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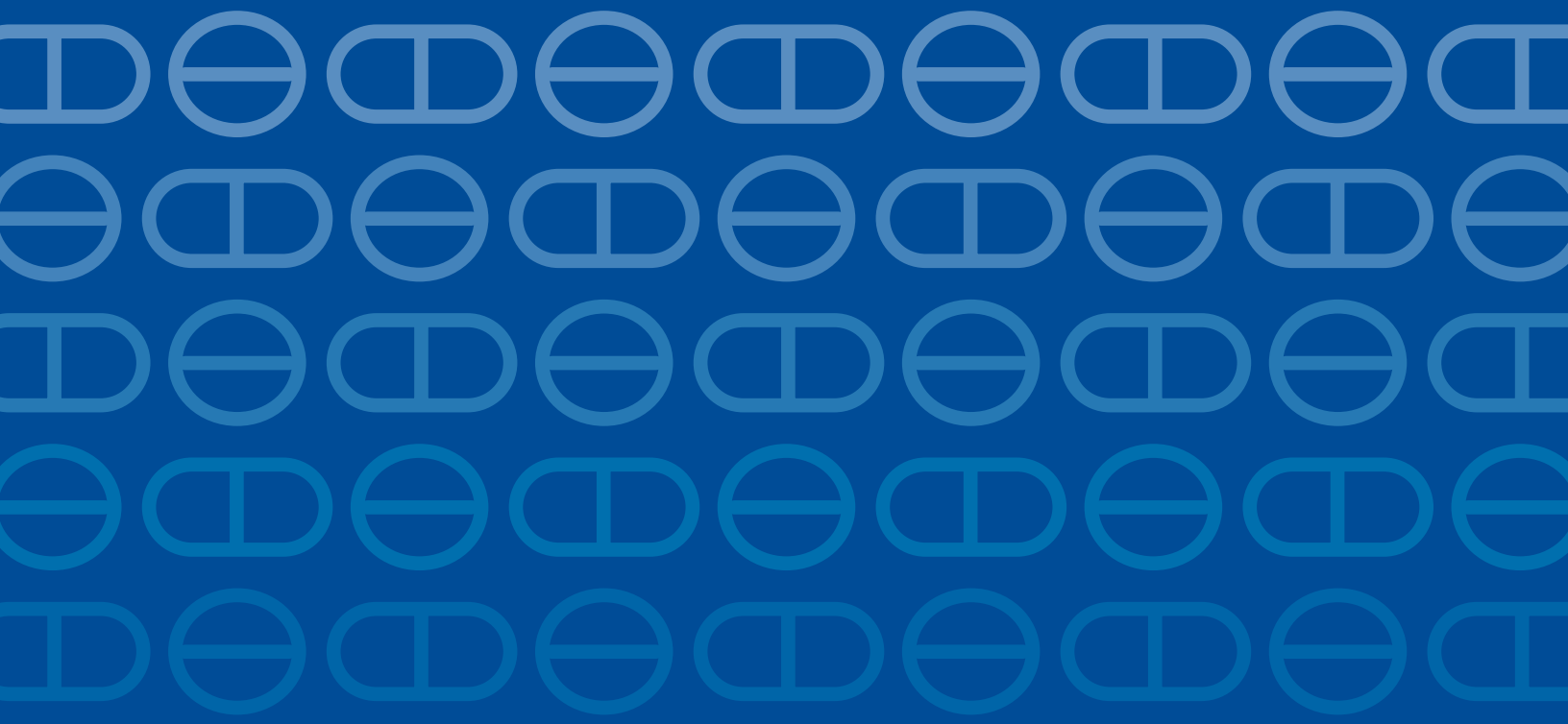
Managing acute pain in the elderly



Managing acute pain in the elderly

Principal Consultants: Brian Bateman M.D., M.Sc.

Series Editors: Jerry Avorn, M.D. (principal editor), Dae Kim, M.D., M.P.H., Sc.D., Jing Luo, M.D., M.P.H., Niteesh K. Choudhry, M.D., Ph.D., Michael Fischer, M.D., M.S., Gregory Curfman, M.D.; Ellen Dancel, PharmD, M.P.H.

Medical Writer: Jenny Cai

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These are general recommendations only; specific clinical decisions should be made by the treating physician based on an individual patient's clinical condition.

Alosa Health
Managing acute pain in the elderly

Accreditation:

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education through the joint providership of Harvard Medical School and Alosa Health. The Harvard Medical School is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation:

The Harvard Medical School designates this enduring material for a maximum of 1.50 *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 without posting 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 completion of this activity, participants will be able to:

- Consider all treatment options to manage pain for different types of acute pain conditions, optimizing the use of non-opioid alternatives before considering opioids.
- Explain the evidence supporting the efficacy and risks of different treatment options for acute pain.
- Follow several general principles for prescribing opioids for acute pain if opioids are necessary.
- Establish realistic expectations for patients to reduce their concerns about their acute pain and contain demands for addictive analgesics.

- Optimize a multimodal pain management strategy for acute pain by combining several approaches, including non-pharmacologic and non-opioid pharmacologic options.
- Develop a strategy to identify patients with possible opioid use disorder or problematic behaviors and provide or refer to appropriate care.
- Recommend naloxone for at-risk patients.

Disclosure Policy:

Harvard Medical School has long held the standard that its continuing medical education courses be free of commercial bias.

In accord with the disclosure policy of the Medical School as well as standards set forth by the Accreditation Council for Continuing Medical Education, course planners, speakers, and content reviewers have been asked to disclose any relevant relationship they, or their spouse or partner, have to companies producing, marketing, re-selling or distributing health care goods or services consumed by, or used on, patients. In addition, faculty have been asked to list any off-label uses of pharmaceuticals and/or devices for investigational or non-FDA approved purposes that they plan to discuss. Such disclosure is not intended to suggest or condone bias in any presentation, but is elicited to provide the course director and participants with information that might be of potential importance to their evaluation of a given presentation.

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Faculty and Planners:

Brian Bateman, M.D., M.Sc., is an Associate Professor of Anesthesia at Harvard Medical School. He is the Chief of the Division of Obstetric Anesthesia in the Department of Anesthesiology, Perioperative and Pain Medicine, and is a researcher in the Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, both at Brigham and Women’s Hospital. Dr. Bateman has no relevant financial relationships to disclose.

Jerry Avorn, M.D., is a Professor of Medicine at Harvard Medical School and Chief of the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital. An internist, he has worked as a primary care physician and geriatrician and has been studying drug use and its outcomes for over 35 years. Dr. Avorn has no relevant financial relationships to disclose.

Dae Kim, M.D., M.P.H., is an Assistant Professor of Medicine at Harvard Medical School and a geriatrician at Beth Israel Deaconess Medical Center. Dr. Kim has no relevant financial relationships to disclose.

Jing Luo, M.D., M.P.H., is an Instructor in Medicine at Harvard Medical School and an urgent care provider at the Brigham and Women’s Hospital. His research focuses on prescription drug pricing and pharmaceutical regulation. Dr. Luo has no relevant financial relationships to disclose.

Niteesh K. Choudhry, M.D., Ph.D. is a Professor of Medicine at Harvard Medical School and a hospitalist at Brigham and Women's Hospital. His research focuses on the use of medications to treat common chronic conditions. Dr. Choudhry has no relevant financial relationships to disclose.

Michael Fischer, M.D., M.S., is an Associate Professor of Medicine at Harvard Medical School and a primary care internist who studies cost–effective drug use in outpatient practices. Dr. Fischer has no relevant financial relationships to disclose.

Gregory Curfman, M.D., is an Assistant Professor of Medicine at Harvard Medical School and board-certified internal medicine physician and cardiologist. Dr. Curfman has no relevant financial relationships to disclose.

Ellen Dancel, Pharm.D., M.P.H., is the Director of Clinical Materials Development at Alosa Health. Dr. Dancel has no relevant financial relationships to disclose.

Jenny Cai, M.Sc., is a medical writer and curriculum specialist with over eight years of experience in medical education. Ms. Cai has no relevant financial relationships to disclose.

Reviewers

Chris Gilligan, M.D., is an Assistant Professor of Anesthesiology at Harvard Medical School and Chief of the Division of Pain Management, Department of Anesthesiology, Perioperative and Pain Medicine at Brigham and Women’s Hospital. Dr. Gilligan has no relevant financial relationships to disclose.

Don Teater, M.D., M.P.H., is a family physician and principal of Teater Health Solutions. He previously held the role of Medical Advisor with the National Safety Council, where he worked to reduce death and injury from prescription opioid overdose. Dr. Teater has no relevant financial relationships to disclose.

Susan O’Brien is a CME Consultant and CME reviewer for Harvard Medical School Department of Continuing Education. Her role is to review CME proposals for compliance with regulatory requirements. Ms. O'Brien has no relevant financial relationships to disclose.

The following committee members from Harvard Medical School’s Continuing Medical Education program also reviewed this educational activity: Gyorgy Baffy, M.D., Ph.D.; James Burnes, M.D.; Laura Collins, M.D.; Louis Pasquale, M.D.; Jane Sillman, M.D.; and Mary Lou Townsend, M.Ed.. Dr. Pasquale is a paid consultant for Bausch & Lomb, an unpaid consultant for Novartis, and a speaker for Allergan. He is the recipient of a grant from NEI and the recipient of an unrestricted grant from Merck. None of the other committee members have any relevant financial relationships to disclose.

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.

Tests and evaluations should be submitted to Alosa Health via email, mail or fax.

Email: cme@alosahealth.org

Mailing address:

Alosa Health
419 Boylston Street, 6th Floor
Boston, MA 02116

Fax: 857-350-9155

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Please email any questions to **cme@alosahealth.org** or call **(617) 948-5997.**

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Scope of acute pain in the elderly

Older patients are at increased risk of pain from degenerative conditions such as osteoarthritis, and often experience pain in multiple sites, compounding pain-related suffering and disability. As the elderly undergo surgery four times more often than other age groups, they are also more likely to suffer from the pain consequences of surgery.[1]

Generalized pain increases in intensity with age.[2] Acute pain in particular is a common reason for emergency department (ED) visits among older adults. In those 65 years and older, acute pain leads to about 4 million U.S. emergency department (ED) visits each year.[3] Potential barriers to assessing and addressing pain during ED visits include cognitive and functional impairments, as well as limitations of physician knowledge about how to address pain in older patients . As a result, many elderly patients experience higher rates of pain and lower rates of effective treatment at the end of the ED visit, and are 20% less likely to receive treatment than younger adults.[4]

In addition to inadequate pain relief, unaddressed acute pain may lead to poorer clinical outcomes, including behavioral problems, longer hospital stays, impaired mobility, complications, as well as the development or intensification of delirium.[4,5] Effective management of acute pain can facilitate patient treatment and recovery, and in some cases, may help prevent chronic pain. In particular, effective early treatment of older adults with acute pain can lead to reduced persistent pain and better long-term function.[6]

Assessment of pain in older patients is often complicated by issues such as age-related physiologic changes, physical accessibility to treatment, psychosocial concerns, frailty, poor memory, coexisting illnesses, use of concomitant medication, and problems of communication with patients with cognitive impairment. Elderly patients may often under- or over-report their experience of pain due to functional impairment or psychological distress. Clinical decision-making must take into account all of these considerations, each of which can increase the risk for adverse outcomes. Opioids are often used to provide acute pain relief but have addictive and euphoric properties that can lead to adverse effects, misuse, abuse, addiction, and overdose. In addition to being bothersome, opioid side effects can also contribute to reduced quality of life and substantial morbidity. Awareness of best practices surrounding opioid use in the elderly is essential to effective acute pain care.[7]

Due to the high prevalence of acute pain, clinicians are challenged with providing effective pain relief while minimizing side effects in this unique population. In particular, opioids are often relied upon to provide adequate relief for acute pain but have addictive and euphoric properties that make patients vulnerable to misuse, abuse, addiction, and overdose. Opioids are also associated with significant adverse side effects. In addition to being bothersome, these side effects can also contribute to reduced quality of life and substantial morbidity, as older adults are more likely to miss doses, overuse opioids, discontinue treatment, or have low compliance. Awareness of best practices surrounding opioid use in the elderly is essential to effective acute pain care.[7]

This evidence document outlines the core principles of acute pain management in the elderly population, with special considerations for the safe, effective and responsible use of prescription opioids. It also reviews evidence for three common pain syndromes common in older adults: acute low back pain, post-operative pain, as well as sprains, strains, fractures and trauma (acute musculoskeletal pain). Finally, it offers recommendations on the management of acute pain in patients who use opioids on a long-term basis for

chronic pain, and the management of acute pain in those with opioid use disorder (formerly referred to as addiction).

Defining acute and chronic pain

Acute pain is defined as having an abrupt onset and is due to an obvious cause, such as an injury or other process that is not ongoing, such as a recent surgical procedure. It has a generally short duration, and usually lasts less than four weeks, improving over time.[8] Acute pain is one of the most common presenting complaints in ambulatory care.[9]

In contrast, chronic pain is defined as pain that typically lasts more than three months or past the time of normal tissue healing. It can be the result of an underlying medical disease or condition, injury, medical treatment, inflammation, or an unknown cause.[10] Chronic pain is addressed in a separate Alosa Health module.

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 illness concern, and ineffective coping strategies regarding the ability to control pain and function despite it.[11] 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).[8]

Assessing acute pain

Appropriate pain management includes a comprehensive initial assessment, as well as frequent reassessments of treatment response. Such assessments include evaluation of pain intensity location, quality and duration, aggravating or alleviating factors, and previous treatments and their efficacy.[12,13] The complexity of pain assessment in geriatric patients often requires a multimodal approach to diagnosis and management.

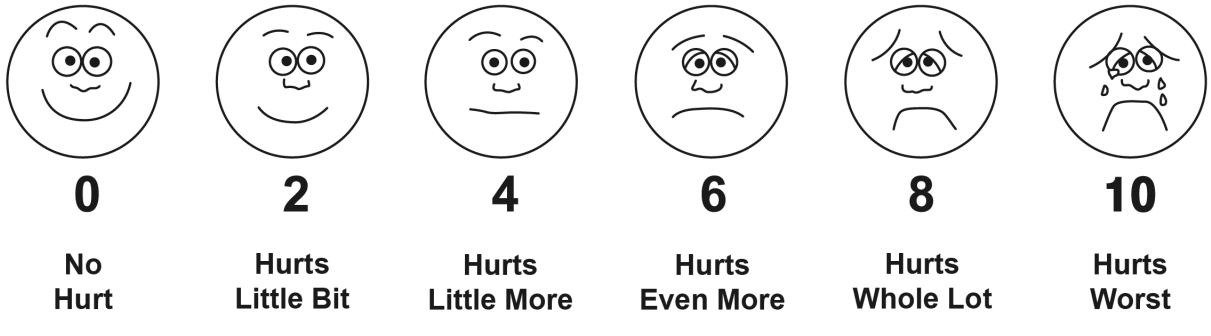
The physical examination includes a complete musculoskeletal examination of the primary site of pain, with particular attention to common conditions such as fibromyalgia, osteoarthritis, and myofascial pain. Types of pain include nociceptive (pain due to tissue injury), neuropathic, and undetermined (multiple etiologies). Older adults are more likely to experience neuropathic pain compared with younger adults because many diseases that cause neuropathic pain increase in incidence with age.[14] Types of neuropathic pain include diabetic neuropathy, postherpetic neuralgia, trigeminal neuralgia, and post-stroke pain. Each of these may be characterized by hypersensitivity, paresthesia, spontaneous (not stimulus-induced) ongoing pain, and shooting, electric shock-like sensations.[15]

Assessing pain intensity

Regular evaluation using a pain scale allows the physician to monitor treatment effectiveness and to determine when changes are needed. It is important to be consistent with evaluations and to use the same scale during follow-up examinations. Generic unidimensional pain questionnaires include the Visual Analog Scale (VAS) and Numeric Rating Scale (NRS), simple measures in which patients rate their current pain intensity from 0 (“no pain”) to 10 (“worst possible pain”).[16] The widely used Wong-Baker FACES Pain Rating

Scale includes a numeric rating scale accompanied by a series of faces depicting various levels of pain (Figure 1).

Figure 1: Wong-Baker FACES Pain Rating Scale



While useful for a quick assessment of pain, 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.[17] In elderly patients, the VAS is associated with more responses that are incomplete or unable to be scored.[13]

Multidimensional pain questionnaires include the Short-form McGill Pain Questionnaire, Chronic Pain Grade Scale, and Short Form 36 Bodily Pain Scale, which assess more aspects of pain, but are mainly used to assess chronic pain rather than acute pain.

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.[18]

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 more fully captures impact of pain on function and quality of life than unidimensional questionnaires, although, like most multidimensional questionnaires, it requires more time (10 minutes) and concentration to complete, which may limit its utility in some elderly patients.[19] See Appendix I for a sample of the BPI.

Assessing pain in patients with cognitive impairment

Self-reports are the most reliable source of information on pain, but if a patient cannot do this adequately because of cognitive impairment or dementia, caregiver's reports can be used. Patients with severe dementia may be unable to report or describe pain, nor request analgesia. Language deficits are a major barrier to adequate pain assessment and treatment in the elderly.[20]

Symptoms of delirium can overlap with manifestation 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, persistent thoughts, anger, or lethargy.[20] In a prospective observational study in 361 patients who had undergone elective non-cardiac surgical procedures, higher pain scores at rest were associated with an increased risk of delirium over the first three

days after surgery (adjusted risk ratio 1.20, p=0.04), although pain with movement and maximal pain score showed no effect.[5]

Careful observation of pain behaviors may be helpful to determine whether there is a treatable cause of pain. For example, the Pain Assessment Checklist for Seniors with Severe Dementia (PACSLAC) is a checklist of six pain behavioral categories:[20]

- 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)

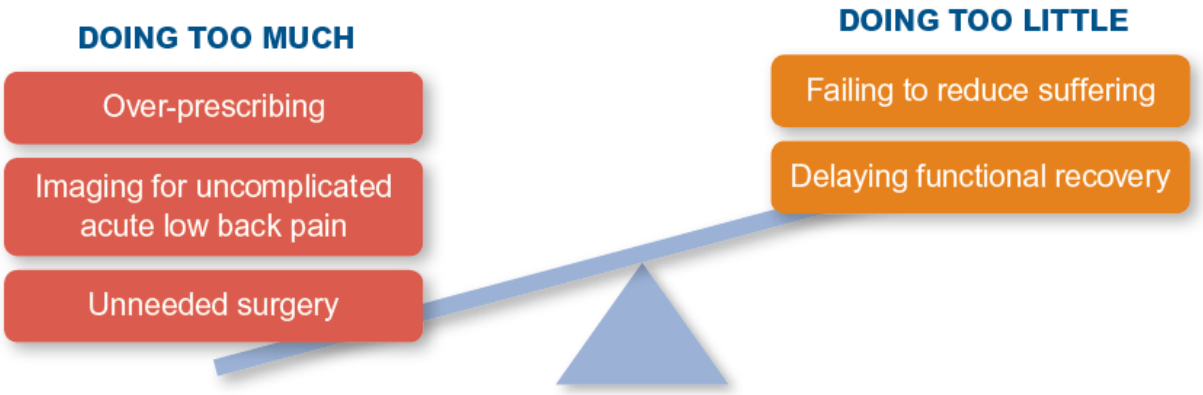
BOTTOM LINE: Assessing acute pain in the elderly can be challenging, and requires the use of validated instruments, caregiver reports, as well as a thorough history and examination.

Managing acute pain

It is important to find the right balance between undertreating acute pain and over-medicating for a self-limited condition. In many cases, the cause of a patient's pain is benign, and the most effective treatment may simply be to provide reassurance to the patient and wait for the underlying condition to improve on its own. In part to address patient concerns or worry, providers may provide too much care, such as unnecessary imaging for uncomplicated acute low back pain, other unneeded diagnostic procedures or surgeries, and prescribing more medication than necessary.

However, in other cases, clinicians may not do enough to treat pain, often leading to missed or delayed diagnosis and management of underlying conditions. Insufficient post-operative pain control may precipitate delirium, especially in the elderly. Therefore, it is important to adequately address acute pain while avoiding over-treatment. The rapid and effective management of acute pain may reduce or prevent adverse physiologic and psychological consequences associated with pain progression, including stress escalation, progression to chronic pain, or inability to comply with medical interventions.[21]

Figure 2: Finding the right balance in management of acute pain



The goal of optimal pain treatment is not to eliminate pain, but rather to relieve suffering and improve function while minimizing the harms and risks associated with treatment. Timely adjustments in treatment for inadequately controlled pain can facilitate recovery from underlying diseases or injuries.

Managing patient expectations

One long-standing rule of thumb states that 90% of patients experience a 90% improvement in pain by 90 days. While not quantitatively rigorous, this concept has some support in the literature. Most forms of acute nociceptive pain (e.g. nonspecific low back pain) are self-limited, subside within weeks, and do not require substantial intervention. In a systematic review evaluating 15 prognosis trials, 82% of people who stopped work due to acute low back pain returned to work within one month.[22] (See Low Back Pain section beginning on p18 for more information on relevant studies).

In a prospective observational study of 1633 patients with acute low back pain, patients showed rapid improvement after the onset of low back pain, with a mean of 16 days to return to a functional status similar to that before onset. Only 5% of patients had not reported functional recovery at six months.[23]

Helping patients manage expectations can reduce fear, worry, concern, and distress, as well as excessive demands for medication. A systematic review of 14 controlled trials of patient education interventions for low back pain showed that structured messaging can reassure patients with acute pain more than usual care/control education both in the short and long term. Messaging was significantly more reassuring to patients when delivered by physicians than other primary care practitioners, and such communication can reduce the frequency of primary care visits.[24] In treating is self-limiting acute pain, such reassurance by physicians is an essential aspect of management.

Examples of effective messaging evaluated in clinical studies:

- “Based on the history and exam, you have a good prognosis.”
- “The acute pain you are experiencing is benign.”
- “Avoid bed-rest.”

Challenges in managing acute pain in the elderly

The clinical approach to acute pain assessment and management differs in older versus younger populations. Elderly patients often have diminished functional status and physiological reserve, with a higher potential to develop complications and adverse reactions to medication than the general public. Concurrent illnesses and conditions may complicate treatment of pain, as patients are more likely to be on several medications at once. In addition, age-related changes in elderly patients result in increased fat mass, decreased muscle mass, and decreased body water compared to the general population; this can have important pharmacodynamic implications for drug dosage and toxicity.[25]

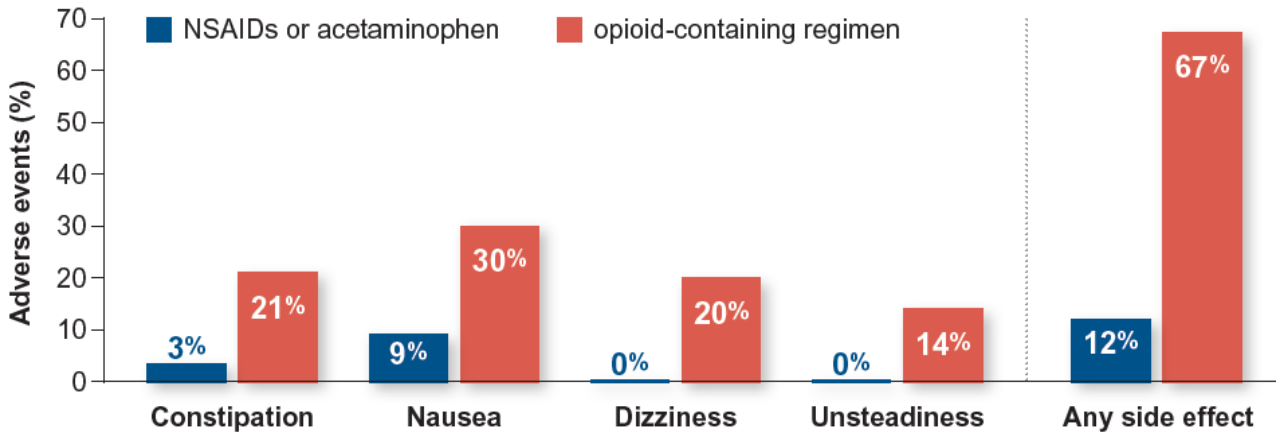
The elderly are at the highest risk for functional decline, medical and surgical complications, and opioid related side effects.[6] Delirium is the most common post-operative complication in older persons and is associated with adverse clinical and economic outcomes, such as higher rates of major complications, poor functional recovery, increased length of hospital stay, and higher costs.[26]

Opioid use can increase the risk of delirium. A prospective cohort study monitored exposure to medications with psychoactive properties such as opioids, benzodiazepines, and anticholinergics in 91 post-operative patients who developed delirium after surgical procedures and 154 controls. All opioids can cause delirium; no significant differences in the rates of delirium have been found among other commonly used opioids, such as morphine, fentanyl, tramadol, hydromorphone, or oxycodone. However, a greater risk of delirium was significantly associated with post-operative use of meperidine (OR 2.7; 95% CI: 1.3-5.5) and benzodiazepines (OR 3.0; 95% CI: 1.3-6.8). For benzodiazepines, long-acting agents and high-dose exposures were more likely to cause delirium than short-acting agents or low-dose exposures.[26,27]

In view of this evidence, clinicians caring for patients at risk for delirium (such as the elderly) should carefully evaluate the use of all psychoactive medications in the post-operative period (e.g., benzodiazepines), choose the lowest effective dose of opioids for a short duration, and employ alternative therapies whenever possible.

Older patients are also at higher risk of complications from opioids. A cross-sectional study compared common side effects experienced during the first week of treatment with opioid-containing analgesics versus non-opioid analgesics (e.g., NSAIDs or acetaminophen) in patients over 65 with acute musculoskeletal pain seen for emergency care. The intensity of six common opioid-related side effects (tiredness, nausea, constipation, vomiting, dizziness, and unsteadiness) was assessed using a 0 to 10 scale. In patients treated with opioid-containing analgesics, 62% (95% CI: 50%-72%) reported at least one side effect of moderate or severe intensity. In addition, both side effects of moderate or severe intensity (62%, 95% CI: 48%-74% vs. 4%, 95% CI: 1%-20%) and medication discontinuation due to side effects (16%, 95% CI: 8%-29% vs. 0%, 95% CI: 0%-13%) were more common in patients prescribed opioids than among those taking only non-opioids. A limitation of this study is that it could not assess severe but less common adverse events associated with NSAIDs and acetaminophen, including the risk for gastrointestinal bleeding, acute kidney injury, and hepatotoxicity. These risks may be reduced through the co-administration of proton pump inhibitors,/ COX-selective NSAIDs and / or keeping acetaminophen doses below three to four grams per day.[3]

Figure 3: Opioid prescriptions are associated with a higher risk of adverse events in older patients[3]



Opioids also greatly increase the likelihood of falls and fracture, a particularly important risk in the elderly. In a retrospective study in 12,840 elderly (mean age 80) patients with arthritis who received different analgesics, opioid use was associated with an increased relative risk of many adverse events compared with nonselective NSAIDs. Although this retrospective comparison would likely have never been made in the setting of an RCT, patients had similar baseline characteristics matched by propensity score methods. Compared with non-selective NSAIDs, the risk of cardiovascular events (hazard ratio (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) were all increased with opioid use. Patients prescribed opioids for arthritic pain had nearly twice the risk of out-of-hospital cardiac death as did comparable patients prescribed nonselective NSAIDs.[28]

These findings were reinforced by the results of another retrospective study of all-cause mortality for 23,308 patients with chronic noncancer pain, in which prescription of long-acting opioids was associated with a significantly increased risk of all-cause mortality compared with prescription of anticonvulsants or cyclic antidepressants. Notably, patients receiving long-acting opioids had a higher risk of death when they also received baseline short-acting opioid doses of ≤30 mg or >30 mg morphine equivalents.[29] Although long-acting opioids should not be prescribed for acute pain, these findings are consistent with those seen with short-acting opioids for arthritis.

Taken together, initial treatment may be especially important for older adults with acute pain, as it serves to reduce suffering as well as improves prognosis. The effective management of initial acute pain has been associated with lower rates of persistent pain and improved long-term function.[6]

Selecting a pain regimen

Several medication choices can relieve acute pain without needing to resort to addictive drugs. For acute musculoskeletal pain, “RICE” (rest, ice, compression, elevation is both safe and effective. Mild exercise as tolerated may also be an option to increase blood flow to the area. Common first-line pharmacologic agents for the symptomatic treatment of mild to moderate pain include acetaminophen, non-steroidal anti-inflammatory drugs (NSAID)s, or topical agents.

The choice between the types of medications 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 first-line

treatments 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. Combining drugs may also provide benefits beyond the additive effects of either drug alone.

Opioids are commonly prescribed for pain, with nearly two thirds (64%) of the public reporting being prescribed an opioid for their painful condition.[30] However, this approach is not as safe and effective as once thought, and high-dose prescriptions or prolonged use often do not improve outcomes and increase the risk of misuse.[31] Opioids should be used cautiously because of the risk of addiction, even with short-term use. For patients with severe pain, such as that following major surgery, the cautious and time-limited use of opioids may be clinically indicated if other measures are not adequate.

Although opioids should be utilized only if there is inadequate response to non-opioid therapies, many clinicians prescribe more opioids than necessary for acute pain.[32] According to the 2015 National Survey on Drug Use and Health, 91.8 million U.S. noninstitutionalized adult civilians reported prescription opioid use (and often opioid misuse), or more than a third of the population.[33] The specific risks associated with overprescribing opioids will be discussed later in this evidence document.

Recent evidence suggests that opioids may not be more effective for moderate to severe pain than non-opioid pain regimens.[34,35] A blinded randomized controlled trial of 416 patients with acute extremity pain found that there were no clinically important differences in pain reduction at two hours after single-dose treatment with ibuprofen and acetaminophen vs. with three different opioid and acetaminophen combination analgesics.[34] This trial is discussed further below (see page 34).

Risks of prescription opioids

Physical dependence on opioids 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. Related risks of opioid use include chronic/persistent use, misuse, abuse, dependence, diversion, and overdose. These risks are particularly pronounced in older patients, who are particularly vulnerable to the associated sedating side effects.

Inappropriate prescribing of medicines, particularly benzodiazepines, tricyclic antidepressants, NSAIDs and opioid analgesics, have been associated with increased adverse drug events in older patients, leading to increased morbidity, mortality and utilization of healthcare resources. As older individuals are more likely to take multiple medications at once to treat multiple concomitant ailments, unnecessary or inappropriate prescriptions add to the number, complexity and cost of the drug regimen, and also reduce compliance.[36]

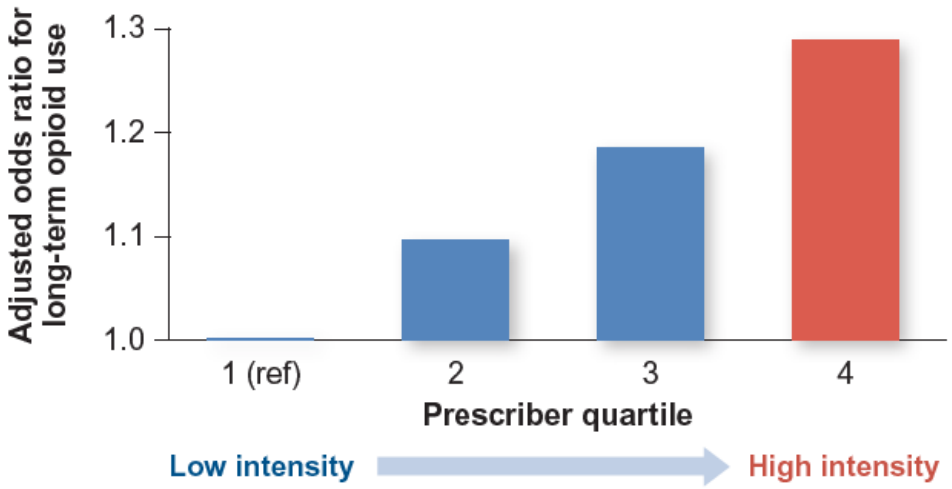
Physician prescribing habits

Despite the known risks of opioids, opioid misuse is remarkably common. In 2016 more than 11 million Americans misused prescription opioids, and opioid-related deaths have more than quadrupled since 1999.[30] According to the 2015 National Survey on Drug Use and Health, of the 91.8 million adults who reported prescription opioid use, 11.5 million (4.7%) misused them; and 1.9 million (0.8%) had an opioid use disorder (opioid dependence). Among adults with misuse, more than half reported using opioids without a prescription, and 40% obtained prescription opioids for free from family members or friends.[33]

The prescribing behavior of physicians has cited as a driver of the opioid epidemic.[30] High intensity prescribing of opioids for acute pain is associated with greater likelihood of long-term opioid use.[37,38] In a retrospective analysis of a national sample of Medicare beneficiaries who received emergency treatment

from 2008 through 2011 who hadn't used prescription opioids within six months before the visit, initial exposure to an opioid was a strong predictor of subsequent outcomes. The study classified rates of physician opioid prescribing behavior as high intensity and low intensity according to relative quartiles of prescribing rates within the same hospital. Overall, 215,678 and 161,951 patients received treatment from low intensity and high intensity prescribers, respectively. Wide variation in rates of opioid prescribing behavior existed among physicians practicing within the same ED (7.3% vs. 24.1% frequency of opioid prescriptions). In addition, long-term opioid use was significantly higher among patients treated by high-intensity prescribers than among those treated by lo -intensity prescribers (adjusted OR 1.30; 95% CI: 1.23-1.37; p<0.001) (Figure 4).[37] This suggests that opioid exposure for the treatment of acute pain may be a trigger for long-term opioid use.

Figure 4: Opioid prescribing rates and long-term opioid use, according to physician prescribing category[37]



The risk of subsequent long-term opioid use increases most sharply based on use in the first days of therapy. An analysis of records from 1,294,247 opioid-naïve, cancer-free patients examined the risk for long-term use based on initial prescribing characteristics. The study quantified the increase in probability of long-term use of opioids with each additional day supplied, day of therapy, or incremental increase in cumulative dose. Patients initiated on long-acting opioids had the highest probabilities of long-term use. The largest incremental increases in the probability of continued opioid pain reliever use were observed when the first prescription exceeded 10- and 30- day supplies, when a patient received a third prescription, or when the cumulative dose was ≥700 morphine milligram equivalents. Patients initiated with tramadol had the next highest probability of long-term use, although tramadol was previously deemed to be a relatively safe opioid agonist thought to have lower abuse potential than other opioids. However, these findings must be weighed in conjunction with several key limitations. This study did not have information on the cause or chronicity of pain prior to the opioid prescription, or whether chronic use was intentional at the time of first prescription, which might all influence the duration of opioid use. In addition, the total cumulative dose of opioid use was calculated, which might have been increasing or decreasing over time. The relationships between days' supply, the cumulative dose, and duration of first episode and the probability of long-term use was also not factored into the analysis.[38]

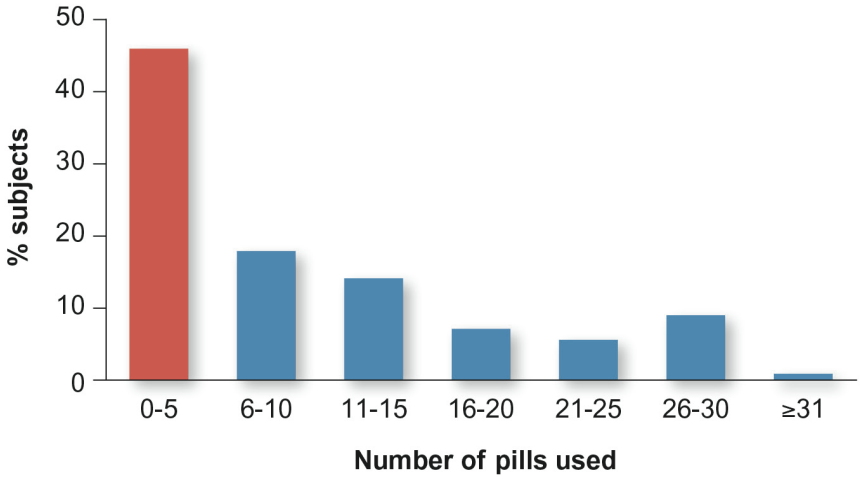
High-risk prescribing practices that have contributed to the overdose epidemic include high-dose prescribing, overlapping opioid and benzodiazepine prescriptions, and inappropriate prescription of extended-release/long-acting (ER/LA) opioids for acute pain.[10]

Leftover medications and disposal education

Low-risk surgical procedures provide an opportunity for opioid-naive patients to receive prescriptions for oxycodone, hydrocodone, or another opioid, often beyond their actual clinical need; there is compelling data that and patients often do not consume all of their prescribed opioid medication.[39-41]

After some types of surgery, the need for opioid analgesic medication may be considerably less than typically dispensed. A phone-based survey of 250 patients following outpatient orthopedic surgery on the hand and wrist found that most patients were dispensed 30 pills and consumed a mean of 10 pills. An average of 19 pills per subject were reported unused, which resulted in 4,639 total leftover tablets for the entire study population (Figure 5).[39]

Figure 5: Opioid prescription vs. consumption after outpatient orthopedic procedure[39]



In a systematic review of post-operative patients who underwent seven different types of surgeries (including obstetric, thoracic, orthopedic, and urologic procedures), 67% to 92% reported unused opioids. Of all the opioid tablets obtained by surgical patients, 42% to 71% went unused. Additionally, unused prescription opioids are not usually stored or disposed of properly. This results in a reservoir of leftover pills that can potentially contribute to the nonmedical use of opioids or drug diversion, resulting in injuries, addiction, or overdose.[41]

In a national survey of U.S. adults with recent opioid medication use, more than half of respondents had or expected to have leftover medication from their prescription, and among those with leftover opioid medications, 61.3% reported keeping them for future use. In addition, 20% reported ever having shared opioid medications with others, with the primary reason (73.0%) being to help the other person manage pain.[42]

Disposal of leftover prescription opioids

When opioids are no longer needed, it is important to dispose of them properly to help reduce harm from accidental exposure or intentional misuse. Current practices related to sharing, storing, and disposing of

opioid medications are suboptimal for preventing misuse. Nearly half of those with recent opioid medication use surveyed in a national survey of U.S. adults did not recall receiving information on safe storage or proper disposal.[42] In one systematic review that examined prevalence of unused prescription opioids in patients following a surgical procedure, most patients (73-77%) stored opioids in unlocked locations, and few (4% to 30%) planned to or actually disposed of their unused prescription opioids. Additionally, fewer patients (4% to 9%) considered or used a disposal method recommended by the FDA.[41]

The U.S. Food and Drug Administration (FDA) has some resources to educate patients on the appropriate disposal of leftover medications, which includes instructions on how to dispose of opioids safely. The guidelines recommend depositing unused opioids in a secure drop-box or mail-back program, if available. Flushing down a toilet or disposal into household trash within used coffee grounds or kitty litter is also an option. The information on the prescription bottle should be removed or blacked out. The U.S. Drug Enforcement Administration (DEA) periodically hosts National Prescription Drug Take-Back events where collection sites are set up in communities for safe disposal of prescription drugs.

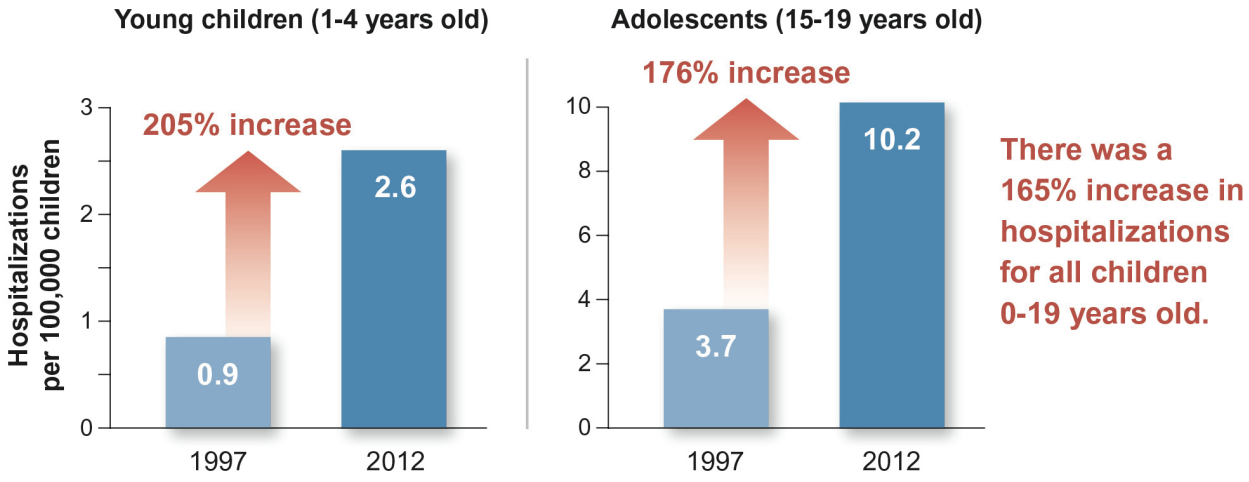
Accidental overdose

One important consequence of excess opioid prescriptions and leftover medications is the increased risk of accidental overdose. Young children and older adolescents are particularly vulnerable to the risks of opioid exposure. Most adolescents and adults reporting recent nonmedical use of opioid medications obtain these medications through their family or friends, including elderly family members.[42]

A population-based, nested case control study in 103 children with opioid overdose whose mothers received publicly funded prescriptions for an opioid or NSAID in the preceding year. Compared with controls, children with an opioid overdose were far more likely to have a mother who received a prescription opioid (unadjusted OR 2.41; 95% CI: 1.68-3.45); that is, children of mothers prescribed opioids were 2.4 times more likely to overdose compared to those prescribed NSAIDs.[43]

In a retrospective analysis that analyzed 13,052 hospital records of children aged one to 19 years hospitalized for opioid poisoning between 1997 and 2012, hospitalizations for opioid poisonings increased by 165% ($p<0.001$). Among children one to four years of age, the incidence increased by 205% ($p<0.001$) ($p<0.001$) (Figure 6).[44]

Figure 6: Percentage increase of hospitalization for opioid poisoning in children[44]



Physicians and patients should take measures to reduce the risk of opioid-related harm to relatives of patients who need opioids, such as children or other elderly relations, by prescribing smaller quantities, as well as facilitating secure storage and prompt disposal of unused opioids.[43]

State policies addressing opioid prescribers

When prescribing, many clinicians do not consistently use practices intended to decrease the risk for opioid misuse, such as prescription drug monitoring programs (PDMPs), urine drug testing, and opioid treatment agreements.[45]

PDMPs are statewide program that collect information about controlled substance prescription drugs that are dispensed to patients within each state. PDMPs aim to improve opioid prescribing, inform clinical practice, and protect patients at risk by tracking controlled substance prescriptions and providing information about prescribing and patient behaviors (e.g. “doctor shopping”, cash fills, combination of opioids and benzodiazepines). However, although a useful benchmark, PDMP data alone should not be a reason to discharge a patient from care. On the contrary, unexpected PDMP findings may open up an opportunity for dialogue, may indicate that pain is inadequately controlled or may indicate a need to refer patients for additional sources of care such as addiction treatment.

Although most states permit or are enacting permissions for interstate sharing, available information may vary based on reporting requirements and restrictions. Reported items vary by differences in dosing schedules, timeliness of pharmacy dispensing information, and detail of information access permissions. All 50 states have an operational prescription drug monitoring program or have enacted legislation to establish a PDMP and are in the process of creating one.

Clinicians should consult the PDMP prior to prescribing opioids, and periodically throughout the course of treatment, with vigilance for opioids and other controlled substances, such as benzodiazepines, that can increase risk of overdose. Drug tests (e.g. urine screens) should be conducted to assess for behaviors of drug abuse or diversion that might place patients at higher risk for opioid use disorder and overdose. Clinicians should also provide specific counseling on increased risks for overdose when opioids are combined with other drugs or alcohol and ensure that patients receive treatment for substance use disorders when needed.[10]

In 2016, the Pennsylvania Legislature enacted new laws aimed at combating the opioid epidemic, which impose new legal requirements for prescription reporting and have a significant impact on practicing physicians statewide. In particular, Act 122 has wide-ranging implications for emergency room and urgent care physicians.[46]

- **Limit of 7-Day Supply:** Emergency room and urgent care physicians may not prescribe opioids in excess of a seven-day supply, (except for prescriptions of >7 days for acute medical conditions) The physician must document that a non-opioid alternative was not appropriate to treat the condition.
- **No Refills:** No matter the amount prescribed, physicians in these settings may not write prescriptions for refills of opioid prescriptions.
- **Substance Abuse Referrals:** Physicians are required to refer people for treatment if the person is believed to be at risk for substance abuse.
- **Use of PDMP:** Physicians must query the PDMP system to determine whether a patient is using an opioid prescribed by another provider. However, this does not apply to patients being treated in an emergency department.

For Pennsylvania-specific PDMP rules, visit: doh.pa.gov/PDMP

BOTTOM LINE: The goal of optimal acute pain treatment is to use non-opioid medications when indicated, limit opioid prescriptions to what is needed, and encourage patients to dispose of unneeded opioids. Prescribers should understand policies regarding medication quantity limits and use of the local PDMP to maximize opioid safety.

Opioids for severe acute pain

Acute pain can often be managed without opioids, which should be considered only if expected benefits for both pain and function outweigh the risks. If opioids are used, they should be initiated with caution and if appropriate, combined with non-pharmacologic therapy and non-opioid pharmacologic therapy.

When required for acute pain, physicians should follow the following general principles, which will be elaborated upon in the next sections.

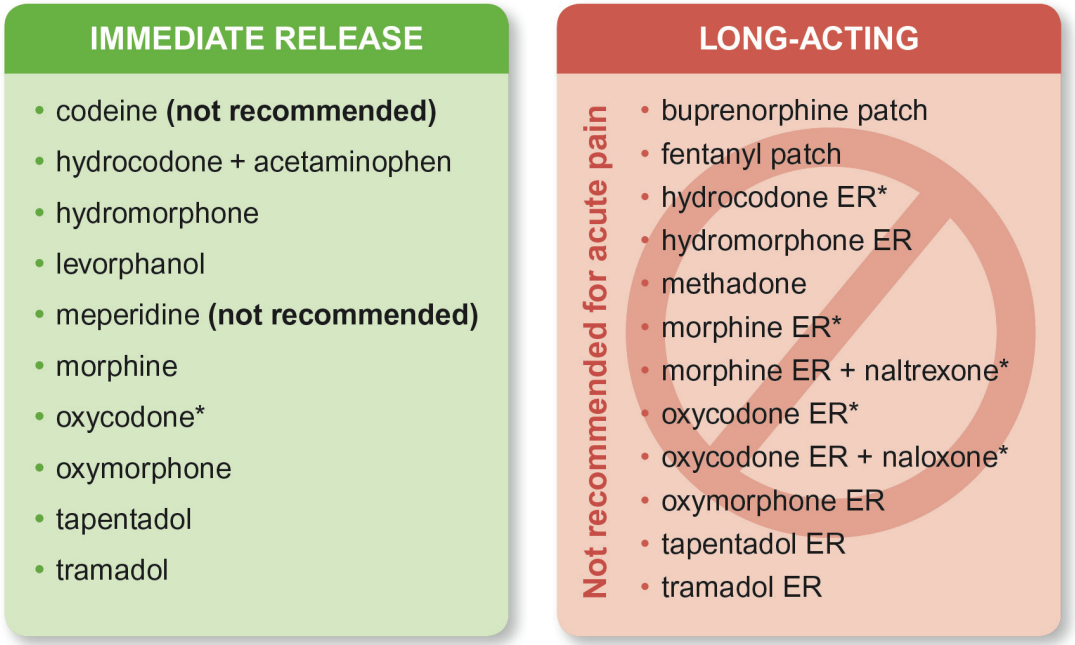
- Consider opioid type:
  - Avoid long-acting or extended release opioids for acute pain.
  - Avoid co-prescribing with agents that depress the CNS (e.g. benzodiazepines).
- Limit dose and quantity: Prescribe short courses, usually less than three days.
- Limit tampering: Consider using a tamper-resistant, short acting formulation (e.g. Roxybond); understanding that these formulations do not affect the risk of abuse by oral ingestion and are typically more expensive than regular opioids (i.e. not abuse-deterrent).
- Combine opioids with other treatments: e.g. non-pharmacologic options, NSAIDs, acetaminophen.

Consider opioid type

Immediate release opioid formulations should be prescribed for patients with acute pain instead of extended release/long-acting (ER/LA) opioids such as methadone, fentanyl patches, or extended release versions of opioids such as oxycodone, oxymorphone, or morphine. These agents have longer half-lives and longer duration of effects and should not be prescribed for the treatment of acute pain.

Opioid medication can be broken down into two classes based on duration of action (Figure 7). Short acting medications are mostly used as initial opioid therapy for acute pain. For chronic pain, short acting opioids are commonly used to treat breakthrough, or episodic pain. Long acting should never be used as initial therapy due to a high risk of respiratory depression, and should only be considered when a patient is on a stable dose of short acting opioids in an effort to improve baseline coverage and decrease pill burden. Occasionally, patients will be on both long and short acting opioids at the same time. If an assessment finds that the patient is taking high amounts of short acting and asking for more, then increasing the long acting is the most appropriate option.[47]

Figure 7: Selected immediate release and long acting opioids



* available in “abuse-deterrent” formulations

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, in individual patients. 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). [48]

The combination of opioids and central nervous system depressants such as benzodiazepines and barbiturates have an additive effect and may lead to over-sedation and respiratory depression in hospitalized patients.[49] In particular, benzodiazepines are commonly prescribed concurrently for patients who receive opioid analgesics and are involved in 30% of overdose deaths related to opioid analgesics in the United states.[50] The risk of death from drug overdose increases almost 4-fold in patients using receiving opioids and benzodiazepines concurrently.[50] Therefore, such combinations should be avoided in at-risk patients, such as the elderly.

Meperidine and benzodiazepines appear to be less safe in the elderly and are associated with the development of post-operative delirium.[26] Meperidine may be particularly likely to cause delirium due to its long half-life and its active metabolite, normeperidine, which is a central nervous system stimulant that can accumulate to toxic levels in some patients.[27] Clinicians caring for older patients at risk for delirium should carefully evaluate the need for agents that have known psychoactive properties and consider alternative therapies if available.

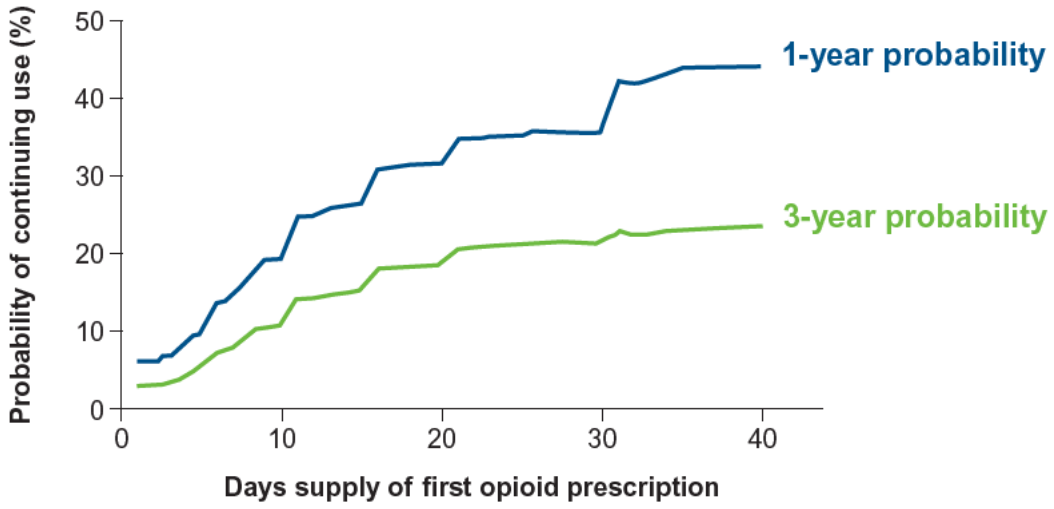
The elimination of opioids must be considered in certain patients. For example, dose reduction of most types of opioids should be considered in patients with reduced renal function to avoid drug accumulation and associated complications. The majority of opioids used for acute pain undergo hepatic biotransformation and renal excretion as the primary route of elimination. Significant renal retention of active or toxic metabolites of

opioids can occur in patients with advanced chronic kidney disease and lead to central nervous system and respiratory depression and hypotension. Serious neurological complications such as myoclonus and seizures can occur with the use of high doses of morphine, hydromorphone, meperidine, fentanyl and diamorphine.[51]

Limit dose and quantity

Long-term opioid use often begins with treatment of acute pain. The risk for long term opioid use seems dose-dependent, a higher number of prescriptions in the first episode of opioid use is associated with greater risk for long-term use (Figure 8). Approximately one in seven patients who received a refill or had a second opioid prescription authorized are still taking opioids one year later. Discussions with patients about the long-term use of opioids to manage pain should occur early in the opioid prescribing process, for example at the first refill. Prescribers should consider individual pain intensity, duration, and etiology when assigning an appropriate dose regimen for each patient.[38]

Figure 8: One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of days' supply in the initial opioid prescriptions*— United States, 2006–2015[38]



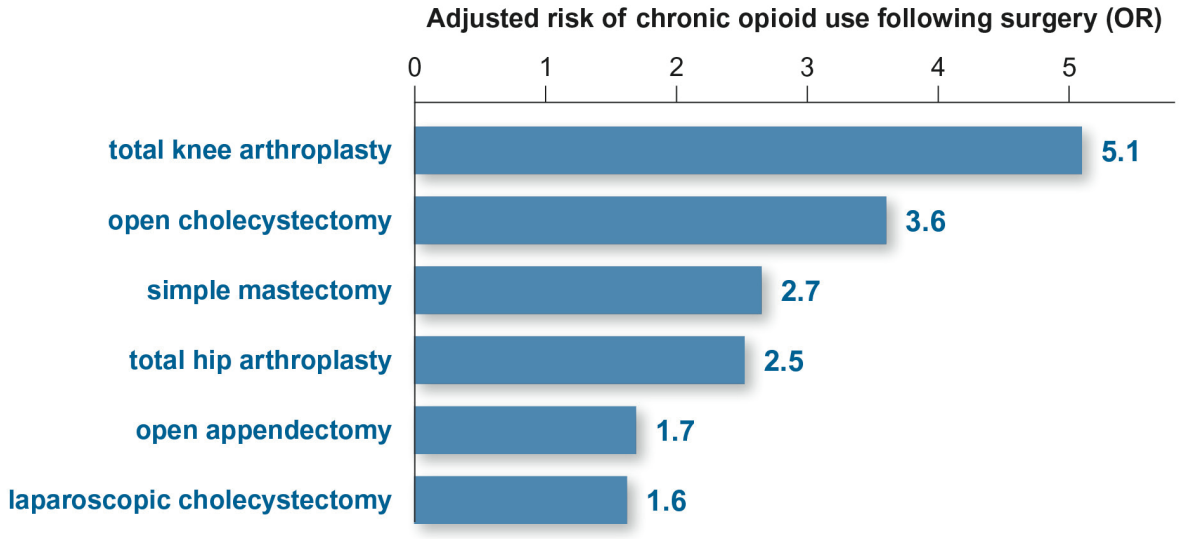
In one key study, between 3% and 10% of opioid naive patients became chronic opioid users. In a retrospective cohort study of opioid naive post-operative patients, the total duration of opioid use was the strongest predictor of misuse (abuse, dependence, overdose), measured by the number of prescription refills. The study estimated an adjusted increase of 44% in the rate of misuse for every refill fulfilled, or a 20% increase for every additional week of prescription. Interestingly, the duration of a prescription was more strongly associated with ultimate misuse rather than the dosage of the opioid.[52]

Among post-operative patients, the use of opioids in the immediate days after surgery has been associated with increased risk of continued opioid use for up to one year, and also an increased likelihood of receiving more frequent opioid prescriptions.[53,54]

A retrospective analysis of 641,941 opioid-naïve surgical patients following 11 types of surgical procedures found an increased rate of chronic opioid use for patients undergoing total knee and hip arthroplasty, open and laparoscopic cholecystectomy, simple mastectomy, open appendectomy (Figure 9). Chronic opioid use was defined as having filled 10 or more prescriptions or more than 120 days' supply of an opioid in the first year after surgery, excluding the first 90 postoperative days. When compared to a reference sample of non-

surgical patients with baseline chronic opioid use in order to estimate the increased risk in chronic opioid use associated with surgery, prescribing post-operative opioids increased the risk of chronic opioid use between 2- and 5- fold. Male sex, age older than 50 years, and preoperative history of drug abuse, alcohol abuse, depression, benzodiazepine use, or antidepressant use were associated with an increased risk of chronic opioid use for most procedures. Elderly men are particularly vulnerable.[54]

Figure 9: Risk of chronic opioid use following surgery[54]



When opioids are needed for acute pain, they should be prescribed at the lowest effective dose, for limited time period to minimize unintentional risks of long-term opioid use. When opioids are used for acute pain, the 2016 CDC guidelines recommend a 3-day prescription, not to exceed a 7-day supply for initial doses of opioids.[10]

Additional opioids should not be prescribed just in case pain continues longer than expected. Even a few days of exposure to opioids significantly increases associated hazards, with each day of unnecessary opioid use (prescription of opioids instead of other, equally effective alternatives) increasing the likelihood of physical dependence without adding benefit.[10,52] Prescriptions with fewer days' supply will minimize the number of pills available for diversion and other misuse.

Tamper-resistant/abuse-deterrent opioids

Completely restricting access to opioid analgesics would prevent patients in need of pain relief from obtaining effective analgesia. One strategy that attempts to mitigate the risk of opioid abuse has been the development of "abuse-deterrent" formulations of opioids that try to make it more difficult to tamper with or altered, such as injecting, snorting, chewing, or smoking. For example, some formulations are more difficult to crush or dissolve, and are thus are less likely to be abused by snorting or injecting.[55] However, these opioids are more aptly named as "tamper-resistant" formulations instead of "abuse-deterrent", as 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.[55] However, while they could potentially contribute to the reduction of the misuse of opioids, they are

still subject to abuse by oral ingestion. Even if taken as indicated, these opioids do not prevent the development of tolerance and addiction to opioids. Abuse-deterrent formulations might make tampering with opioids more difficult for drug misusers but does little to address population-level issues related to overprescribing, overuse, and harm of opioid medicines taken via the intended route.[56]

At the time of writing, only one short acting opioid is abuse determent (RoxyBond). This formulation contains oxycodone and includes inactive ingredients that make the tablets harder to misuse by physical manipulation, chemical extraction, or injection.[55]

Combination with other treatments

A multimodal approach to analgesia involves combinations of two or more analgesics with different mechanisms of action and is more effective than monotherapy with any one agent. Combination therapy allows for lower individual doses, reduced side effects, and shorter hospital stays.[57] Opioids should be part of this multimodal approach, in which sufficient analgesia is achieved due to the additive or synergistic effects between different classes of analgesics, which allows for a reduction in the doses of individual drugs and thus a lower incidence of adverse effects.

A Cochrane review of three RCTs assessed the analgesic efficacy and adverse effects of ibuprofen plus oxycodone for moderate to severe post-operative pain. The proportion of participants achieving at least 50% pain relief over six hours was 60% with ibuprofen 400 mg and oxycodone 5 mg and 17% with placebo, giving a number needed to treat (NNT) of 2.3 (2.0 to 2.8). There was no significant difference between ibuprofen and oxycodone and ibuprofen 400 mg alone. For oxycodone 5 mg alone the proportion was 23%, giving an NNT for ibuprofen 400 mg + oxycodone 5 mg compared with oxycodone alone of 2.9 (2.3 to 4.0). The NNT for low-dose ibuprofen (200 mg) plus acetaminophen 5000 mg is 1.6, which is better than any of the opioid combinations. This suggests that multimodal analgesia is probably more effective than an opioid alone for acute post-operative pain.[58,59]

Multimodal perioperative treatment can also be useful for decreasing postoperative pain and limiting opioid use. For example, perioperative administration of gabapentin may reduce the incidence and intensity of postoperative pain up to six months after surgical procedures such as otolaryngology, orthopedic, mastectomy, and abdominal/pelvic operations. In a recent RCT of 422 patients undergoing surgery, gabapentin had a modest effect on promoting opioid cessation after surgery. (See expanded description in Post-operative pain section on page 28) [60]

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 to reduce risks of opioid misuse, abuse, and overdose.

Acute pain conditions

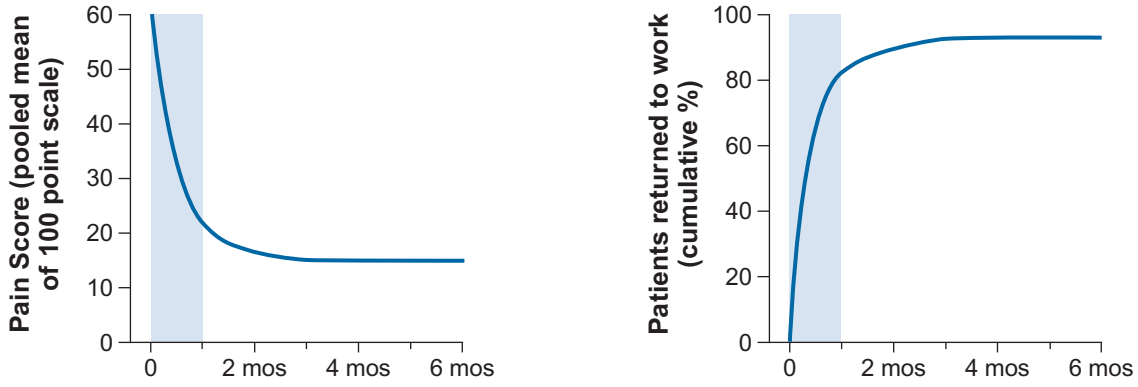
Acute low back pain

Musculoskeletal conditions such as back pain affect more than 1.7 billion people worldwide and have the fourth greatest impact on the overall health of the world population, considering both death and disability.[61] Acute lower back pain is defined as spinal and paraspinal symptoms in the lumbosacral region that lasts for a duration of less than four weeks.[62] Low back pain is responsible for more than 2.7 million emergency room visits per year, which constitutes about 2.4% of all visits to emergency departments in the U.S.[63] The total costs of low back pain in the U.S. were estimated to be $100 billion in 2006, much of which were indirect costs of lost wages and productivity.[64,65]

Back pain is a symptom rather than a disease. The majority of all etiologies are non-specific, with no evidence of underlying disease. Up to 85% of patients cannot be given a definitive disease diagnosis because of the weak associations among back symptoms, pathologic changes, and imaging results. As most patients with acute back pain get better after a short time, many do not seek medical care. Consequently, it is difficult to estimate the exact prevalence of low back pain.[66]

Episodes of non-specific low back pain are usually self-limited, and most patients resolve their pain on their own. A systematic review evaluated 15 prognosis trials, which included nine RCTs that evaluated exercise, manual therapy, an educational pamphlet, medical care, NSAIDs and bed rest, one controlled trial that evaluated an early intervention in the workplace, and five cohort studies. Most studies reported a rapid decrease in pain (by between 12% and 84% of initial levels) within one month, with an average reduction of 58% of initial pain scores. Of note, 82% of people who stopped work due to acute low back pain returned to work within one month. Improvement continued until about three months, although recurrences were common, with 73% reporting additional symptoms over 12 months.[22] (Figure 10).

Figure 10: Course of acute pain (left) and return to work after onset (right)



Rarely, low back pain may be indicative of an underlying or systemic medical illness or condition, such as sciatica or herniated disc. Red-flag symptoms include severe progressive neurologic deficits such as loss of continence of stool/urine, and saddle anesthesia, and signs of underlying conditions such as osteomyelitis (such as fever, leukocytosis, elevated erythrocyte sedimentation rate (ESR)).

Contrary to common belief, excessive imaging of the spine after reports of low back pain may not be required, and is often not helpful in identifying a cause, as image findings are poorly associated with symptoms. Imaging of the lower spine before six weeks does not improve outcomes but does increase costs. Early use of imaging or opioids, which contradicts current practice guidelines, is associated with higher rates of prolonged disability and invasive procedures.[67] Physicians should not image for low back pain within the first six weeks, unless red flags are present. Red flags include, but are not limited to, severe or progressive neurological deficits or when serious underlying conditions such as osteomyelitis are suspected.[68,69]

Acute low back pain affects the psychological well-being of patients, which can lead to risky behaviors and associated comorbidities. The 2002 National Health Interview Survey was a cross-sectional, population-based survey of U.S. adults, in which the 3-month prevalence of low back pain was found to be 34 million, with the frequency increasing with patient age. Adults with low back pain reported more comorbid conditions, exhibited more psychological distress (including serious mental illness), and engaged in more risky health behaviors than adults without either condition.[70]

Non-drug treatment options

Non-pharmacologic treatment with superficial heat, massage, acupuncture, or spinal manipulation are often recommended to treat acute low back pain. Most non-drug options are generally recognized as safe, with the exception of spinal manipulation, which has been associated with adverse events such as stiffness, spasm, pain, and fatigue. However, the frequency of serious events may be 1 in 20,000 to 2,000,000 manipulations.[71,72]

Bed rest or exercise?

Although bed rest and back-extension exercises are often prescribed for patients with acute low back pain, they have not actually been found to be more effective than continuing regular activities.

A controlled trial examined the efficacy of different interventions in 186 patients with nonspecific acute low back pain by randomly assigning them to one of three treatments: bed rest for two days (67 patients), back-mobilizing exercises (52 patients), or continuation of ordinary activities (67 patients). After three and 12 weeks, continuing ordinary activities within the limits permitted by the pain leads to more rapid recovery than either bed rest or back-mobilizing exercises, showing statistically significant differences in the duration of pain, pain intensity, lumbar flexion, ability to work as measured subjectively, the Oswestry back-disability index, and number of days absent from work. Contrary to common belief, recovery was slowest among the patients assigned to bed rest. Bed-rest should specifically be avoided for acute low-back pain. The authors concluded that just continuing ordinary activities as tolerated leads to more rapid recovery than either intervention.[73]

Analysis of six RCTs showed essentially no difference between exercise and usual care. Further moderate-quality evidence showed no clear differences between different exercise regimens in more than 20 head-to-head RCTs in patients with acute low back pain.[64]

Heat (thermal treatments)

Heat and cold treatments are often used to relieve symptoms of low back pain, most frequently applied heat wraps or hot water bottles, rice bags or heated blankets.[74] However, the evidence to support practice of superficial heat and cold for low back pain is limited.

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 low back pain. One trial of 100 patients with acute and subacute low back pain found that adding exercise to heat wraps provided significantly more pain relief at day seven (weighted mean difference (WMD) 2.00; 95% CI: 1.29-2.71), and also led to improvements in function than either heat or exercise alone.[74,75]

The application of cold treatment to low back pain is even more limited, and there is conflicting evidence. No solid, well-supported conclusions can be drawn. However, despite the lack of convincing benefit, there were also no major adverse events reported with treatment with heat or cold, aside from effects from contact such as skin pinkness.[74]

Massage

Massage, the manual manipulation of the body to promote relaxation, is utilized to relieve low back pain by reducing muscle tone and improving local circulation to remove algesic substances.[76] Only one study has looked at the effect of massage on patients with acute low back pain (n=51) and suggests the short-term benefit of massage versus inactive control in these patients (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).[77]

Myofascial trigger points (MTrPs) are palpable hyperirritable nodules in skeletal muscle that are associated with chronic musculoskeletal pain.[78] Pressure massage targeting compression of MTrPs has been thought to reduce symptoms associated with acute low back pain. A small randomized open-label study of 63 patients with acute low back pain randomized to MTrP massage (compression at MTrPs), non-MTrP massage (compression at non-trigger points) and effleurage (massage of superficial areas) showed that MTrP massage significantly improved scores measuring pain intensity (VAS 0 (no pain) to 100 (worst pain possible), pressure pain threshold, as well as range of motion compared to either non-MTrP or effleurage massage.[76]

Acupuncture

Acupuncture involves the stimulation of specific points on the body, most often involving skin penetration by fine metallic needles or lasers and has been used to treat acute non-specific low back pain. However, there is inconsistent evidence that acupuncture is more effective than medication at relieving symptoms of acute low back pain. This treatment appears to be associated with few adverse events, but the evidence is also limited.

Acupuncture may be more effective than medication for symptom improvement or relieve pain better than sham acupuncture in acute low back pain. Low-quality evidence from five RCTs showed that acupuncture may more effectively improve symptoms of acute low back pain compared with NSAIDs (RR 1.11; 95% CI: 1.06-1.16). 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; 95% CI: -17.00 to -1.76), but there were no clear effects on function/disability.[79]

Spinal manipulation

Spinal manipulation is the use of hands or a device to provide controlled force to a joint of the spine, often performed by chiropractors, physical therapists, and some physicians. There have been conflicting conclusions from RCTs and meta-analyses have reported different conclusions about the effectiveness of spinal manipulation in treating acute low back pain, suggesting either no effect or small effect on pain and

function. Spinal manipulation of the cervical spine has rarely been associated with adverse events, such as stroke, headache, and vertebral artery dissection.[72]

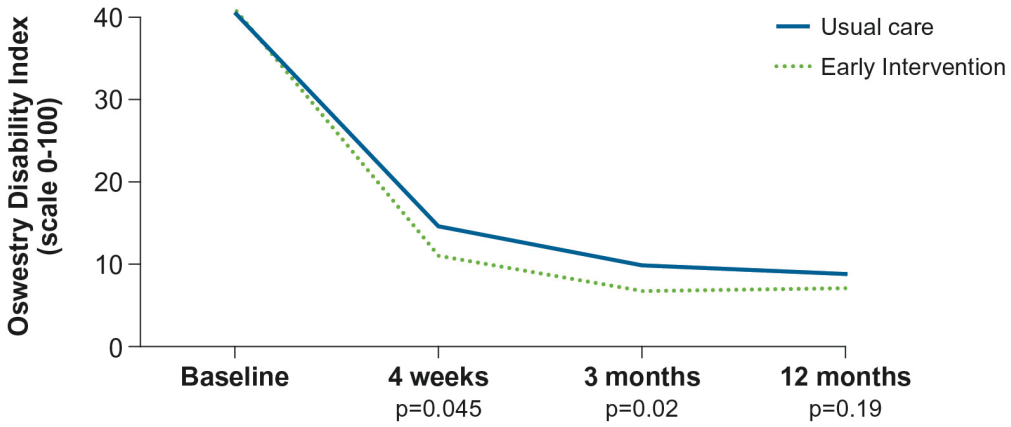
A 2017 systematic review and meta-analysis of 26 randomized clinical trials found a modest improvement in both pain and function, at up to six weeks (SMD -0.39; 95% CI: -0.71 to -0.07) in patients with acute low back pain who underwent spinal manipulation. However, minor transient musculoskeletal harms such as increased pain, stiffness, and headache were reported in more than half of patients.[71]

Physical therapy

The effect of early physical therapy on acute back pain is unclear, although some guidelines advise delaying referral to physical therapy or other specialists for a few weeks to allow for spontaneous recovery.[80]

An RCT of 220 patients randomized to four sessions of early physical therapy or usual care evaluated whether early physical therapy (manipulation and exercise) is more effective than usual care (no additional intervention beyond patient education) in improving disability for patients with acute low back pain. At four weeks and three months, patients receiving early physical therapy had a small improvement in disability scores (between-group difference in ODI score, −3.2; 95% CI: -5.9 to -0.47; p=0.02). However, the improvement was modest, and did not achieve the minimum clinically important difference compared with usual care and was not sustained at one year.[67]

Figure 11: Effect of early physical therapy on disability



Drug options

Several systemic pharmacologic therapies are available for low back pain, and are associated with small to moderate but mostly short-term effects on pain. The most commonly prescribed medications for low back pain are nonsteroidal anti-inflammatory drugs (NSAIDs), skeletal muscle relaxants, and opioid analgesics. However, research has found only limited evidence to support use of most medications for low back pain.[81]

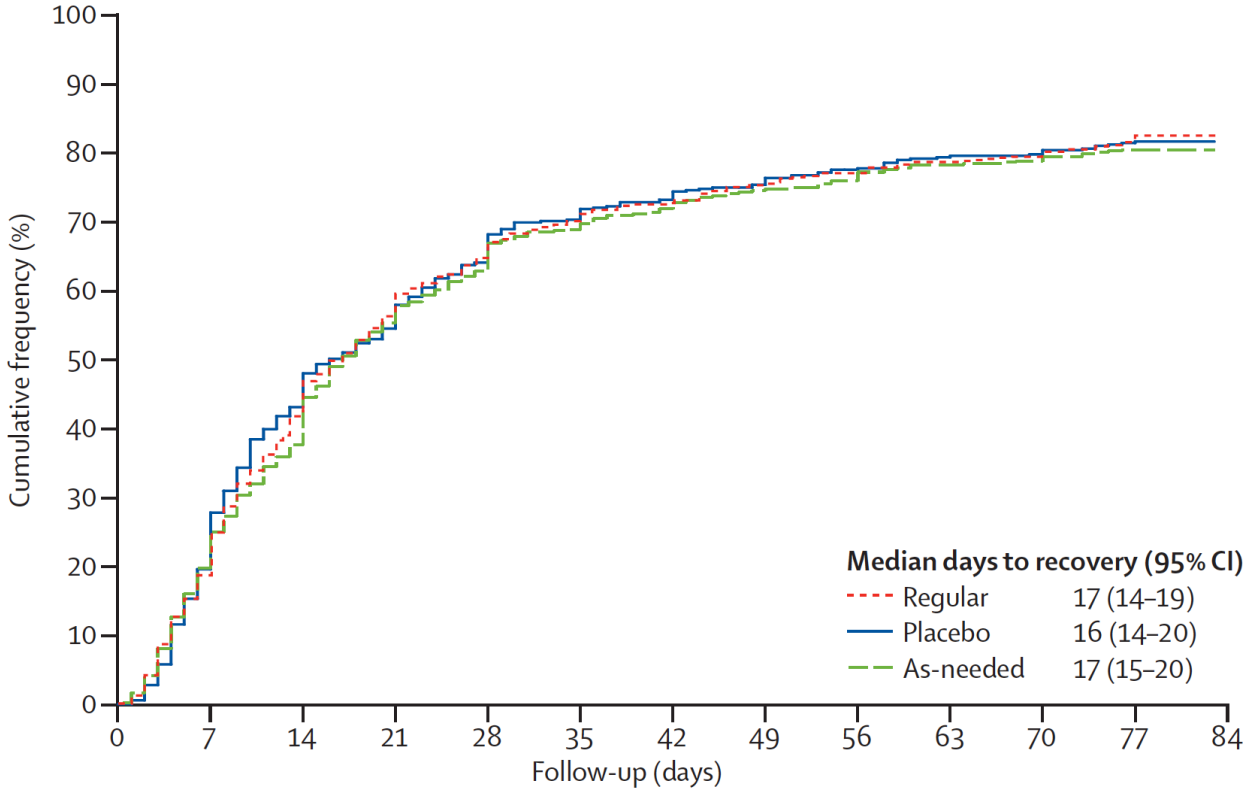
Acetaminophen

Acetaminophen is often used to relieve the symptoms of acute low back pain. The greatest safety concern with acetaminophen use is the risk of hepatotoxicity, which can be avoided by keeping doses below 4000 mg/day in healthy adults and below 3000 mg/day in the elderly.

Acetaminophen and NSAIDs are equally effective for acute low back pain, although NSAIDs are associated with a higher incidence of adverse effects, such as gastrointestinal bleeding and peptic ulcer disease.[32] The American College of Physicians Clinical Practice Guidelines found no difference between acetaminophen and NSAIDs in pain intensity (SMD 0.21; 95% CI: -0.02 to 0.43) at three weeks or less. It was concluded that acetaminophen has a lower risk for adverse events than NSAIDs (relative risk 0.57; CI: 0.36-0.89).[81,82]

Others question whether acetaminophen is really better than no treatment for low back pain. An RCT in 1652 patients compared the efficacy of acetaminophen to improve time to recovery from acute low back pain in patients who received scheduled therapy (three times per day; equivalent to 3990 mg acetaminophen per day) or as needed doses (taken when needed for pain relief; maximum 4000 mg acetaminophen per day), compared to placebo. The study found no difference between either regimen of acetaminophen and placebo in terms of days to recovery, or mean pain scores (Figure 12). Neither regular nor as-needed acetaminophen significantly speed recovery from acute low-back pain.[83]

Figure 12: Pattern of sustained recovery of patients receiving acetaminophen and placebo[83]



Oral NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs) are effective analgesics, but can increase the risk of cardiovascular and gastrointestinal adverse effects.[84] A Cochrane review of 65 RCTs of NSAIDs in non-specific acute low-back pain with or without sciatica were analyzed to assess the effectiveness of treatment with NSAIDs. NSAID use was associated with significantly more pain relief than placebo, but also significantly more side effects.[82]

Clinical evidence shows that NSAIDs have a small improvement on pain intensity than placebo (4 trials: WMD -8.39 points on a 0- to 100-point scale (CI: -12.68 to -4.10 points) but have little effect on function (2.4-

2.9 point improvement on the Roland-Morris Disability Questionnaire), as shown in a 7-day trial.[82,85] There is moderate evidence that NSAIDs are not more effective than acetaminophen for acute low-back pain, but the latter is associated with fewer side effects.[81,82]

COX-2 selective NSAIDs do not seem to be more effective than traditional NSAIDs, but do produce fewer side effects, particularly gastrointestinal bleeding.[82] An RCT of 24,081 patients examined the cardiovascular safety of celecoxib, as compared with nonselective NSAIDs. Esomeprazole (20-40 mg) was provided to all patients for gastric protection. Patients were randomized to receive celecoxib (mean daily dose 209 mg), naproxen (mean daily dose 852 mg), or ibuprofen (mean daily dose 2045 mg). While there were no differences between the three treatments in cardiovascular outcomes, celecoxib produced fewer gastrointestinal events than naproxen (p=0.01) and ibuprofen (p=0.002), and fewer renal events than ibuprofen (p=0.004). These results confirm that at moderate doses, celecoxib was not inferior to ibuprofen or naproxen with respect to cardiovascular safety in patients with arthritis.[84]

Skeletal muscle relaxants

Skeletal muscle relaxants include carisoprodol (SOMA), cyclobenzaprine (Amrix, Flexaril), and metaxalone (Skelaxin), which together account for more than 45% of all prescriptions written for management of musculoskeletal pain.[86] 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 low back pain is debated, and there are concerns about potential adverse effects.

A 2003 Cochrane Review found that skeletal muscle relaxants were more effective than placebo for short-term relief of acute low back pain after two to four days. The pooled relative risk for non-benzodiazepines versus 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. However, there were also significantly more associated adverse effects, particularly in the central nervous system.[87]

However, a more recent RCT of over 323 patients found that adding a muscle relaxant to naproxen was no better than naproxen alone for acute low back pain. This trial also found that opioids may not be any more effective in patients with severe acute musculoskeletal pain than a combination of ibuprofen and acetaminophen (Figure 13).[88]

Common side effects of skeletal muscle relaxants include dizziness, dry mouth, drowsiness, and somnolence. The presence of potential adverse events of skeletal muscle relaxants necessitates that they be used with caution, especially if taken with other sedating medications, particularly opioids.[89]

Systemic corticosteroids

Oral steroids may provide some analgesic effect due to their anti-inflammatory activity. The available evidence suggests that non-epidural steroids do not improve pain among patients with acute nonspecific low back pain. One RCT of 82 young adults with recent onset radicular low back pain found that a single intramuscular corticosteroid injection in the emergency room was no better than placebo at reducing pain intensity one month after discharge from emergency.[90]

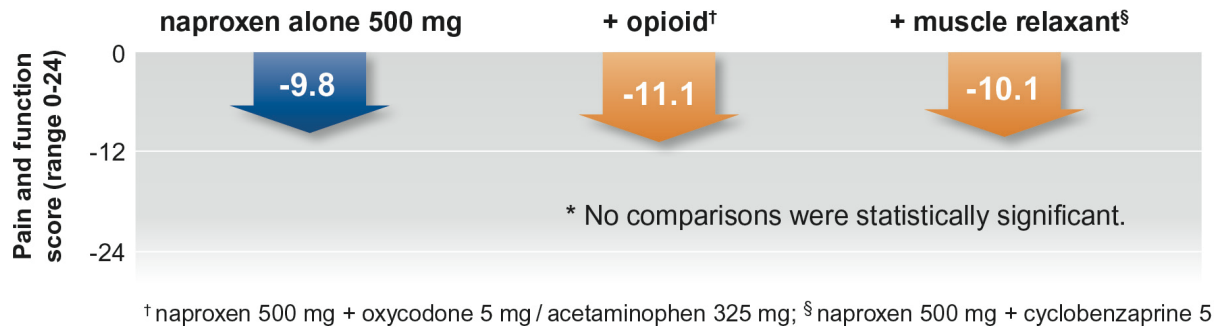
Another trial of 269 patients with acute radicular low back pain due to herniated lumbar disk found a small improvement in function (6.4 points on a 100-point scale) with a short course of oral prednisone but no significant improvement in pain compared to placebo.[91]

For patients with radiculopathy (sciatica), a trial of 23 RCTs conducted between 1970 and 2012 involving 2,334 participants compared the efficacy of epidural corticosteroid injections with placebo in patients with sciatica. Results showed that epidural corticosteroid injections may provide some short-term improvement in pain and disability, compared with placebo, but long-term results were non-significant, in that pain relief did not persist for one year. The effect size in this study was small and might not have been clinically significant.[92]

Opioids

Almost all placebo controlled RCTs of opioids have been conducted for chronic rather than acute low back pain. One RCT in 107 patients found that opioids may not be any more effective in patients with severe acute musculoskeletal pain than a combination of ibuprofen and acetaminophen. The trial compared functional outcomes and pain at one week and three months after an emergency department visit for acute low back pain among patients receiving naproxen together with either placebo, cyclobenzaprine, or oxycodone/acetaminophen. Results revealed 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 13). There was also no difference in patient reported satisfaction with treatment nor in time to return to usual activities between treatment groups.[63]

Figure 13: Adding oxycodone/acetaminophen to naproxen was no better than naproxen alone for pain or function scores at 1 week[63]



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

A retrospective cohort study of workers' compensation claims from 8443 patients with acute disabling low back pain evaluated the associations between early opioid prescription and outcomes. Mean disability duration, mean medical costs, and risk of surgery and late opioid use increased with increasing opioid dose, measured in morphine equivalent amounts. Compared with those receiving no opioids, the risk for subsequent surgery was three times greater (95% CI, 2.4–4.0) in those receiving the highest dose of opioids, and the risk of receiving late 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.[53]

Managing acute low back pain

Given that most patients with acute low back pain improve over time regardless of treatment, clinicians should educate patients of the favorable prognosis of acute low back pain, highlighting the high likelihood for improvement in the first month. Non-pharmacologic treatment with superficial heat, massage, acupuncture, or spinal manipulation could be recommended as potential ways to relieve symptoms of acute low back pain

and improve function. If pharmacologic treatment is required, nonsteroidal anti-inflammatory drugs or skeletal muscle relaxants could be considered.[64]

Table 1: Managing acute low back pain: an evidence-based checklist

	INTERVENTION	Efficacy	Harm	Comment
NON-DRUG OPTIONS	massage	●	○	Limited evidence from **small studies suggest short-term benefits** for pain but not function.[76,77]
	acupuncture	●	○	**Superior to sham acupuncture** based on results from 2 RCTs[64]
	spinal manipulation	●	○	**Small improvements in pain and function** based on systematic review of 12 RCTs[71]
	exercise	○	○	A review of 6 RCTs showed **no difference between exercise and usual care** for acute LBP.[64]
	physical therapy	○	○	**Did not improve pain intensity at 3 months** in an RCT of 220 patients randomized to 3 weeks of PT sessions or usual care[67]
DRUG OPTIONS	NSAIDs	●	●	**A small effect on pain intensity and function** versus placebo.[82] Cox-2 selective NSAIDs reduce the risk of gastrointestinal bleeding.[93]
	acetaminophen	●	○	In a randomized trial of over 1500 patients with acute LBP, **acetaminophen (~4000 mg total) was not better than placebo** for any pain outcome.[83]
	systemic oral steroids	●	○	**Do not improve pain severity** among patients with acute LBP without radiculopathy[90]
	epidural steroids (for sciatica)	●	●	May provide **small or short-term benefits** for acute low back pain with **radicular symptoms (sciatica)**[92]
	opioids	●	●	Offer no benefit beyond NSAIDs,[63] but with greater risk
	muscle relaxants	●	●	Shown to be more effective than placebo[87]

● = strong evidence of efficacy; ● = some evidence of efficacy or harm; ● = evidence of lack of efficacy or evidence of harm; ○ = inadequate evidence

Post-operative pain

Over 48 million surgical procedures performed annually in the U.S.[94,95] More than 80% of patients who undergo surgical procedures experience acute post-operative pain and approximately 75% of those with post-operative pain report the severity as moderate, severe, or extreme.[96] A national survey on patient satisfaction with post-op pain management indicated that post-surgical pain was the most prominent pre-surgical patient concern, and nearly half of patients reported they had high or very high anxiety levels about pain before surgery.[97]

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-op pain scores had increased lengths of hospital stay, more missed physical therapy sessions, delayed ambulation, and impaired function (locomotion) at six months.[6] 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.

Patients' perceptions regarding post-operative pain management have changed. Results from national surveys on patient satisfaction with post-op pain management indicate that more patients prefer opioids and believe them to be more effective. However, disproportionately more side effects from analgesic medications were reported in 2013 (79%) compared to 1995 (23%). From the 2003 survey, adverse events included drowsiness (56%), constipation (35%), and nausea (28%) (Table 2).[95-97]

Table 2: Patient reports of analgesic use after surgery in 1995, 2003, and 2013[97]

Survey Year	Prefer Opioids	Use of non-pharm therapies	Reported side-effects
1995	29%	46%	23%
2003	28%	n/a	23%
2013	43%	60%	79%

After administration of high doses of potent opioids, patients may develop a paradoxical response to opioids and actually become more sensitive to painful stimuli, resulting in **hyperalgesia** rather than analgesia. This acute opioid-induced hyperalgesia in the post-operative period can lead to increased post-operative pain despite an increase in opioid use. Although distinct from analgesic tolerance to opioids, hyperalgesia can also result in an increase in opioid use.[98]

The development of persistent postsurgical pain can also occur. This condition is diagnosed when pain persists beyond the expected healing period—longer than two months for most surgeries. Many factors that contribute to persistent pain have been identified, but no one factor seems to be predominant. Persistent post-surgical pain may delay or hinder recovery and warrants further investigation into underlying causes.[99]

Non-drug options

Non-pharmaceutical options for relief of post-operative pain include transcutaneous electrical nerve stimulation (TENS), acupuncture and related interventions, massage, cold therapy (with and without compression), localized heat, warm insufflation, 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 many are not covered by most health insurance.[100]

Acupuncture

Acupuncture is often used to treat pain, and it has been investigated as adjuvant treatment for post-operative analgesia.[101]

The 2016 American Pain Society guideline neither recommends nor discourages acupuncture, citing mixed evidence supporting efficacy.[100] However, several systematic reviews have found that acupuncture compared to controls or sham acupuncture can reduce opioid use. A recent systematic review of 13 studies of post-operative adults receiving acupuncture evaluated the effectiveness of acupuncture and acupuncture-related techniques in treating pain after surgical procedures. Compared with sham acupuncture or control, patients treated with acupuncture or related techniques had less pain (SMD -1.27, 95% CI: -1.83 to -0.71;

p<0.001) and used less opioid analgesics (SMD -0.72; 95% CI: -1.21 to -0.22, p=0.005) on day one after surgery compared with those treated with control.[102]

One key meta-analysis of 15 trials evaluated the efficacy of acupuncture and related techniques as adjunctive therapy for acute post-operative pain management, and found that post-operative pain intensity, as measured by a visual analogue scale (0–100 mm), was significantly reduced in the acupuncture group compared with control group at eight hours (WMD -14.57 mm; 95% CI: -23.02 to -6.13] and 72 hours (WMD -9.75 mm; 95% CI: -13.82 to -5.68) after surgery. 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 stimulation was 21%-29%.[103]

Some elderly patients suffering from a higher incidence of postoperative morbidity and mortality might benefit from perioperative acupuncture, which could help ameliorate opioid-induced respiratory depression, pain, ileus, sedation and immobility. However, acupuncture is rarely available in perioperative settings, and clinical application needs to be optimized.[104]

Transcutaneous electrical nerve stimulation (TENS)

TENS is delivered through small portable devices that deliver low-voltage electrical currents through the skin that activates endogenous descending inhibitory pathways activating opioid receptors to produce reduced central excitability and reduce pain through stimulatory effects on large diameter afferent fibers.

A systematic review of 21 RCTs found that use of TENS administered with a strong, subnoxious intensity at an adequate frequency in the wound area was associated with 26.5% (range -6 to +51%) less post-operative analgesic use compared with no TENS.[105] In view of this evidence, TENS is recommended by the 2016 American Pain Society guideline as an adjunct to other post-operative pain treatments.[100]

Drug options

Acetaminophen

Acetaminophen is more effective than placebo at reducing post-procedural pain, and is associated with mild, mostly transient, adverse events.[106] In a Cochrane review of 21 RCTs of acute post-operative pain, acetaminophen provided a statistically significant benefit when compared with 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) post-surgery. Higher doses gave greater benefit for each measure at both time points. There was no difference between groups in reported adverse events.[107]

A 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 needed additional analgesia over four to six hours, compared with about 70% with placebo.[106]

NSAIDs

NSAIDs are beneficial in mild to moderate, acute pain and inflammation. 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 paracetamol at conventional doses in acute pain. Single-dose oral NSAIDs (ibuprofen 400mg, diclofenac 50mg, naproxen 500mg or celecoxib 400mg) are

beneficial in mild to moderate acute pain and inflammation (NNT 2-3 to achieve a 50% reduction in acute post-op pain vs. placebo).[59,108]

The combination of acetaminophen and NSAID may offer superior analgesia compared with either drug alone. In a systematic review of 21 studies (n=1909), combination of acetaminophen and NSAID was more effective than acetaminophen alone (85% of studies) or NSAID alone (64% of studies). Pain intensity was reduced by 35% when comparing combination vs acetaminophen alone, and 39% less when comparing combination vs NSAIDs alone.[109]

A review of 39 separate Cochrane Reviews that analyzed single dose oral analgesics after acute post-operative pain found that the number needed-to-treat (NNT) varied from about 1.5 to 20 for at least 50% maximum pain relief over four to six hours compared with placebo. Efficacy was seen with ibuprofen 200 mg plus acetaminophen 500 mg (NNT compared with placebo 1.6; 95% CI: 1.5-1.8), ibuprofen fast-acting 200 mg (95% CI: 2.1; 1.9-2.3); ibuprofen 200 mg plus caffeine 100 mg (2.1; 95% CI: 1.9-3.1), diclofenac potassium 50 mg (2.1; 95% CI: 1.9-2.5), and etoricoxib 120 mg (1.8; 95% CI: 1.7-2.0). For comparison, ibuprofen acid 400 mg had an NNT of 2.5 (95% CI: 2.4-2.6).[110]

Gabapentinoids

Concomitant use of nonopioid adjuvants for pain relief has been explored as an option to limit opioid use. Gabapentinoids (e.g., gabapentin [Neurontin] or pregabalin [Lyrica]) are frequently prescribed with opioids and are used as potential components of multimodal opioid-sparing analgesic regimes. They may help reduce central sensitization induced by surgery as well as post-operative inflammation.

Gabapentin is an antiepileptic and analgesic medication that has been shown to have analgesic and opioid-sparing effects when administered following surgery.[111,112] It may also increase other side effects such as sedation, visual disturbances, and dizziness.[113] Pain reduction by gabapentin or pregabalin alone is inconsistent, with some studies showing benefit to 24 hours while others showing no difference vs. placebo. However, gabapentin and pregabalin have been most studied in the immediate post-operative period as an add on to standard pain regimens (e.g., opioids, NSAIDs), resulting in reduced doses of opioids.[111,113,114]

The first RCT of perioperative use of gabapentin with extensive postoperative longitudinal follow-up was reported in 2018 in 422 patients who had undergone various types of surgery. The study examined the effect of perioperative gabapentin on postoperative time to pain resolution and cessation of opioid use. Patients received 1200 mg of preoperative gabapentin followed by 600 mg every eight hours for 72 hours, or active placebo. Although gabapentin use did not significantly affect postoperative pain resolution (84 days vs. 73 days for placebo for patients to give five consecutive reports of zero average pain at the surgical site; HR 1.04, 95% CI 0.82-1.33), participants receiving gabapentin had a 24% increase in the rate of opioid cessation after surgery (25 days vs. 32 with placebo; HR=1.24; 95% CI, 1.00-1.54; p=0.05). Adverse events were similar between the two groups. The use of perioperative gabapentin in conjunction with opioid use may be an effective strategy to promote opioid cessation and prevent chronic opioid use.[60]

Of note, the conduct of anesthesia and prescribing of opioids following surgery were not standardized, which may have affected the patient's pain experience and perhaps influence the development of chronic pain following surgery. Additional investigation is needed to determine if gabapentin administration might be clinically valuable in perioperative setting.[115]

Combining gabapentinoids with opioids may increase risk of respiratory depression, as patients are at a higher risk after surgery. A retrospective study of 125 patients who were prescribed opioids and at least one dose of naloxone compared the frequency of respiratory depression among patients who received naloxone

and opioids (non-gabapentinoid group) with those who received naloxone, opioids, and gabapentinoids (gabapentinoid group). Results indicated no significant difference between respiratory depression and sedation among those who received gabapentinoids (17/51=33.3%) and those who did not (33/102=32.4%) (p=0.128). However, there was an increased risk of respiratory depression in the gabapentinoid group in patients who had surgery within the last 24 hours.[49]

Lidocaine patch

The topical lidocaine 5% patch is used for the treatment of chronic neuropathic pain syndrome and post-herpetic neuralgia and has potential as a possible local anesthetic to treat post-operative pain. However, the evidence supporting this is limited, and there is no clear role for transdermal lidocaine for post-operative pain.[57]

A meta-analysis of five trials comparing the lidocaine patch with control for treatment of acute or post-operative pain found no significant differences in pain score, opioid consumption, or length of hospital stay. Given this evidence, application of a lidocaine patch may not be an effective adjunct for acute and post-operative pain management.[57]

Opioids

Due to their potent analgesic efficacy in severe post-operative pain, opioids are frequently prescribed after many types of surgery. Opioid analgesics such as morphine, hydromorphone, meperidine, or fentanyl are commonly used to treat post-operative pain. However, as noted these drugs are associated with a number of undesirable side effects, such as nausea, vomiting, gastrointestinal ileus, dizziness, sedation, immunosuppression, and respiratory depression, which may delay patient recovery.[116]

Exposure to opioids after surgery increases the risk of chronic opioid use, especially in elderly men.[54] A recent observational retrospective study using commercial insurance claims estimated that approximately 56% of members received a prescription opioid after surgery, with 90% of these prescriptions being filled within three days of discharge. Subsequent opioid dependence, abuse, or overdose was 0.6%, which was low, but rates of misuse grew rapidly with increasing opioid use. Risk factors for opioid misuse include the number of refills (each additional refill increased the rate of misuse by 70.7%), as well as the duration of use (more so than initial dose).[52]

Oxycodone is a strong opioid agonist used to treat severe pain and is two to three times stronger than codeine. A systematic review of 20 RCTs (n=2641) of single dose oxycodone in adult 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 for ≥50% pain relief of oxycodone 15 mg, 4.6 (95% CI: 2.9-11). Efficacy was found to increase when combined with acetaminophen (NNT for oxycodone 10 mg plus acetaminophen 650 mg, 2.7 (95% CI: 2.4-3.1). Adverse events were more frequently with combination therapy than placebo, and included nausea, vomiting, and dizziness. These were generally mild to moderate in severity and rarely led to withdrawal.[117]

Opioids are also frequently prescribed following surgical tooth extraction and represent a key area of excessive opioid prescribing in the United States. Although some patients may require a limited supply of opioids after tooth extraction, a disproportionally large number of opioids are frequently prescribed. In a cohort of U.S. Medicaid patients from throughout the United States, prescriptions for opioids were filled by 42% of patients within seven days following surgical tooth extraction. The most commonly dispensed opioid was hydrocodone (78%), followed by oxycodone (15.4%), propoxyphene (3.5%), and codeine (1.6%). The median amount of morphine equivalents dispensed to adults following extraction was 120 mg which

represents 24 5-mg tablets of hydrocodone or 16 5-mg tablets of oxycodone. Considering the expected intensity and duration of pain after tooth extraction, alternatives with fewer adverse effects, such as non-opioid analgesics, may be more effective in this setting.[118]

Contrary to logic, the prescription of opioids at a higher quantity and strength in the attempt to reduce pain and improve satisfaction with pain relief in the acute setting has not been shown to be efficacious. In fact, patients who used more opioids post-operatively actually reported greater pain intensity, and administration of more opioids did not improve satisfaction with pain relief.[119]

Managing post-operative pain

Contemporary post-operative pain management aims to enhance pain relief and reduce opioid requirements by combining non-drug options, non-opioid analgesics and techniques with different mechanisms of action.[113]

Evidence for non-drug options are limited, however acupuncture may offer superior analgesia to controls and may reduce opioid use after surgery. Among drug options, multimodal analgesia may be superior than any single drug intervention alone, such as combining NSAIDs and acetaminophen. Gabapentinoids may be added to first line therapies in the immediate post-op period, however do confer more side effects. Opioids are effective in moderate to severe post-op pain but should be used judiciously. Physicians should acknowledge patient concerns about pain after surgical procedures and offer reassurance that the pain will be self-limited and can often be managed without the need for potentially addictive drugs.

Table 3. Efficacy and harms of treatment of acute post-operative pain

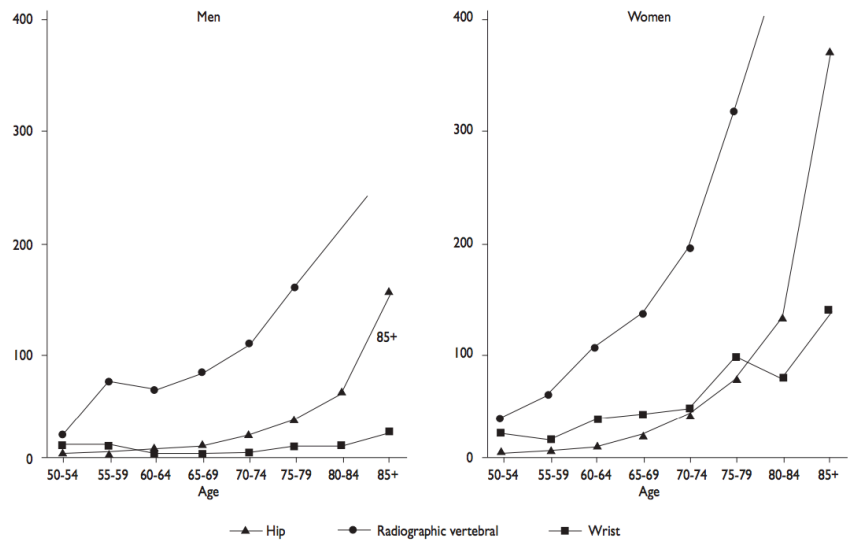
	INTERVENTION	Efficacy	Harm	Comment
NON-DRUG	**acupuncture**	●	○	Compared to controls or sham acupuncture, **can reduce opioid use by 21% to 29% after surgery.**[102]
NON-DRUG	**TENS***	●	○	**Recommended by the American Pain Society** as an adjunct to other treatments.
DRUG OPTIONS	**NSAIDs** (ibuprofen 400 mg, diclofenac 50 mg, naproxen 500 mg or celecoxib 400 mg)	●	○	**Beneficial in mild to moderate acute pain and inflammation** (NNT† 2-3 to achieve a 50% reduction in acute post-op pain vs placebo).[110]
DRUG OPTIONS	**acetaminophen**	●	○	In a review of 51 studies, **46% of patients achieved at least 50% pain relief after surgery**, compared to 20% for placebo (NNT† = 4).[106]
DRUG OPTIONS	**NSAID + acetaminophen**	●	○	A review of 21 studies indicates **combining NSAIDs with acetaminophen offers better pain relief** compared with either drug alone.[109]
DRUG OPTIONS	**gabapentin (e.g., Neurontin); pregabalin (e.g., Lyrica)**	●	●	Evidence for efficacy is mixed. One study found **adding gabapentin** for patients already taking acetaminophen and celecoxib after total knee replacement **was no different than adding placebo.**[113]
DRUG OPTIONS	**opioids**	●	●	In 20 RCTs, oxycodone provided **more effective analgesia than placebo.**[117] **Adverse events included nausea, vomiting, dizziness.**

● = strong evidence of efficacy; ● = some evidence of efficacy or harm; ● = evidence of lack of efficacy or evidence of harm; ○ = inadequate evidence

Sprains, strains, fractures, and trauma

In addition to low back pain, pain due to joint disorders, injury, sprains, strains and fractures is one of the most common musculoskeletal injuries in the elderly (Figure 14). There is a heightened risk of almost all types of fracture in individuals with low bone density, regardless of the site of injury. Acute ankle sprains are among the most common cause of primary care office and emergency department visits, with an incidence in 5,840 per 100,000 people a year in the United States.[120]

Figure 14: Incidence of spinal, hip, and wrist fractures by age and gender[121]



Non-drug options

Standard (conventional) therapy

The optimal non-drug treatment for sprains and strains remains uncertain. Rest, ice, compression, and elevation (RICE) is a foundational management approach, but since there are few RCTs of each component, it may not be supported in its entirety by strong clinical evidence.[122]

- *Rest:* Avoiding any activity that induces stress or strain to the injured area, reducing the metabolic demands of the injured tissue and avoiding increased blood flow. For some injuries, such as acute ankle sprain, graduated exercises may offer faster recovery of function than rest alone.
- *Ice:* Application of cryotherapy to limit injury-induced damage by reducing the temperature of the tissues at the site of injury, reducing metabolic demand, inducing vasoconstriction, and limiting the bleeding. Standard protocols recommend icing for 20 minutes every two hours, or every 10 minutes alternating between ice and rest.
- *Compression:* Application of pressure around the injured site to stop hemorrhage, reduce swelling, limit the amount of tissue edema, and helps control the osmotic pressure of the tissue.
- *Elevation:* Increasing the height of the injured part lowers pressure in local blood vessels, limits bleeding, increases drainage, and limits edema.

Surprisingly, there does not actually exist much convincing clinical evidence to support the effectiveness of RICE therapy in improving strains and sprains. A meta-analysis of 24 RCTs analyzed the effectiveness of applying RICE therapy within 72 hours after 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.[122]

Ice has been shown to be better than heat for sprains and 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 started within 36 hours after the injury (full activity in 13.2 days) is an effective treatment of ankle sprains, yielding earlier

complete recovery than late cryotherapy initiated 36 hours after injury (30.4 days) or heat therapy (33.3 days).[123]

In a prospective RCT of patients with mild to moderate sprains who underwent functional treatment with different types of external supports, treatment with an Air-Stirrup ankle brace (Aircast Inc., Summit, NJ) combined with an elastic wrap was more effective for functional improvement compared to use of the Air-Stirrup brace alone, an elastic wrap alone, or a walking cast. Treatment with the Air-Stirrup brace combined with the elastic wrap of grade II sprains (decreased motion and some loss of function, a torn anterior talofibular ligament with an intact calcaneofibular ligament, some ligamentous instability (e.g., positive anterior drawer and negative talar tilt results), swelling and hemorrhage, and point tenderness) allowed patients to return to pre-sprain function in the shortest time interval.[124]

Functional treatment

Several studies have challenged the utility of the RICE approach, suggesting that early movement, including manual therapy techniques, may be better for recovery.[122,125] A small RCT of 101 patients with mild ankle sprains observed that functional treatment involving moderate therapeutic 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. Activity level was significantly higher in the exercise group than in the standard treatment group, as measured by time spent walking (1.2 hours, 95% CI: 0.9-1.4 vs. 1.6 hours, 1.3-1.9, respectively), step count (5621 steps, 95% CI: 4399-6843 vs. 7886 steps, 95% CI: 6357-9416, respectively), and time spent doing light intensity activity (53 minutes, 95% CI: 44-60 vs. 76 minutes, 95%: 58-95, respectively). However, there remain risks related to functional treatment, such as reinjury or delay of soft tissue recovery.[125]

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 a simple grade one or two ankle sprains found that addition of early supervised physiotherapy to usual care (RICE treatment) did not lead to clinically important improvements in functional recovery up to six months after injury.[126]

Joint mobilization

It is commonly believed that early controlled mobilization of the joint (most often using a tubular compression bandage) for severe ankle sprains is effective in promoting recovery and limiting chronic symptoms. 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 (MD 9%; 95% CI: 2.4-15.0) than if the patient is only given a tubular compression bandage. Improvements in pain, symptoms, and activity was also observed.[127]

Drug options for sprains and strains

NSAIDs

NSAIDs may be beneficial when used with immobilisation for people with acute sprain by reducing inflammation, but some have expressed concern that early use in the first 48 hours after injury may impair healing. Possible side effects including gastrointestinal bleeding and heart failure should be taken into consideration, particularly in susceptible populations such as the elderly.[128,129]

A Cochrane review of 16 trials involving 2144 patients with acute soft tissue injury (sprain, strain or contusion of a joint, ligament, tendon or muscle that occurred up to 48 hours prior) compared oral NSAIDs with

acetaminophen, opioid, acetaminophen plus opioid, or complementary and alternative medicine. These results show consistent evidence of no clinically important difference 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.[130]

- 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 over. There was little difference between the two groups in return to function at day seven or over. There was slightly lower risk of gastrointestinal adverse events in the acetaminophen group based on an assumed risk of gastrointestinal adverse events (16 per 1000 participants for acetaminophen vs. 13 more participants per 1000 in the NSAID group; 95% CI: 0-35 more).
- 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 over 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, and in gastrointestinal adverse events.

Topical NSAIDs such as diclofenac gel also can provide effective initial pain control for acute musculoskeletal pain resulting from sprains and strains. These agents have been shown to be safe and effective for acute musculoskeletal pain, with fewer systemic adverse effects than oral NSAIDs. However, long term impact of topical NSAID use has not been determined.[108]

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. Nine studies (n=991) compared acetaminophen against NSAIDs and found little difference in pain at 24 hours, welling or function at seven days. NSAIDs were associated with a higher risk of gastrointestinal bleeding (13 more events per 1000 people) than acetaminophen.[130]

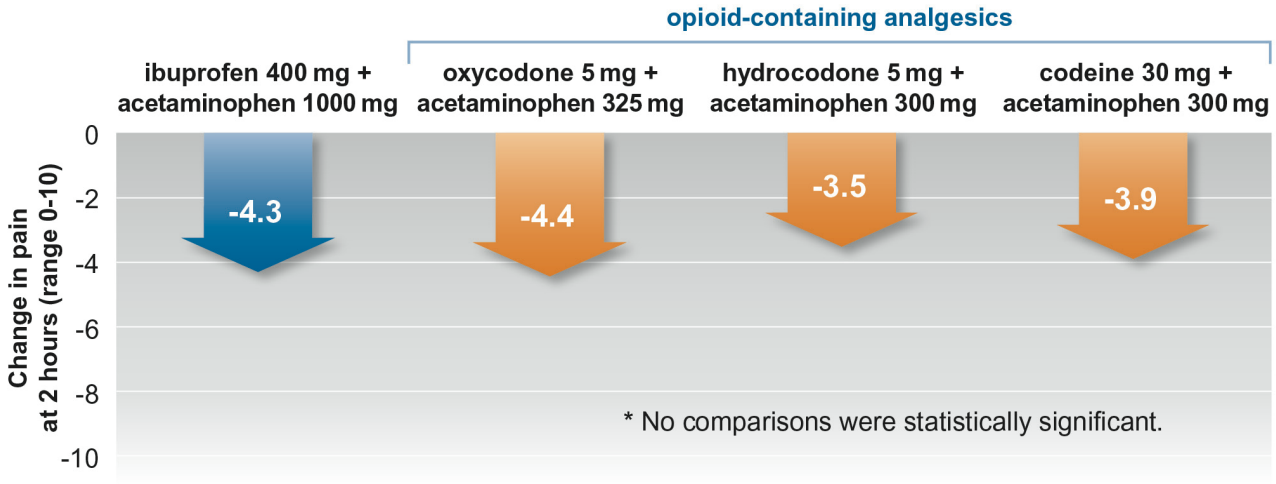
Opioids

Opioid analgesics are often prescribed for moderate to severe acute pain due to sprains and strains. Although they are thought to be stronger analgesics than NSAIDs, opioids were found in a recent RCT to be no more effective in patients with severe acute musculoskeletal pain than a combination of ibuprofen + acetaminophen.[34]

This RCT was conducted in 416 patients with acute extremity pain (mean score, 8.7 on the 11-point numerical rating scale [NRS]), who were assigned to one of four regimens: 1) ibuprofen 400 mg and acetaminophen 1000mg; 2) oxycodone 5mg and acetaminophen 325mg; 3) hydrocodone 5mg and acetaminophen 300mg; or 4) codeine 30mg and acetaminophen 300mg. The mean pain scores at two hours after ingestion (primary endpoint) decreased by 4.3 (95% CI: 3.6-4.9) with ibuprofen and acetaminophen; by 4.4 (95% CI: 3.7 to 5.0) with oxycodone and acetaminophen; by 3.5 (95% CI: 2.9-4.2) with hydrocodone and acetaminophen; and by 3.9 (95% CI: 3.2-4.5) with codeine and acetaminophen (p=0.053). (Figure 15) None of the differences between analgesics was statistically significant or met the definition of a minimally clinically important difference in mean NRS pain score of 1.3. These results suggest that there were no clinically

important differences in pain reduction at two hours after blinded ingestion among single-dose treatment with ibuprofen and acetaminophen or with three different opioid and acetaminophen combination analgesics.[34]

Figure 15: Effectiveness of ibuprofen and acetaminophen compared with three opioid containing regimens in patients with severe musculoskeletal pain[34]



Thus, it is not clear that opioids result in greater pain relief for the patient compared to other analgesics. For acute post-operative orthopedic pain, opioid medication has been associated with less satisfaction with pain relief. In a prospective comparative study in 60 patients following ankle fracture surgery, it was found that patients that did not use opioids had less pain and equivalent satisfaction with pain relief compared to patients that used opioids.[131] Additionally, another prospective study in 100 patients who had undergone primary total hip arthroplasty showed lower mean pain scores during the first 24 hours after surgery in those using a non-opioid oral regimen, compared to opioid-based patient-controlled analgesia.[132]

Instead, opioids have been shown to be associated with an 88% increase in fracture risk.[133] This association was reported in cohort studies examining the association between chronic opioid use and later fracture risk for patients with chronic noncancer pain. Adverse effects of opioid use, such as sedation and dizziness, can increase the likelihood of falling, while decreased bone mineral density from opioid use may weaken bone structure. As elderly persons have a higher risk of developing osteoporosis and pain, opioids used to treat pain in this population may increase the risk of subsequent fractures.[133]

Management of sprains, strains, fractures and trauma

Non-drug recommendations for treating acute pain caused by sprains, strains, fractures and trauma include ice, compression, elevation, and early mobilization to reduce pain and improve function. Physical therapy may not be better than usual care alone for mild ankle sprains. However, casting or air-casting may improve short-term function for most the most severe ankle sprains.

When pharmaceutical intervention is required, acetaminophen and NSAIDs are equally effective, although NSAIDs are associated with more adverse events. Topical NSAIDs reduce pain and may be an option to avoid the systemic side effects of oral NSAIDs. Opioids have been found to be no better in ultra-acute settings than a regimen of ibuprofen and acetaminophen.

Opioid monotherapy has been commonly used by orthopedic surgeons due to a belief that NSAIDs suppress the healing and formation of long bones. While isolated clinical investigations have been cited as evidence to withhold NSAIDs during treatment of fractures, critical examination of the clinical literature does not support this belief. According to the American Orthopedic Association, this is an important point to emphasize, as NSAIDs represent a safer and equally effective alternative to opioids for pain control during fracture treatment.[134]

Table 4. Efficacy and harms in the treatment of acute pain due to sprains and strains

	INTERVENTION	Efficacy	Harm	Comment
NON-DRUG OPTIONS	**compression**	●	○	Compression with an elastic wrap or air-stirrup brace **improves function in mild ankle sprains**.[124]
	exercise	●	○	Incorporating therapeutic exercises in the first week after ankle sprain **improves short term function**.[122,125]
	casting (severe sprains)	●	○	For the most severe ankle sprains (unable to bear weight for 3 days), **a hard cast or air cast was more effective for foot/ankle function** compared to compression bandage alone.[127]
	physical therapy	○	○	**May not be better than usual care** for mild ankle sprains.[126]
DRUG OPTIONS	**acetaminophen**	●	○	**Keep daily dose of acetaminophen below 3000 mg/day** for most older patients.[130]
	oral NSAIDs	●	●	**Co-prescribe a PPI or H2 blocker** for patients at higher risk of **gastrointestinal bleeding**.[130]
	topical NSAIDs	●	○	Number needed to treat for acute musculoskeletal pain: 1.8–4.4[108]
	opioids	●	●	A systematic review found that **opioids are no better than NSAIDs** for acute sprain, strain, or contusions, **while posing important risks**.[34]

● = strong evidence of efficacy; ● = some evidence of efficacy or harm; ● = evidence of lack of efficacy or evidence of harm; ○ = inadequate evidence

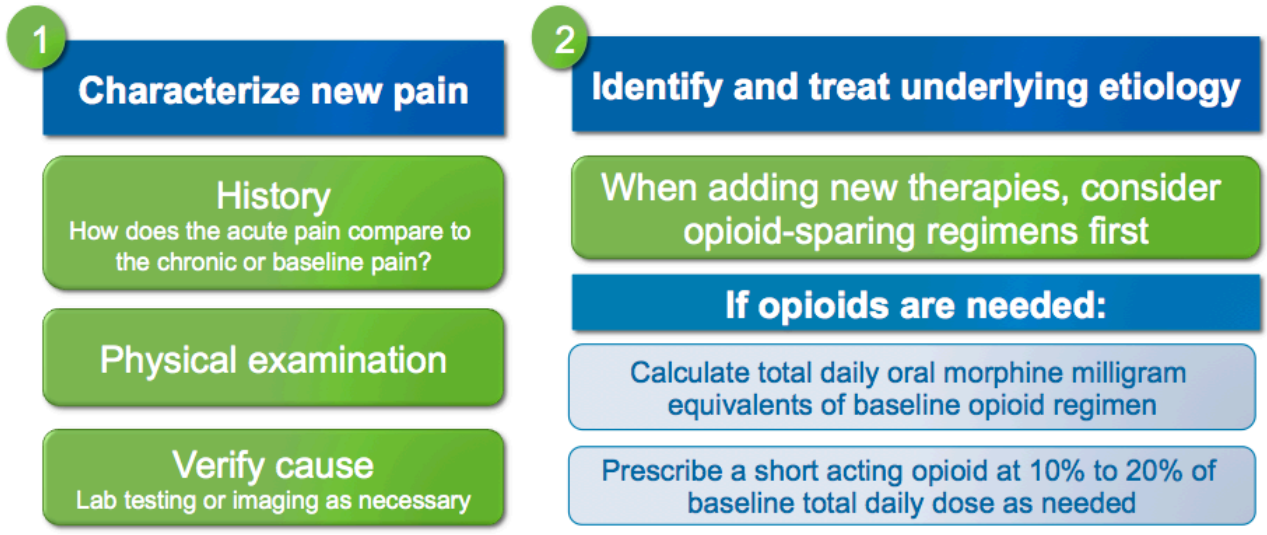
Acute pain management in special populations

Chronic opioid users

Long-term opioid users are those engaging in persistent opioid use for six months (180 days) or longer.[37] Treating new acute pain in this population poses a unique challenge, as patients are already dependent on opioids. These patients often need higher doses to achieve the same analgesic effect, and also may have heightened sensitivity to painful or less noxious stimuli. The acute pain in these patients is often undertreated, yet they are at a higher risk for overdose.

When new-onset, acute pain develops in these patients, such as a sudden ankle fracture, goals of acute pain management include pain relief, improvement of function, and hastening return to baseline while preventing withdrawal and relapse in patients with substance use disorders. The main objective is to ensure that baseline opioid requirements are met, and additional analgesia are provided to manage the acute pain.[135]

Figure 16: Suggested clinical algorithm for acute pain in patients chronically using opioids[7,135]



As the risk of overdose is higher with increasing total daily opioid dosages, some clinicians may be hesitant to prescribe additional opioids due to concerns about respiratory depression, opioid addiction, misuse, and diversion. There remains some clinical ambiguity in determining optimal analgesic therapy in this complex population.

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 dosing regimens such as frequent repeat doses.[135]

Expert opinion suggests that when prescribing new or additional opioids, choosing a different type of opioid may improve analgesia due to different receptors affected (opioid rotation). However, the cross-tolerance of different opioids varies, and caution is crucial to select the appropriate dose.[7,135] Selecting an appropriate, safe dose of methadone is particularly challenging due to its long and highly variable half-life and numerous

interactions with other medications, and effects on the electrocardiographic QTc interval and respiratory depression.[89]

To select a dose, clinicians should estimate the daily morphine equivalent dose of the baseline opioid regimen and convert the newly prescribed opioid to an equivalent morphine dose. Appropriate rescue dosing for breakthrough pain should be provided by prescribing a short acting opioid at 10% to 20% of the baseline total daily dose as needed.[7,136]

Patients on opioid agonist maintenance therapy

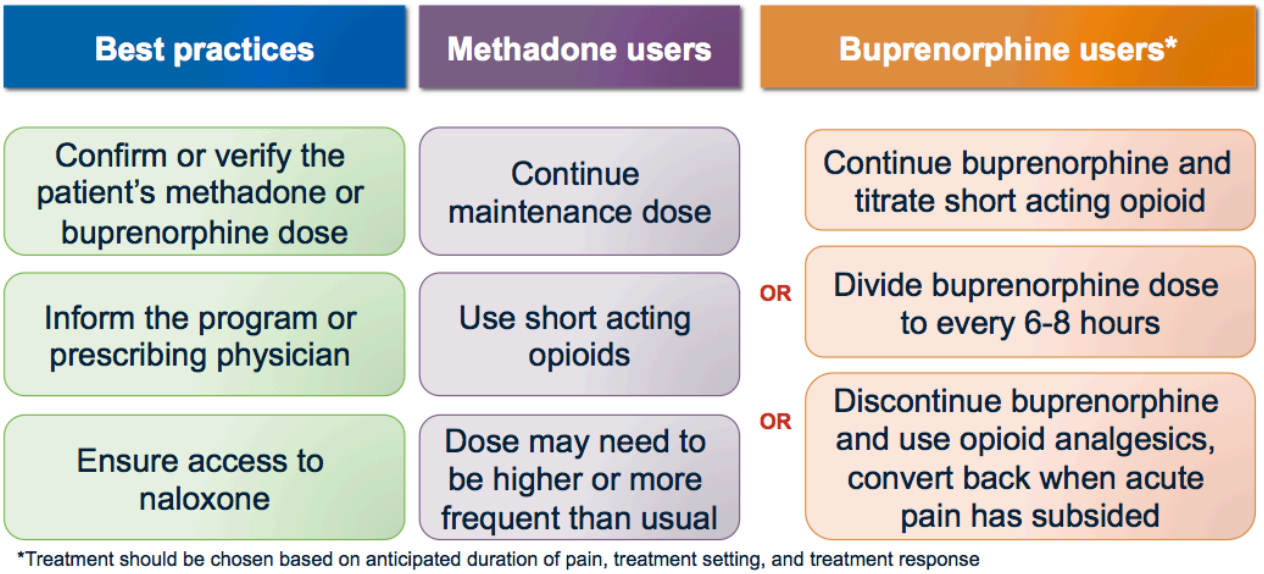
Patients with opioid dependence (opioid use disorder or addiction) receiving long-term opioid agonist therapy (OAT) with methadone and buprenorphine sometimes develop acutely painful conditions that need treatment. In patients with a known history of a substance use disorder, physicians may not prescribe effective opioid analgesia due to concerns of side effects, iatrogenic drug addiction, and prescription drug diversion. As a result, this population is at particular risk of under-treatment for their acute pain.

There is also a tendency to assume that acute pain is adequately controlled with the long-term opioid agonist. In reality, opioid agonists *at* usual doses for treatment of opioid use disorder is insufficient to treat severe or persistent pain. Although 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).[137]

Patients in this population generally have a higher cross-tolerance for analgesia and may require higher doses of opioids for pain control, while analgesic effects may be shorter in duration than for patients without tolerance. Higher opioid analgesic doses administered at shorter intervals may be necessary.

When opioids are necessary for patients on methadone or buprenorphine, clinicians should verify the patient's methadone or buprenorphine dose, and ensure that naloxone is available. Clinicians should inform the program or prescribing physician about the addition of new opioids or benzodiazepines, as this may affect subsequent urine screening.

Figure 17: Suggested clinical algorithm for acute pain in patients receiving opioid agonist therapy who require analgesics[137]



Patients with history of opioid addiction or dependence (off medication assisted treatments)

Patients with history of active or past opioid use disorder or dependence may seek prescription opioids after experiencing acute pain after injury or surgery. Mismanagement of these patients my lead to relapse to active drug use or intensification of withdrawal symptoms.

If opioids are required, clinicians should balance the benefits for analgesia against the risk of relapse and ensure consistent access to naloxone. Consulting or co-managing with an addiction specialist may provide optimal comprehensive care. In opioid-dependent patients, naloxone is used in the treatment of opioid-overdose-induced respiratory depression, in rapid detoxification and in combination with buprenorphine for maintenance therapy to prevent intravenous abuse. However, naloxone use in opioid-dependent patients is also associated with risks such as induction of an acute withdrawal and possible catecholamine release leading to pulmonary edema and cardiac arrhythmias. Therefore, naloxone should be used with caution and monitored.[138]

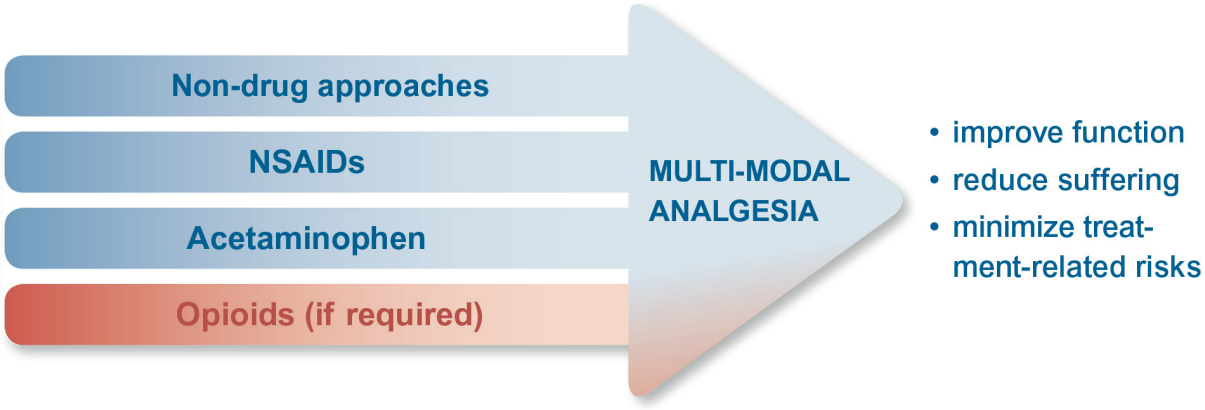
A detailed clinical assessment for objective evidence of pain will decrease the chance of being misled by a drug-seeking patient and if appropriate, will enable careful use of opioid analgesics in patients with a history of opioid dependence. Clinicians should strongly consider opioid-sparing or interventional treatments for planned surgery, which is associated with acute post-operative pain.

Putting it all together

As acute pain is a self-limiting disease, most patients experience a natural relief of symptoms within a month. Helping patients manage their expectations about their acute pain with structured messaging can provide reassurance and reduce fear, worry, and distress.

A multimodal approach is recommended to for optimal management of acute pain in elderly populations, including non-drug (e.g. interventional procedures, physical rehabilitation, and psychological support) and drug-based options (Figure 18). Clinicians should explore different pain management options before resorting to opioids, which lack any anti-inflammatory effects and may not be any more effective to treat acute pain than NSAIDs and/or acetaminophen, while conferring important risks.

Figure 18: Combining pharmacologic and non-pharmacologic approaches to manage acute pain



When opioids are required, clinicians should utilize strategies to limit opioid misuse and maximize analgesic effectiveness, such as titrating to effect with a limited day's supply of short-acting opioids and rotating different types of opioids to provide additional analgesic effect as needed. Clinicians should avoid co-prescribing benzodiazepines in this setting, and should check the local PDMP as required by state law. So-called abuse-deterrent opioid formulations are no less addictive than regular opioids when taken by mouth. Patients prescribed opioids for acute pain should be followed closely because of an increased risk of overdose, which is dose dependent.

Clinicians should tailor the amount of opioid needed to the need for analgesic in order to minimize the amount of leftover medication. Leftover prescription opioids may increase the risk of opioid misuse, mishandling, and accidental overdose by the patient or others.

Appendix I: Brief Pain Inventory

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

Brief Pain Inventory (Short Form)

Date:_____/_____/_____ Time:_____

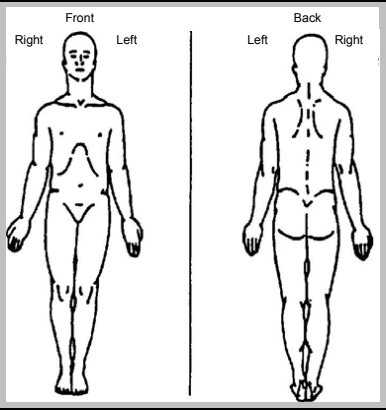
Name:_____ _____ _____

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

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

A. General Activity

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

B. Mood

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

C. Walking Ability

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

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

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

E. Relations with other people

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

F. Sleep

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

G. Enjoyment of life

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

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About this publication

These are general recommendations only; specific clinical decisions should be made by the treating physician based on an individual patient's clinical condition.

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This material was produced by Jing Luo, M.D., M.P.H., Instructor in Medicine; Jerry Avorn, M.D., Professor of Medicine (principal editor); Brian Bateman, M.D., M.Sc., Associate Professor of Anesthesia; Michael A. Fischer, M.D., M.S., Associate Professor of Medicine; Gregory Curfman, M.D., Assistant Professor of Medicine; Niteesh K. Choudhry, M.D., Ph.D., Professor of Medicine; Dae Kim, M.D., M.P.H., Sc.D., Assistant Professor of Medicine; all at Harvard Medical School; and Ellen Dancel, PharmD, M.P.H., Director of Clinical Materials Development at Alosa Health. Drs. Avorn, Bateman, Choudhry, Fischer, and Luo are physicians at the Brigham and Women's Hospital, and Dr. Kim practices at the Beth Israel Deaconess Medical Center, both in Boston. None of the authors accepts any personal compensation from any drug company.

Medical writer: Jenny Cai

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