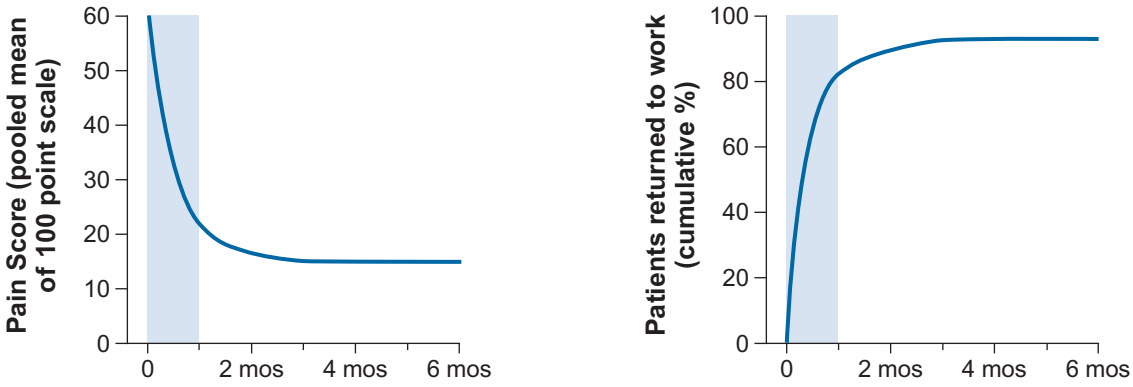
prescribing opioids for acute pain, the minimum effective dose should be prescribed for the shortest period of time (typically <3 days) to reduce risks of opioid misuse, abuse, and overdose.

Acute pain conditions

Acute low back pain

Most low back pain (LBP) etiologies are non-specific with no evidence of underlying disease, are usually self-limited, and resolve within weeks. A systematic review of 15 trials evaluating a range of treatments for LBP found rapid pain reductions within a month, regardless of treatment used (Figure 5).[33]

Figure 5: Course of acute pain (left) and return to work after onset (right)[33]



Rarely, low back pain may indicate an underlying or systemic medical illness or condition, such as sciatica or herniated disc. Red-flag symptoms include severe progressive neurologic deficits such as urinary or fecal incontinence, saddle anesthesia, and signs of underlying conditions such as osteomyelitis.

Imaging for acute low back pain is rarely indicated because image findings are poorly associated with symptoms.[79] Imaging of the lower spine before six weeks does not improve outcomes but does increase costs.[79]

Non-drug treatment options

Non-pharmacologic treatment with heat, massage, acupuncture, or spinal manipulation are often recommended to treat acute LBP. Most non-drug options are generally safe, although spinal manipulation may rarely produce stiffness, spasms, or increased pain.[80,81]

Bed rest or exercise?

Although bed rest and back-extension exercises are often prescribed for patients with acute LBP, they have not been found to be more effective than continuing regular activities. Staying in bed won't speed healing and long bed rest may make back pain worse.[82]

One trial randomized 186 patients with nonspecific acute LBP to bed rest for two days, back-mobilizing exercises, or continuation of ordinary activities.[83] At three-weeks and 12-weeks follow-up, patients who continued ordinary activities had statistically significant reductions in pain duration and pain intensity, improved lumbar flexion, and returned to work more quickly compared to the other two groups.

A Cochrane review of 61 randomized trials involving 6,390 patients with acute and chronic LBP comparing a variety of exercise regimens to no exercise found that exercise was slightly more effective for reducing pain and improving function, particularly when patients were in some kind of healthcare setting.[84] The pooled mean improvement in pain with exercise vs. no exercise was 7.3 points (0-100 scale), 95% CI: 3.7-10.9 points, and the mean improvement in function was 2.5 points (out of 100) 95% CI: 1-3.9 points. In another review of 20 head-to-head trials of different exercise programs for LBP, there were no significant differences in outcomes between regimens.[85]

Thermal treatments

Heat and cold treatments are often used to relieve symptoms of low back pain, most frequently heat wraps or hot water bottles, rice bags, or heated blankets.[86]

Heat wrap therapy has been found by a small number of trials to provide a minor short-term reduction in pain and disability in a population with a mix of acute and subacute LBP. One trial of 100 patients found that adding exercise to heat wraps provided significantly more pain relief at day seven (weighted mean difference (WMD) 2 points; 95% CI: 1.29-2.71 points) and also led to greater improvements in function than either heat or exercise alone.[86,87]

The application of cold treatment to LBP is even more limited, and a 2017 review concluded that there is insufficient evidence for using cold treatments.[86]

Massage

Only one study has looked at the effect of massage on patients with acute LBP (n=51), and it suggested a short-term benefit of massage vs. inactive control (standard mean difference [SMD] -1.24; 95% CI: -1.85 to -0.64). However, massage had no benefit on function (SMD -0.50; 95% CI: -1.06 to 0.06).[88] A 2015 Cochrane review of 25 trials comparing massage to active or inactive controls in 3,096 patients with acute, subacute, or chronic LBP found low-quality evidence that massage modestly reduced pain and improved function in the short-term (0-6 months), but not long-term (6-12 months).[89]

Myofascial trigger points (MTrPs) are palpable hyperirritable nodules in skeletal muscle that are associated with chronic musculoskeletal pain.[90] Pressure massage targeting compression of MTrPs has been thought to reduce symptoms associated with acute LBP. A small randomized, unblinded study of 63 patients with acute LBP randomized to MTrP massage, non-MTrP massage (compression at non-trigger points), or effleurage (massage of superficial areas) showed that MTrP massage significantly reduced pain intensity (0-100 scale), pressure pain threshold, and range of motion compared to either non-MTrP or effleurage massage.[91]

Acupuncture

Low-quality evidence from five randomized controlled trials (RCTs) showed that acupuncture may improve symptoms of acute LBP to a greater extent than (RR 1.11; 95% CI: 1.06-1.16) than NSAIDs.[92] Additionally, evidence from two RCTs showed that acupuncture may more effectively relieve pain

compared with sham acupuncture, resulting in a small decrease in pain intensity (mean difference -9.38 points; 95% CI: -17.00 to -1.76 points), but there were no significant effects on function/disability.[92]

Spinal manipulation

RCTs and meta-analyses have provided conflicting conclusions about the effectiveness of spinal manipulation in treating acute LBP, suggesting either no effect or small effect on pain and function. Spinal manipulation of the cervical spine has been associated with rare adverse events, such as stroke, headache, and vertebral artery dissection.[81]

A 2017 systematic review and meta-analysis of 26 randomized trials found a modest improvement in both pain and function at up to six weeks after the procedure (SMD -0.39; 95% CI: -0.71 to -0.07) in patients with acute LBP who underwent spinal manipulation. Minor, transient musculoskeletal adverse events such as increased pain, stiffness, and headache were reported in more than half of patients.[80]

Transcutaneous electrical nerve stimulation (TENS)

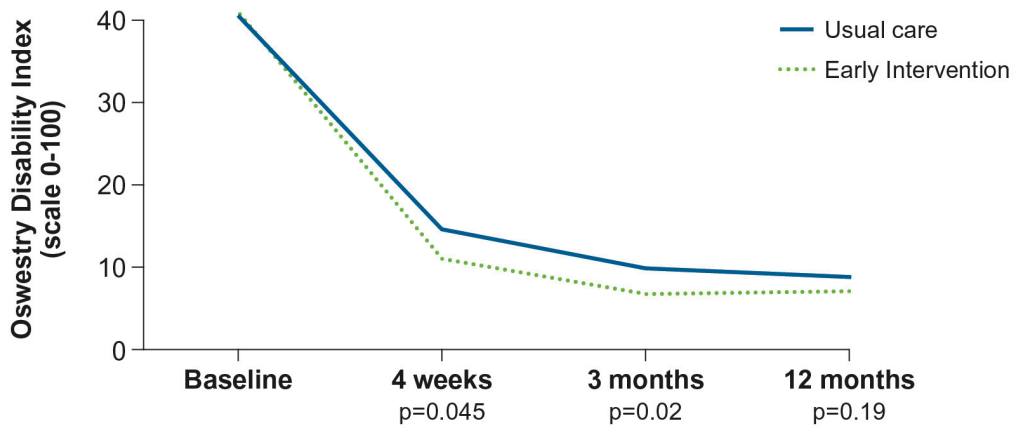
A meta-analysis of two trials comparing TENS vs. placebo in 121 patients with acute LBP found no significant differences in analgesic efficacy (mean difference on 100-point scale -15 points; 95% CI: -40 points to 10 points).[93] A randomized trial of 74 patients with acute LBP being transported to a hospital compared enroute TENS vs. sham TENS and found significant differences in mean pain scores upon arrival (49 mm on a 100 mm scale with TENS vs. 77 mm with sham; $P<0.01$) and mean anxiety scores (69 mm on 100 mm scale vs. 84 mm; $P<0.01$).[94]

Physical therapy

The effect of early physical therapy on acute back pain is unclear, and some guidelines advise delaying referral to physical therapy or other specialists for a few weeks to allow for spontaneous recovery.[95]

An RCT randomized 220 patients with acute LBP to four sessions of early physical therapy or usual care (Figure 6).[96] At three months, patients receiving early physical therapy had a small improvement in disability scores (between-group difference −3.2 points on 0-100 scale; 95% CI: -5.9 to -0.47 points), which was less than the author-defined minimum clinically important difference for this outcome.[96] At 1 year, there were no significant between-group differences.

Figure 6: Effect of early physical therapy on disability[96]



Drug options

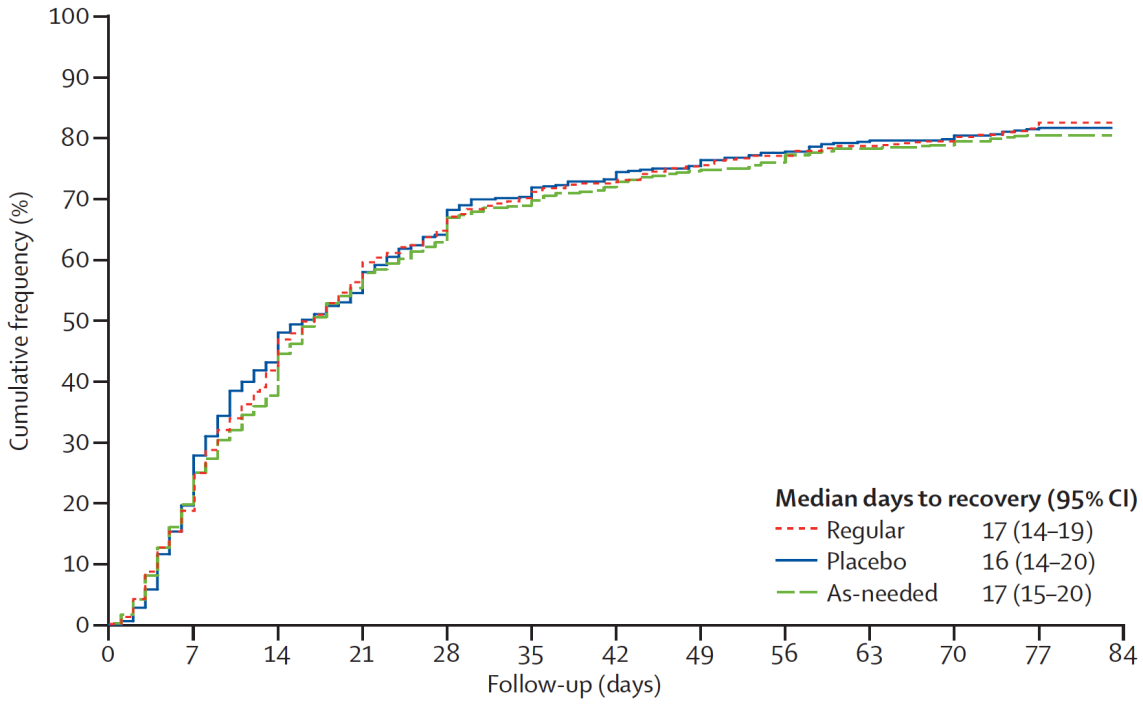
Several systemic pharmacologic therapies are available for low back pain and are associated with small to moderate, mostly short-term effects on pain. The most commonly-used medications for LBP are NSAIDs, acetaminophen, skeletal muscle relaxants, and opioids. However, research has found only limited evidence to support use of these medications for LBP.[97]

Acetaminophen

Evidence for the analgesic efficacy of acetaminophen for acute LBP is mixed. The American College of Physicians Clinical Practice Guidelines found no difference between acetaminophen and NSAIDs in reducing pain intensity (SMD 0.21; 95% CI: -0.02 to 0.43) at three weeks or less and a lower risk of adverse events with acetaminophen vs. NSAIDs (RR 0.57; 95% CI: 0.36-0.89).[97,98]

Observed improvements in pain with acetaminophen may, however, be strongly influenced by the placebo effect. For example, an RCT of 1,652 patients compared acetaminophen 4000 mg/day in two different regimens vs. placebo and found no differences between either regimen and placebo in days to recovery, or mean pain scores (Figure 7 on next page).[99]

Figure 7: Pattern of sustained recovery of patients receiving acetaminophen and placebo[99]



NSAIDs

A Cochrane review of 65 RCTs of oral NSAIDs for non-specific acute LBP with or without sciatica found that NSAIDs were associated with significantly more pain relief vs. placebo but also significantly more side effects.[98]

In an analysis of four trials, mean pain reduction with NSAIDs was 8.39 points (0-100 scale); 95% CI: -12.68 to -4.10 points). There was no significant improvement in function with NSAIDs in a single 7-day trial.[98,100]

COX-2 selective NSAIDs do not seem to be more effective than traditional NSAIDs for pain relief but are associated with fewer side effects, particularly gastrointestinal bleeding.[98] An RCT of 24,081 patients with arthritis pain examined the safety of celecoxib, compared with nonselective NSAIDs.[101] Esomeprazole (20-40 mg) was provided to all patients for gastric protection. Patients were randomized to celecoxib (mean daily dose 209 mg), naproxen (mean daily dose 852 mg), or ibuprofen (mean daily dose 2,045 mg). There were no differences among the three treatments in cardiovascular outcomes, but celecoxib produced fewer gastrointestinal events than either naproxen (P=0.01) or ibuprofen (P=0.002), and celecoxib was associated with fewer renal events compared to ibuprofen (P=0.004).

Skeletal muscle relaxants

Skeletal muscle relaxants account for more than 45% of all prescriptions written for management of musculoskeletal pain.[102] These are commonly used to treat spasticity from upper motor neuron syndromes and muscular pain or spasms from peripheral musculoskeletal conditions. Their efficacy in the management of non-specific acute LBP is debated, however, and there are concerns about potential adverse effects.

A 2003 Cochrane Review found that skeletal muscle relaxants (both benzodiazepines and non-benzodiazepines) were more effective than placebo for short-term relief of acute LBP after two to four days. The pooled relative risk for non-benzodiazepines vs. placebo was 0.80 (95% CI: 0.71-0.89) for pain relief and 0.49 (95% CI: 0.25-0.95) for global efficacy.[103]

However, a 2018 RCT of 240 patients with LBP presenting to emergency rooms found that adding the muscle relaxants orphenadrine or methocarbamol to naproxen was no better than naproxen alone for improving function at one week.[104] In addition, a 2019 RCT of 320 patients with acute LBP randomized to ibuprofen or ibuprofen and one of three skeletal muscle relaxants (baclofen, metaxalone, or tizanidine) found no significant differences between groups in pain or functional impairment at one-week follow-up.[105]

Common side effects of skeletal muscle relaxants include dizziness, dry mouth, drowsiness, and somnolence, necessitating cautious use, particularly if taken with other sedating medications such as opioids.

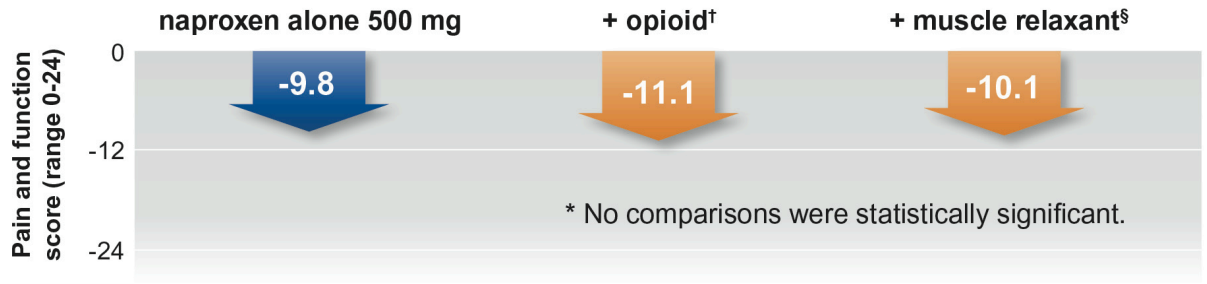
Systemic corticosteroids

Oral steroids are commonly used to treat acute sciatica and may provide some analgesic effect due to their anti-inflammatory activity. However, evidence suggests that non-epidural steroids do not improve pain in patients with acute nonspecific LBP.[85] One RCT of 269 patients with acute radicular LBP due to herniated lumbar disk found a small improvement in function with a three-week course of oral prednisone (mean difference 6.4 points on a 100-point scale vs. placebo) but no significant improvement in pain.[106]

Opioids

Almost all RCTs of opioids have been conducted for chronic, rather than acute, LBP. One RCT in 107 patients with acute LBP found that opioids may be no more effective than a combination of ibuprofen and acetaminophen.[107] The trial compared functional outcomes and pain at one week and three months after randomization to naproxen, naproxen plus cyclobenzaprine, or naproxen plus oxycodone/acetaminophen. Results showed that adding cyclobenzaprine or oxycodone/acetaminophen to naproxen did not improve functional outcomes or pain at 1-week follow-up more than naproxen alone (Figure 8). There was also no difference in patient-reported satisfaction with treatment nor in time to return to usual activities between treatment groups.[107]

Figure 8: Naproxen vs. naproxen plus oxycodone/acetaminophen vs. naproxen plus muscle relaxant at 1 week[107]



† naproxen 500 mg + oxycodone 5 mg / acetaminophen 325 mg; § naproxen 500 mg + cyclobenzaprine 5 mg

A retrospective cohort study of workers' compensation claims from 8,443 patients with acute disabling LBP evaluated the associations between early opioid prescription and outcomes.[108] Mean disability duration, mean medical costs, and risk of surgery and late opioid use *increased* with increasing opioid dose measured in morphine equivalent units. Compared with those receiving no opioids, the risk for subsequent surgery was three times greater (RR 3; 95% CI: 2.4–4.0) in those receiving the highest dose of opioids, and the risk of receiving late-term opioids (≥5 prescriptions from 30 to 730 days) was six times greater (95% CI: 4.9–7.7). These results suggest that the use of opioids to manage acute LBP may be counterproductive to recovery.[108]

Other therapies

Although there is moderate evidence supporting cannabinoids use for chronic pain, current evidence is inadequate for drawing conclusions about effectiveness for treating acute LBP.[109] No studies have evaluated the use of gabapentin/pregabalin as treatments for LBP.[97]

BOTTOM LINE: Since most cases of acute LBP remit regardless of treatment, clinicians should educate patients about the favorable prognosis and avoid unnecessary imaging or treatments. Non-pharmacologic treatment with superficial heat, massage, acupuncture, or spinal manipulation could be considered, along with acetaminophen, NSAIDs, or skeletal muscle relaxants. Opioids are unlikely to reduce pain or improve function relative to other treatments and should be avoided due to their high risks.

Post-operative pain

Post-operative pain can have a significant effect on patient recovery and healthcare burden. Among 411 older adults (mean age 82) with recent hip fracture, a prospective cohort study found that patients with higher post-operative pain scores had increased lengths of hospital stay, more missed physical therapy sessions, delayed ambulation, and impaired locomotion at six months.[17] Poor pain control can delay post-operative functional improvement, whereas improved pain control may decrease length of stay, enhance functional recovery, and improve long-term functional outcomes.

Non-drug options

Non-pharmaceutical options for relief of post-operative pain include transcutaneous electrical nerve stimulation (TENS), acupuncture, massage, cold therapy (with and without compression), localized heat, continuous passive motion, and immobilization or bracing. Although these are generally safe, their effectiveness as an adjunct to post-operative pain management is variable, and treatments may not be covered by health insurance.[110]

Acupuncture

Acupuncture has been investigated as adjuvant treatment for post-operative analgesia.[111] A 2016 systematic review of 13 trials (682 patients) of post-operative acupuncture and acupuncture-related techniques vs. sham acupuncture or control found reduced pain within 24 hours of surgery with acupuncture or related techniques (SMD -1.27; 95% CI: -1.83 to -0.71) and lower mean use of opioid analgesics (SMD -0.72; 95% CI: -1.21 to -0.22).[112]

A meta-analysis of 15 trials evaluating acupuncture and related techniques as adjunctive therapy for acute post-operative pain management, found that pain intensity (0–100 mm scale) was significantly reduced in the acupuncture group vs. control at eight hours (WMD -14.57 mm; 95% CI: -23.02 to -6.13) and at 72 hours (WMD -9.75 mm; 95% CI: -13.82 to -5.68).[113] A reduction in opioid-related adverse events was also seen in patients receiving acupuncture, including nausea, dizziness, sedation, pruritus, and urinary retention. The relative reduction in opioid use with acupuncture was 21%-29%.

Although older adults, who have higher rates of postoperative morbidity and mortality, might benefit from perioperative acupuncture, this option is rarely available, and acupuncture procedures and regimens have not been standardized.[114]

Transcutaneous electrical nerve stimulation (TENS)

A systematic review of 21 RCTs found that TENS administered with a strong, subnoxious intensity at an adequate frequency in the wound area was associated with a non-significant 26.5% reduction (range -6 to +51%) in post-operative analgesic use compared with no TENS.[115] Despite the limited evidence base, TENS is recommended by the 2016 American Pain Society guideline as an adjunct to other post-operative pain treatments.[110]

Exercise/physical therapy

Evidence for the analgesic benefits of exercise or stretching for post-operative pain is mixed. A trial of 63 patients who had arthroscopic shoulder surgery found that horizontal adduction stretching twice daily for 48-72 hours post-surgery significantly reduced posterior shoulder tightness compared to either standard care or supine sleeper stretching.[116] A prospective observational study of 231 patients having total knee arthroplasty compared participation in group-based exercise programs plus usual ambulation and activities-of-daily-living exercises vs. a historical control group who did not do group-based exercise and found significant improvements in knee range-of-motion and extension and quadriceps strength with group exercise.[117]

A non-randomized study in 30 patients with total knee arthroplasty found that exercise/mobilization on first post-operative morning (25 meter walking twice, with 20-min. interval) was associated with significantly less pain at rest and during knee flexion at 5 minutes and 20 minutes after the exercise compared to baseline pain scores.[118] Whether physical rehabilitation following total knee replacement occurs at home or in an inpatient setting may not matter, according to results of the HIHO randomized trial.[119] In total, 165 patients were randomized to 10 days of hospital inpatient rehabilitation followed by 8 weeks of clinician-monitored home-based exercises vs. the home-based program alone. At 26 weeks of follow-up, there were no significant differences between groups in results from the 6-minute walk test, patient-reported pain and function, or quality of life.[119]

A systematic review of 6 trials compared focused physiotherapy exercise vs. standard care or standard physiotherapy in 614 patients with total knee arthroscopy.[120] The meta-analyses of 5 trials found small effect sizes at 3-4 months for functional improvement (effect size 0.33; 95% CI: 0.07-0.58) and range of motion (mean difference 2.9 degrees; 95% CI: 0.61-5.2 degrees), but no significant differences in walking ability or quality of life. At one-year follow-up, there were no significant differences in any outcome measures between groups.

Massage

Massage therapy appears safe in post-operative patients, but evidence suggests it has little effect on key outcomes such as pain or consumption of opioid analgesics. One trial randomized 605 veterans undergoing sternotomy or major abdominal surgery to one of three groups: standard post-operative care; individual attention from a massage therapies (without massage); or daily back massage for up to five postoperative days.[121] All three groups experienced reductions in pain, pain unpleasantness, and consumption of opioid analgesics, and at five-day follow-up, there were no significant differences between groups in these outcomes. Another trial randomized 252 adults having cardiac surgery to usual care or usual care plus two massages and found no significant differences in pain or any other outcomes.[122] A 2019 structured review of evidence about massage for post-surgical outcomes found weak methodologies among existing trials and high clinical heterogeneity, leading the authors to conclude that massage is not recommended as an effective therapy at this time.[123]

Drug options

Acetaminophen

Acetaminophen is more effective than placebo at reducing post-procedural pain, and is associated with mild, mostly transient, adverse events.[124] In a Cochrane review of 21 RCTs of acute pain following wisdom teeth extraction, acetaminophen provided a statistically significant benefit vs. placebo for pain relief at both four hours (RR 2.85; 95% CI: 1.89-4.29) and six hours (RR 3.32; 95% CI: 1.88-5.87). Higher doses gave greater benefit for each measure at both time points. There was no difference between groups in reported adverse events.[125]

A separate Cochrane review of 51 studies assessed the efficacy of acetaminophen for the treatment of acute post-operative pain and found that about half of participants treated with acetaminophen at standard doses achieved at least 50% pain relief over four to six hours, compared with about 20% treated with placebo. Additionally, about half of participants using acetaminophen needed additional analgesia over four to six hours, compared with about 70% with placebo.[124]

NSAIDs

An overview of 16 systematic reviews and meta-analyses that directly and indirectly compared ibuprofen and acetaminophen at standard doses showed that ibuprofen was consistently superior to acetaminophen at conventional doses in acute post-operative pain. Single-dose oral NSAIDs (ibuprofen 400 mg, diclofenac 50 mg, naproxen 500 mg or celecoxib 400 mg) were shown to reduce mild to moderate acute pain and inflammation vs. acetaminophen (Number Needed to Treat (NNT) of 2-3 to achieve a 50% reduction in acute post-op pain vs. placebo).[126,127]

The combination of acetaminophen and NSAID may offer superior analgesia compared with either drug alone. In a systematic review of 21 studies (n=1,909), combining acetaminophen and NSAID was more effective than acetaminophen alone (85% of studies) or NSAID alone (64% of studies). Pain intensity with combination treatment was reduced by 35% vs. acetaminophen alone, and by 39% vs. NSAIDs alone.[128]

Topical NSAIDs may be an effective option for post-surgical pain. One trial randomized 120 women having laparoscopic gynecologic surgery to diclofenac patch vs. placebo at all incisional areas.[129] Mean pain intensity was significantly lower in the diclofenac group at 12 hours post-surgery (3.7 points vs. 5.7 points on 10-point scale; P=0.002) and 24 hours post-surgery (2 points vs. 4.6 points; P<0.001).

Significantly fewer patients in the diclofenac group required additional analgesics in the first 36 hours post-surgery (35% vs. 71.7%; P<0.001).

Anticonvulsants

Anticonvulsants (e.g., gabapentin or pregabalin) may be prescribed with opioids as part of multimodal opioid-sparing analgesic regimes to help reduce central sensitization induced by surgery.[130,131] Gabapentin, however, may also increase side effects such as sedation, visual disturbances, and dizziness, especially at higher doses.[132] Pain reduction with gabapentin or pregabalin alone is inconsistent, with some studies showing benefit to 24 hours while others showing no difference vs. placebo. However, adjunctive use of gabapentin and pregabalin in the immediate post-operative period has been shown to reduced overall opioid doses.[130,132,133]

A 2018 RCT randomized 422 surgical patients to 1200 mg of preoperative gabapentin followed by 600 mg every eight hours for 72 hours vs. active placebo.[134] Gabapentin did not significantly affect time to postoperative pain resolution (84 days vs. 73 days for placebo), but patients receiving gabapentin had a marginally significant reduction in time to opioid cessation after surgery (25 days vs. 32 with placebo, P=0.05). Adverse events were similar between the two groups.

Lidocaine patch/gel

Topical lidocaine patches or gels may help manage chronic neuropathic pain syndrome and post-herpetic neuralgia and have potential for treating post-operative pain, however evidence is insufficient for recommendations of transdermal lidocaine for this indication.[135]

Skeletal muscle relaxants

Skeletal muscle relaxants are not currently included as therapeutic options in clinical guidelines on postoperative pain management,[110] and evidence from clinical trials is limited. One trial randomized 60 patients undergoing inguinal hernia report to tizanidine 4 mg orally 1 hour before surgery and twice daily in first postoperative week vs. placebo.[136] At one-week follow-up, pain scores at rest and during movement were significantly lower in the tizanidine group, and analgesic consumption was also lower with tizanidine (33% vs. 77% in placebo group; P<0.001). Skeletal muscle relaxants are not effective for reducing pain in patients having third molar extractions.[137,138]

Opioids

Due to their potent analgesic efficacy in moderate-to-severe post-operative pain, opioids are frequently prescribed after many types of surgery. However, as noted previously, these drugs are not only associated with risks for addiction, they can exert a number of undesirable side effects, such as nausea, vomiting, gastrointestinal ileus, immunosuppression, and respiratory depression, which may delay patient recovery.[139]

A systematic review of 20 RCTs (2,641 adults with moderate-to-severe post-operative pain) found that single-dose oxycodone is an effective analgesic in acute post-operative pain at doses over 5 mg (NNT 4.6 for ≥50% pain relief with oxycodone 15 mg). Efficacy increased when combined with acetaminophen (NNT 2.7 for oxycodone 10 mg plus acetaminophen 650 mg).[140]

BOTTOM LINE: Multi-modal post-operative pain management may be superior than any single drug intervention alone, such as combining NSAIDs and acetaminophen. Anticonvulsants may be

considered both pre- and post-operatively. Opioids are effective in moderate-to-severe post-op pain but should be used judiciously and with non-opioid analgesics to minimize adverse events and risks of addiction.

Sprains, strains, fractures, and trauma

Non-drug options

The optimal non-drug treatment for sprains and strains remains uncertain. Rest, ice, compression, and elevation (RICE) is a foundational management approach for musculoskeletal trauma, but these techniques are supported by surprisingly little clinical evidence.[141]

A meta-analysis of 24 RCTs analyzed the effectiveness of RICE therapy within 72 hours of trauma for patients after ankle sprain and found moderate evidence for the benefit of immediate posttraumatic mobilization to treat acute ankle sprains, limited evidence for the benefits of ice and compression, and no evidence to support the use of elevation.[141]

Ice has been shown to be better than heat for sprains because it reduces swelling. In a comparison study of 37 patients with ankle sprains, cryotherapy (15 minutes, one to three times per day) was compared with heat therapy (15 minutes, one to three times per day). Results showed that early cryotherapy was associated with shorter time to complete recovery vs. heat therapy (30.4 days vs. 33.3 days, no P-value reported).[142]

Functional treatment

Several studies suggest that early movement, including manual therapy techniques, may be better for recovery from strains or sprains.[141,143] An RCT of 101 patients with mild ankle sprains found that functional treatment (moderate exercises during the first week after ankle sprain) led to significant improvements in short-term ankle function compared with patients who received standard RICE treatment.[143] Activity levels were significantly higher in the exercise group than in the standard treatment group, as measured by time spent walking (1.6 hours vs. 1.2 hours, P=0.029), step count (7,886 steps vs. 5,621 steps, P=0.021), and time spent doing light-intensity activity (76.2 minutes v. 53 minutes, P=0.047).

Supervised physical therapy, long thought to speed up the recovery from sprains, may not be better than usual care for mild ankle sprains. An RCT of 503 patients with simple ankle sprains found that addition of early supervised physiotherapy to RICE treatment did not lead to clinically important improvements in functional recovery up to six months after injury.[144]

Joint mobilization

An RCT in 584 patients with the most severe ankle sprains (unable to bear weight for three days) found that a short period of immobilization with below-the-knee cast or air cast may result in better quality of ankle function at three months than if the patient is only given a tubular compression bandage. Improvements in pain, symptoms, and activity was also observed in the cast groups.[145]

Other therapies

Insufficient evidence exists to recommend massage, acupuncture, or TENS for the treatment of strains or sprains.[146,147]

Drug options for sprains and strains

NSAIDs

A Cochrane review of 16 trials involving 2,144 patients with acute soft tissue injury compared oral NSAIDs with acetaminophen, opioids, acetaminophen plus opioid, or complementary and alternative medicine. These results showed no clinically important differences in analgesic efficacy between NSAIDs and other oral analgesics, with some very low-quality evidence of better function and fewer adverse events with NSAIDs compared with opioid-containing analgesics.[148]

- When NSAIDs were compared with acetaminophen (nine studies, involving 991 participants), there was a lack of clinically important differences in pain at less than 24 hours, at days one through three, and at day seven or later. There was little difference between the two groups in return to function at day seven or later. There was slightly lower risk of gastrointestinal adverse events in the acetaminophen group (16 per 1000 participants for acetaminophen vs. 13 more participants per 1000 in the NSAID group).
- When NSAIDs were compared with opioids (4 studies, involving 958 participants), there was a lack of clinically important differences in pain at less than 24 hours, at days four through six, and at day seven. Return to function at day seven or later favored the NSAID group (low quality evidence), with fewer gastrointestinal adverse events in those receiving selective COX-2 inhibitor NSAIDs.
- When NSAIDs were compared with the combination of acetaminophen and an opioid (four studies, involving 240 participants), there was no difference in pain, swelling, return to function at day seven, or in gastrointestinal adverse events.

Topical NSAIDs such as diclofenac gel or patch (Flector) can also provide effective initial pain control for acute musculoskeletal pain resulting from sprains and strains.[149] These agents have been shown to be safe and effective for acute musculoskeletal pain, with fewer systemic adverse effects than oral NSAIDs.[150] However, the long term impact of topical NSAID use has not been determined.[127]

Acetaminophen

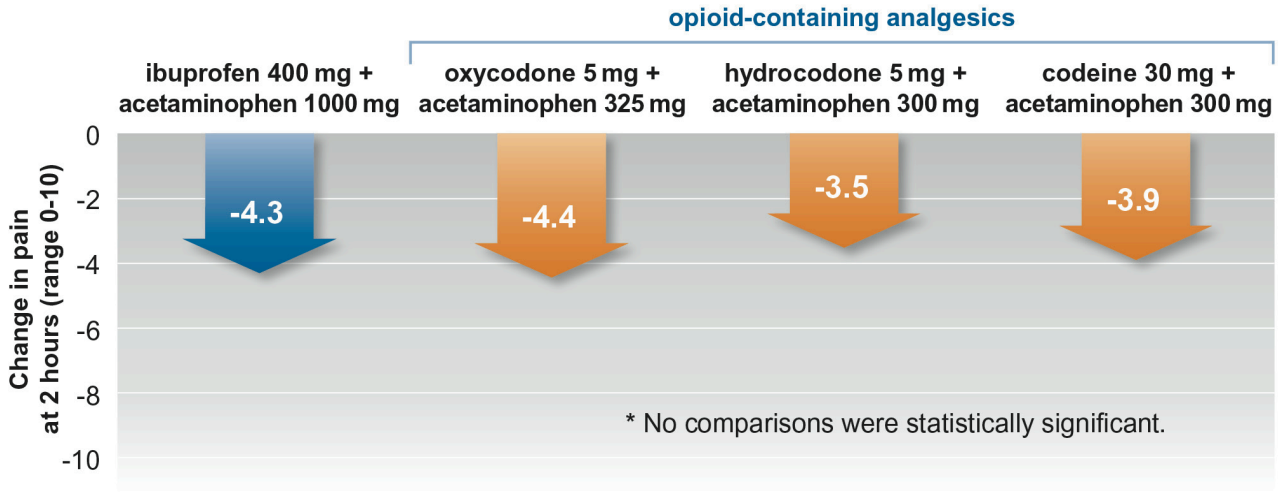
When the efficacy of acetaminophen or combination acetaminophen plus opioids was compared to NSAIDs for the treatment of acute soft tissue injuries, no clinically important differences were observed for pain or function. An Cochrane analysis of nine studies (n=991) comparing acetaminophen vs. NSAIDs found little difference in pain at 24 hours, or in swelling, or function at seven days, although the study authors downgraded the evidence for these outcomes due to the possibility of suboptimal dosing of the analgesics.[148] NSAIDs were associated with a higher risk of gastrointestinal bleeding (13 more events per 1000 people) than acetaminophen.

Opioids

A 2017 RCT found that opioid analgesics were no more effective in patients with severe acute musculoskeletal pain than a combination of ibuprofen plus acetaminophen.[62] In total, 416 patients with acute extremity pain were randomized to one of the following four regimens: 1) ibuprofen 400 mg and acetaminophen 1000 mg; 2) oxycodone 5 mg and acetaminophen 325 mg; 3) hydrocodone 5 mg and acetaminophen 300 mg; or 4) codeine 30 mg and acetaminophen 300 mg.[62] The mean pain scores at two hours after ingestion decreased by 4.3 points (95% CI: 3.6-4.9) with ibuprofen and acetaminophen; by 4.4 points (95% CI: 3.7 to 5.0) with oxycodone and acetaminophen; by 3.5 points (95% CI: 2.9-4.2) with

hydrocodone and acetaminophen; and by 3.9 points (95% CI: 3.2-4.5) with codeine and acetaminophen (Figure 9). None of the differences between analgesics were statistically significant.[62]

Figure 9: Effectiveness of ibuprofen and acetaminophen compared with three opioid-containing regimens in patients with severe musculoskeletal pain[62]



Other therapies

No studies have evaluated the use of gabapentin/pregabalin or skeletal muscle relaxants as treatments for acute strains or sprains.

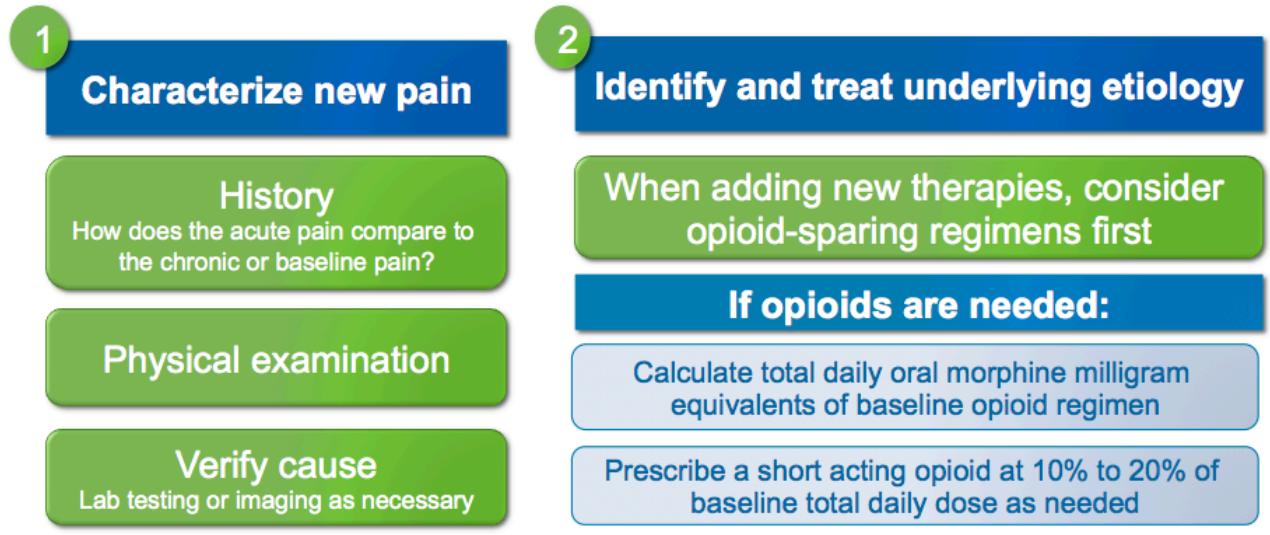
BOTTOM LINE: Treat acute pain caused by sprains, strains, fractures and trauma with non-drug therapies (RICE) and non-opioid analgesics. Combining an NSAID with acetaminophen may have positive synergistic analgesic effects. Topical NSAIDs reduce pain and may be an option to avoid the systemic side effects of oral NSAIDs. Physical therapy may not be better than usual care alone for mild ankle sprains, but casting or air-casting may improve short-term function for severe ankle sprains. Opioids are no more effective for pain relief than a combination of acetaminophen and an NSAID and should be avoided due to known risks and adverse events.

Acute pain management in special populations

Chronic opioid users

Treating acute pain in patients on long-term (i.e., >6 months) opioids for chronic pain is challenging since patients are already opioid-tolerant. These patients often need higher doses to achieve the same analgesic effect and also may have opioid-induced hyperalgesia. The main goal in treating acute pain in this population is to ensure that baseline opioid requirements are met and then additional analgesia is provided to manage the acute pain.[151]

Figure 10: Suggested clinical algorithm for acute pain in patients chronically using opioids[151,152]



A multimodal combination of medications, such as non-opioid analgesics and short-acting opioids, can be used to address acute pain in chronic opioid users. It is important to note that switching from long-acting opioids to intermittent doses of a short-acting opioid medication may trigger adverse reactions in dependent patients. This may require frequent repeat doses.[151]

Expert opinion suggests that when prescribing additional opioids, choosing a different type of opioid may improve analgesia due to different receptors affected (opioid rotation).[153] However, the cross-tolerance of different opioids varies, and caution is crucial to select the appropriate dose.[151,152]

To select a dose to treat acute breakthrough pain, clinicians may estimate the daily morphine equivalent dose of the baseline opioid regimen and prescribe a short-acting opioid at 10% to 20% of the baseline total daily dose for the duration of expected pain.[152,154]

Selecting an appropriate, safe dose of methadone is particularly challenging due to its long and highly variable half-life, numerous interactions with other medications, and effects on the QTc interval and respiratory depression.[155]

Patients with OUD

Some physicians may not prescribe effective opioid analgesia for patients with OUD on medication-based treatment due to concerns about respiratory depression, overdose, or drug diversion. As a result, this population is at particular risk of under-treatment for acute pain.

Physicians may also assume that acute pain is adequately controlled with the long-term opioid agonist (i.e., methadone) or partial-agonist (i.e., buprenorphine). In reality, these agents at usual doses used to treat OUD are insufficient to treat severe or persistent pain. Although they are potent analgesics, methadone and buprenorphine have a duration of action for analgesia (four to eight hours) that is substantially shorter than their suppression of opioid withdrawal (24 to 48 hours).[156]

Therefore, non-opioid analgesics (e.g., acetaminophen and NSAIDs) are first-line options for treating acute pain in this population. For moderate-to-severe pain not adequately controlled with non-opioids,

however, judicious use of opioid analgesics should be considered. Patients on medication-based treatment generally have a high cross-tolerance for analgesia, leading to shorter durations of analgesic effects. Higher opioid doses administered at shorter intervals may thus be necessary.

Because extended-release naltrexone will block the effects of any opioid analgesics, acute pain in such patients (e.g., that associated with dental work, surgery, or traumatic injury) should be treated with regional analgesia, conscious sedation, non-opioid analgesics, or general anesthesia, and consultation with a pain specialist may be warranted.[157]

If opioids are deemed necessary for patients on methadone or buprenorphine, clinicians should verify the patient's methadone or buprenorphine dose, and ensure that naloxone is available. Primary care providers should prescribe naloxone to patients at risk of overdose, including those:

- with renal or hepatic dysfunction
- taking opioid doses >50 MMED
- co-prescribed benzodiazepines or other sedating medications
- with a history of overdose or OUD
- starting treatment for opioid use disorder

In many states, including Illinois, Maine, Ohio, Pennsylvania, and West Virginia, a standing order or protocol allows patients, family members, caregivers, and/or friends to request naloxone from their local pharmacist. Anyone receiving naloxone should be taught how to use the device and about the common signs of overdose.

If a new opioid is added to an existing OUD regimen to treat acute pain, clinicians should inform the program or prescribing physician about the addition, as this may affect subsequent urine screening. As with any patient with acute pain, it's important to remind patients that the goal is not "zero pain" but, rather, a level of analgesia that maximizes physical and mental functioning.[158]

Patients susceptible to respiratory depression

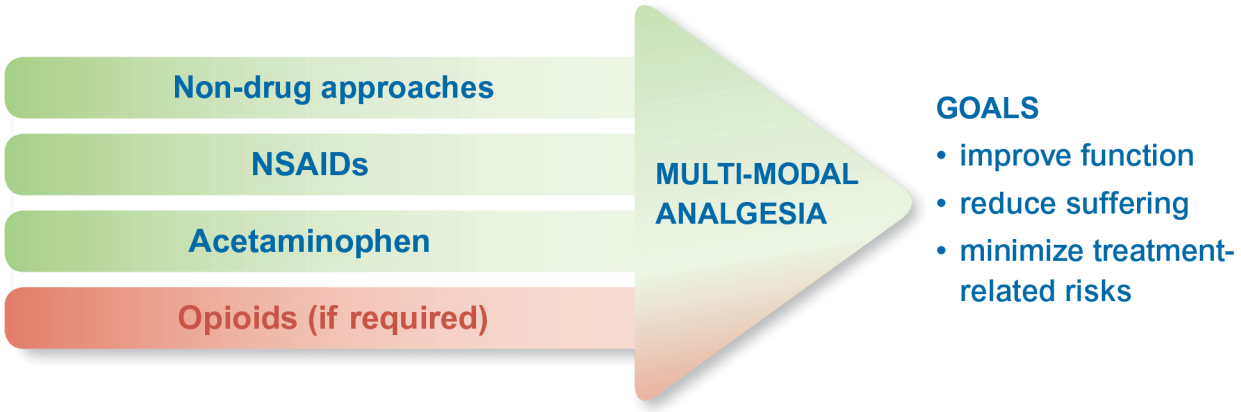
Opioid-induced respiratory function is a particular concern in patients with obstructive sleep apnea (OSA), who are at increased risk for opioid-induced respiratory depression (OIRD) compared to the general population. A systematic review of 40 studies assessed perioperative outcomes among patients with sleep apnea receiving opioids for acute pain, and although it did not find any high-quality randomized studies, poorer outcomes were observed among patients with sleep apnea who took opioids.[159] The risk of OIRD was highest in the 24 hours after opioid administration, suggesting that enhanced monitoring is essential. In addition, patients with OSA were found to have enhanced opioid sensitivity and increased pain perception, both of which can complicate treatment and warrant a cautious approach if opioids are deemed necessary.

Putting it all together

Since much acute pain is self-limiting and remits with healing (typically within a month), helping patients frame expectations about pain and pain relief can provide reassurance and reduce fear, worry, and distress.

Use multimodal approaches to manage acute pain, combining non-drug (e.g. interventional procedures, physical rehabilitation, and psychological support) and drug-based options (Figure 11). Opioid analgesics should be reserved for pain that is non-responsive to all other approaches, and then should be used at the lowest doses and shortest durations that are appropriate for the pain intensity expected with the precipitating event.

Figure 11: Combining pharmacologic and non-pharmacologic approaches to manage acute pain



Clinicians should avoid co-prescribing benzodiazepines and should check their state PDMP (whether or not this is required by law).

Table 2 on the next page summarizes the evidence for drug and non-drug approaches to managing the acute pain conditions reviewed previously.

Table 2: Summary of treatment options for acute pain conditions

	INTERVENTION	Acute strains and sprains	Acute low back pain	Acute post-op pain
NON-DRUG OPTIONS	compression	🟢	⊘	⊘
	exercise	🟢	🟡	○
	casting (severe sprains)	🟢	⊘	⊘
	physical therapy	○	○	○
	massage	○	🟢	🟡
	acupuncture	○	🟢	🟢
	spinal manipulation	⊘	🟡	⊘
	TENS*	○	⊘	🟢
DRUG OPTIONS	acetaminophen	🟢	○	🟢
	oral NSAIDs	🟢	🟢	🟢
	topical NSAIDs	🟢	⊘	○
	opioids	🔴	🔴	🟡
	skeletal muscle relaxants	⊘	○	○
	systemic oral steroids	⊘	○	⊘
	epidural steroids (for sciatica)	○	🟡	○
	NSAID + acetaminophen	🟢	🟢	🟢
	gabapentin; pregabalin	⊘	⊘	🟡

Risk/benefit: 🟢 = favorable; 🟡 = potentially favorable; 🔴 = unfavorable; ○ = neutral; ⊘ = not studied

* **TENS:** transcutaneous electrical nerve stimulation

As with treating chronic pain, the appropriate deployment of opioids for acute pain calls for balancing the potential benefits of an analgesic option against the risks that can reasonably be expected in a specific patient with a specific set of physical, emotional, or cognitive characteristics. With proper pain assessment, primary reliance on non-pharmacologic and non-opioid analgesics and a holistic view of pain that considers critical psychological and social dimensions of pain, clinicians can both relieve immediate suffering and maximize their patients' long-term health.

Appendix I: Brief Pain Inventory

STUDY ID #:_____ DO NOT WRITE ABOVE THIS LINE HOSPITAL #: _____

Brief Pain Inventory (Short Form)

Date: ____/____/____ Time: _____

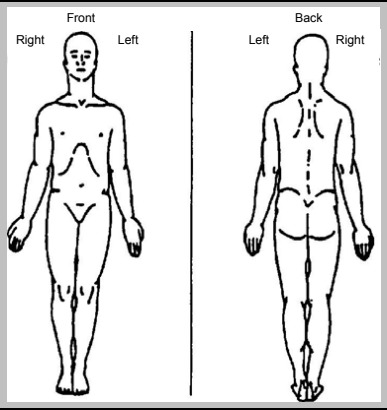
Name: _____ _____ _____

Last First Middle Initial

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these every-day kinds of pain today?

1. Yes 2. No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by circling the one number that best describes your pain at its worst in the last 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No Pain — Pain as bad as you can imagine

4. Please rate your pain by circling the one number that best describes your pain at its least in the last 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No Pain — Pain as bad as you can imagine

5. Please rate your pain by circling the one number that best describes your pain on the average.

0 1 2 3 4 5 6 7 8 9 10
No Pain — Pain as bad as you can imagine

6. Please rate your pain by circling the one number that tells how much pain you have right now.

0 1 2 3 4 5 6 7 8 9 10
No Pain — Pain as bad as you can imagine

Page 1 of 2

STUDY ID #:_____ DO NOT WRITE ABOVE THIS LINE HOSPITAL #: _____

Date: ____/____/____ Time: _____

Name: _____ _____ _____

Last First Middle Initial

7. What treatments or medications are you receiving for your pain?

8. In the last 24 hours, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0% No Relief 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% Complete Relief

9. Circle the one number that describes how, during the past 24 hours, pain has interfered with your:

A. General Activity

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

B. Mood

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

C. Walking Ability

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

D. Normal Work (includes both work outside the home and housework)

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

E. Relations with other people

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

F. Sleep

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

G. Enjoyment of life

0 Does not Interfere 1 2 3 4 5 6 7 8 9 10 Completely Interferes

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