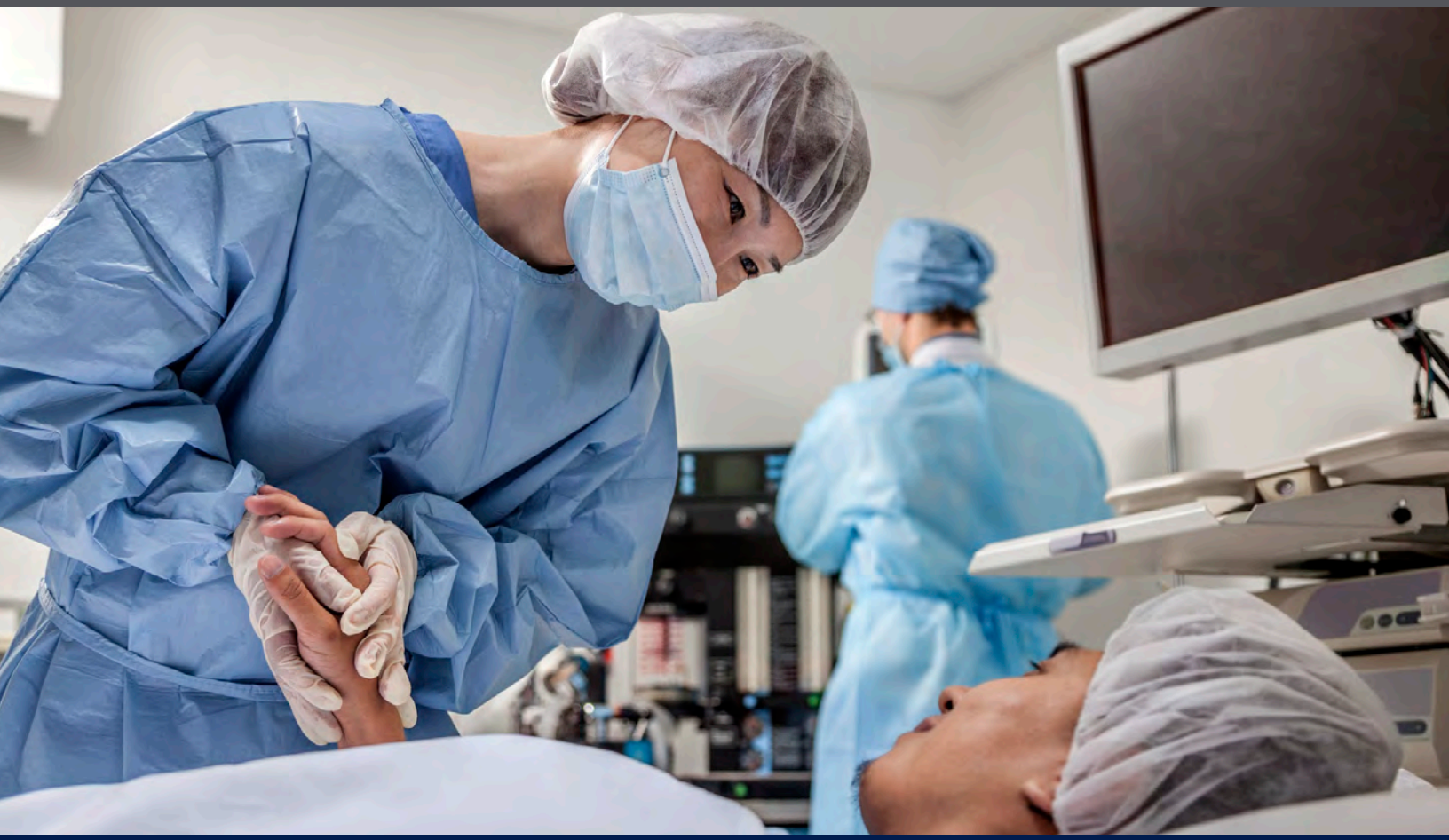
Colorado's Opioid Solution: Clinicians United to Resolve the Epidemic (CO's CURE)

The Colorado Chapter of the American College of Surgeons and
The Colorado Society of Anesthesiology

2020 Opioid Prescribing and Treatment Guidelines



Developed by Colorado American College of Surgeons and the Colorado Society of Anesthesiology in partnership with Colorado Hospital Association, Colorado Medical Society and Colorado Consortium for Prescription Drug Abuse Prevention

COLORADO MEDICAL SOCIETY

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Colorado Chapter of the American College of Surgeons

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ARTS Addiction Research & Treatment Services

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Dedicated to the clinicians across Colorado and the patients for whom they care

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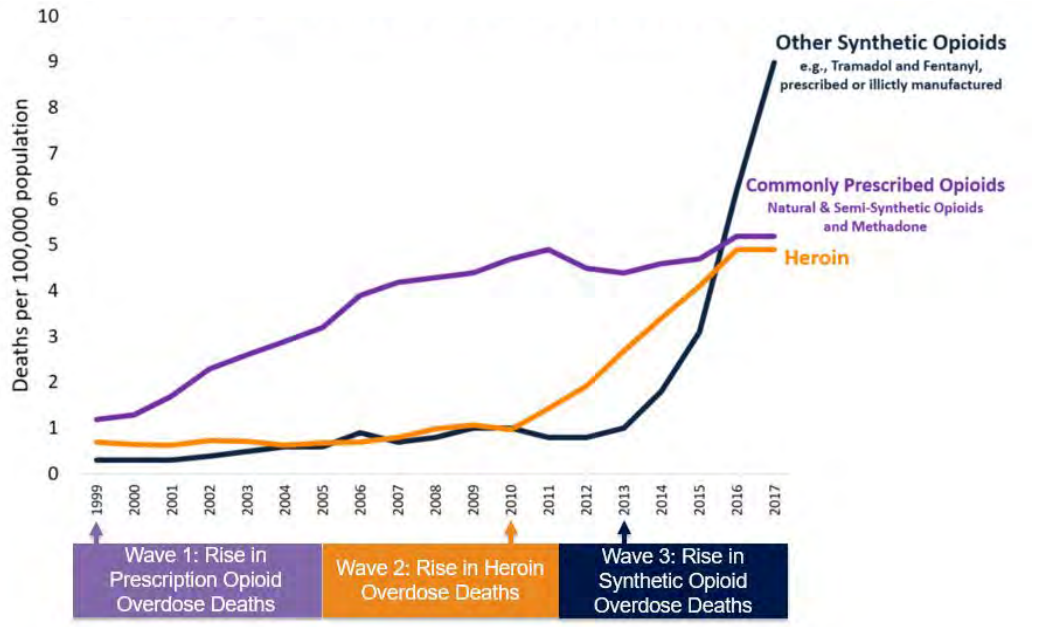
Introduction

Clinicians across Colorado and the nation are facing one of the most devastating public health crises in decades. Opioids, both prescription and illicit, have become the leading cause of accidental death in the United States for adults 50 years of age or younger.[1] Opioid-related adverse drug events (ORADEs), opioid overdose, physical dependence and the development of opioid use disorder (OUD), have become an increasingly common part of medical practice. The number of lives impacted by the crisis is astonishing. The Centers for Disease Control and Prevention (CDC) reports that opioid overdose killed nearly 400,000 Americans between 2000 and 2017, and currently an average of 130 Americans die every day of opioid overdose **(FIGURE 1)**.[2,3] The economic costs of this epidemic are projected to exceed $1.5 trillion by next year; the human costs are incalculable (Figure 2).[10]

(FIGURE 1)

Three Waves of the Rise in Opioid Overdose Deaths, 1999-2017



SOURCE: CDC MMWR[3]

More than 10.3 million people over the age of 12 years self-reported misusing opioids in 2018, with 9.9 million misusing prescription pain relievers and 808,000 using heroin.[4] The pharmaceutical use of opioids skyrocketed between 1990 and 1996: prescriptions for fentanyl rose 1,000%, followed by morphine (49%), oxycodone (15%) and hydromorphone (12%).[5] The number of prescription opioids sold in the United States increased five-fold between 1999 and 2017, and prescription opioids were involved in 218,000 overdose deaths over this time period. In 2017, there were 58 opioid prescriptions written for every 100 patients in the United States, with an average prescription length of 18 days.[6]

The dire consequences of the widespread availability of prescription opioids emerged over time. The "lag period" between a patient's first exposure to an opioid (either medical or nonmedical) and their first treatment admission is an average of seven years. For patients who die of an overdose, the time between their first exposure to an opioid and death is between nine and 13 years.[7,8] In 2017, opioids were responsible for 34% of all substance use disorder (SUD) treatment admissions for patients aged 12 years and older.[9] The economic implications of this epidemic are staggering. The nonmedical use of opioid pain relievers has cost society approximately $1 trillion between 2001 and 2016; unless major changes are made, the economic toll is projected to grow by another $500 billion by the end of 2020 (Figure 2).[10]

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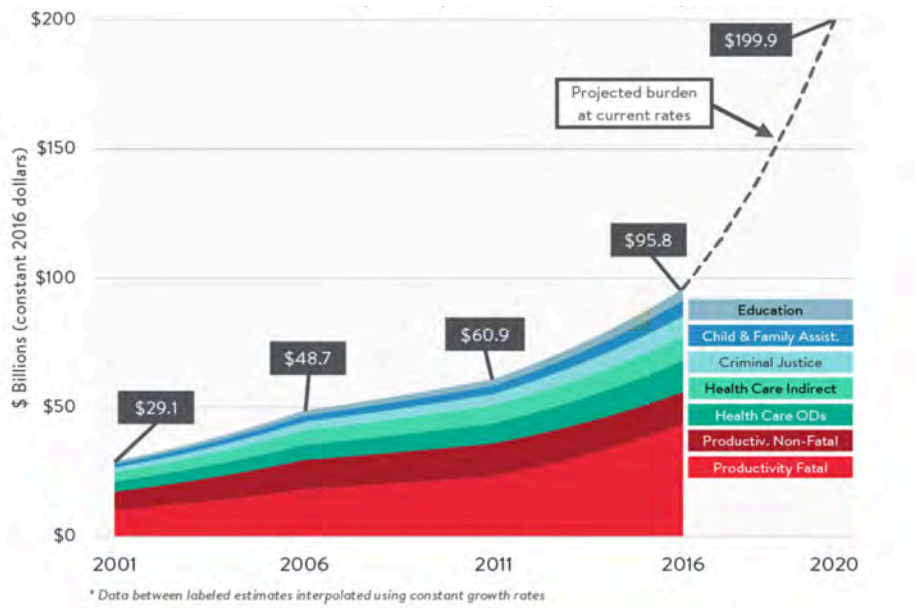
(FIGURE 2)

Total and Projected Costs of the Opioid Epidemic, 2001-2016



SOURCE: Altarum[10]

While a number of external factors have contributed to the liberal use of these potentially lethal drugs, the medical community is compelled to acknowledge its role in creating this crisis. Fortunately, clinicians and health care systems also have the power to reverse these grim statistics by reforming their practices with resolve and innovation.

The Origins of the Opioid Epidemic

Concerned about potential adverse effects, including addiction and overdose, few physicians prescribed opioids for chronic noncancer pain throughout most of the 20th century.[15] That changed in 1986, however, when pain expert Russell Portenoy published a limited case series of 38 hospital patients that suggested that chronic noncancer pain could be managed safely with high doses of opioids without posing a risk of addiction.[16] Since then, the scientific validity of Portenoy's original work has been called into question; in recent years, the researcher himself has publicly doubted the relative efficacy and safety of long-term opioid use for the treatment of chronic noncancer pain.[17–20] Portenoy's findings were endorsed by both the American Academy of Pain Medicine and the American Pain Society, which further legitimized his assertions about the safety of opioid medications.[21] As a result, many pharmaceutical companies began to aggressively market their opioids for wider use at increased dosages and in extended-release formulations.

This shift in perspective was reinforced by the Veterans Health Administration, which adopted pain as the "fifth vital sign" in 1999.[22] The Joint Commission, a governing body responsible for hospital accreditation, added pain management as a requirement for accreditation in 2000.[2,15] During the same period, a report by the Institute of Medicine, *Relieving Pain in America,* painted pain management as a "moral imperative, a professional responsibility, and the duty of people in the healing professions."[23] In addition to these mounting institutional pressures, patient satisfaction surveys increasingly compelled medical clinicians to place a premium on pain management. These highly subjective scorecards, which were routinely linked to remuneration, used the management of pain as a marker for patients' satisfaction with the care they received.[2,24] Once reserved for the treatment of severe pain, opioid analgesics became routinely prescribed for a wide range of pain complaints.

Introduction continued

These guidelines are meant to inform and augment clinical judgment, not replace it. Although CO's CURE acknowledges the value of opioids in certain clinical situations, such as for end-of-life care and the treatment of pain associated with sickle cell disease, severe trauma, burns and cancer, it advocates using extreme caution in all cases. What follows is a compilation of ideas and suggestions that can be implemented by hospitals and clinicians to aid in the prevention of opioid misuse and addiction and the identification, treatment and support of patients with OUD. It is unlikely that a hospital or surgical practice can or will attempt to implement each strategy or idea included in these guidelines. Rather, hospitals and clinicians are encouraged to consider which of these suggestions are appropriate given their unique processes and resources. The recommendations in these guidelines are not intended to be a substitute for the oversight of legal counsel and compliance leaders.

The Opioid Epidemic in Colorado

Coloradans have been significantly affected by this national public health crisis. Since 2000, Colorado has seen 6,030 overdose deaths from opioids.[11] There was a total of 1,635 prescription opioid-related overdose deaths in the state from 2013 to 2017, which translates to 5.8 deaths per 100,000 residents. Heroin-related opioid overdose deaths have increased 76% since 2017.[12]

Colorado Statistics

In 2017 in the state of Colorado:

- There were over 3.7 million opioid prescriptions dispensed to 1 million patients at retail **(TABLE 1)**. These numbers were down slightly from a high of 4.3 million opioid prescriptions for 1.1 million patients in 2015.[12]
- There were 1,012 drug overdose deaths, 57% of which involved an opioid.[12]
- 15% of opioid-naïve patients were prescribed long-acting opioids.[13]
- 10% of patient prescription days involved overlapping opioid and benzodiazepine prescription use.[13]
- There were 671.3 opioid prescriptions filled per 1,000 residents.[13]
- There were 134.3 treatment admissions for heroin per 100,000 people and 40.6 treatment admissions for pharmaceutical opioids per 100,000 people.[1]

While there is considerable variation from county to county in Colorado, with some rural counties particularly affected, the impact of the opioid crisis is felt in all regions and communities. No county is untouched, and the need to address the effects of the crisis is universal. All Colorado physicians, health care practitioners and hospitals must work together to turn the tide and resolve the crisis.

(TABLE 1)

Characteristics of Opioid Prescriptions Dispensed, Colorado 2014-2017

Characteristics	2014	2015	2016	2017
Number of Prescriptions Dispensed	4,039,048	4,310,254	4,159,575	3,765,253
Number of Unique Patients	1,085,551	1,131,781	1,102,297	1,027,685
Number of Unique Prescribers	25,011	24,784	28,063	27,676
Number of Unique Pharmacies	941	839	1,039	1,097

Excludes buprenorphine drugs commonly used to treat opioid use disorder
In 2014 NPI was used to identify unique prescribers and pharmacies as DEA numbers were not available until 2015
Data Source: Colorado Prescription Drug Monitoring Program, Colorado Department of Regulatory Agencies Analysis by: Colorado Department of Public Health and Environment, 2018

SOURCE: Colorado Opioid Profile[12]

Introduction continued

(TABLE 2)

High-Risk Prescribing Practices and Patient Behaviors, Colorado 2014-2017

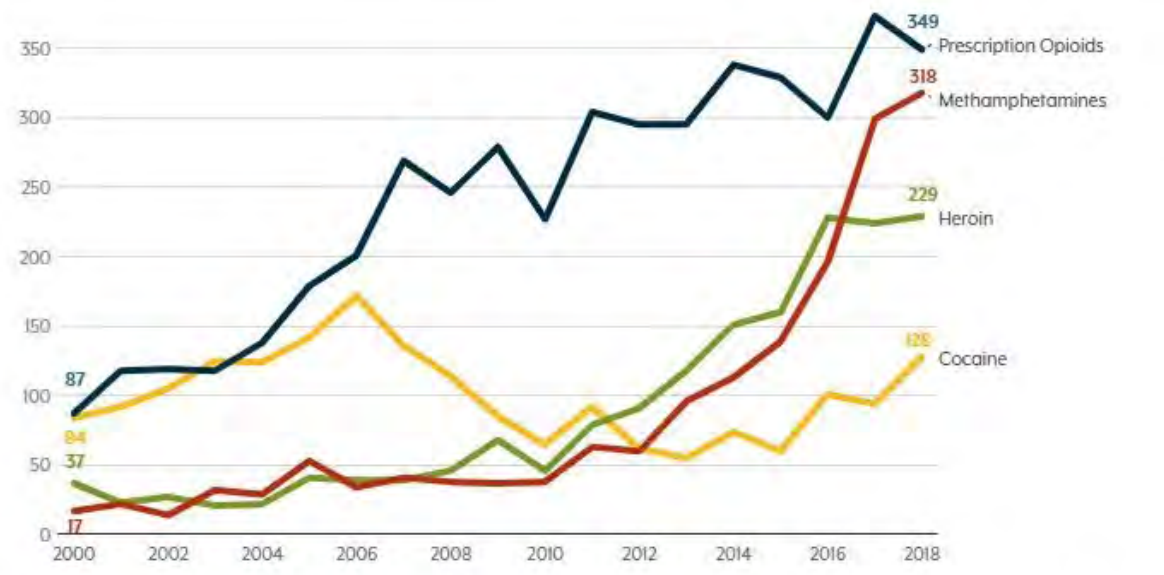
Indicators	2014	2015	2016	2017	2014-2017 % Change
Patients receiving more than 90 MME (%)	10.3	8.9	8.7	8.2	-20.5
Patients with MPEs (rate/100,000 residents)	170.1	124.0	93.6	68.0	-60.0
Patients prescribed LA/ER opioids who were opioid-naive (%)	18.2	17.6	15.8	15.1	-17.3
Patient prescription days with overlapping opioid prescriptions (%)	22.3	21.5	21.4	20.5	-7.8
Patient prescription days with overlapping opioid and benzodiazepine prescriptions (%)	12.1	11.6	11.2	9.9	-18.0

Schedule II-IV Controlled Substances
Excludes Buprenorphine drugs commonly used for treatment
Annual percentages are based on average of quarterly percentages
Data Source: Vital Statistics Program, CDPHE and the Colorado Prescription Drug Monitoring Program, DORA
Data Analysis by: CDPHE, 2018

SOURCE: Colorado Opioid Profile[12]

(FIGURE 3)

Number of Drug Poisoning Deaths by Drug Type, 2000-2018



Categories are not mutually exclusive (may total to more than 100% of total drug overdoses) or comprehensive (other drugs not listed).

SOURCE: Colorado Health Institute[14]

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CO's CURE

Faced with the greatest public health crisis of a generation, Colorado is taking a stand for the benefit of all. CO's CURE is the nation's first set of comprehensive, multispecialty medical guidelines designed to end the opioid epidemic. Within each specialty, there is room for specific nuances of practices, and across all CO's CURE guidelines there is multispecialty collaboration with input from content experts. The unique structure of these evidence-based recommendations is anchored by objectives that can be shared by all medical specialties.

The Four Pillars of CO's CURE:

1. Limiting opioid usage
2. Using alternatives to opioids (ALTOs) for the treatment of pain
3. Implementing harm reduction strategies
4. Improving treatment and referral of patients with OUD

These pillars were conceived by the Colorado Chapter of the American College of Emergency Physicians (ACEP) and published as part of Colorado *ACEP's 2017 Opioid Prescribing & Treatment Guidelines.* When implemented in 10 Colorado emergency departments as part of the Colorado Opioid Safety Pilot by Colorado Hospital Association, the approach entailed in these guidelines resulted in a 36% decrease in opioid use and a 31% increase in the use of opioid alternatives for pain management.[25] The success experienced in Colorado emergency departments through those initiatives represents just one front in efforts to address the opioid epidemic in Colorado. To fully resolve the epidemic, Colorado clinicians will need to adopt a more inclusive, coordinated and ambitious approach.

Now is the time for all specialties and clinicians to unite to create better treatment paradigms for the benefit of patients and communities across Colorado. The guidelines developed under CO's CURE represent some of the most forward-thinking and comprehensive strategies in the nation. They belong to not one specialty, but to all specialties; rather than divide clinicians into their respective tribes and silos, they unite them in a common cause: to resolve the opioid epidemic in Colorado and beyond.

Limiting Opioid Use in Surgical and Anesthesia Practice

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Limiting Opioid Use in Surgical and Anesthesia Practice

The majority of patients who develop OUD report that their first exposure to an opioid involved a pain medication that was prescribed to them or diverted from a family member or friend.[26] General surgeons are responsible for approximately 5% of the opioid prescriptions dispensed in the United States, and the vast majority of hospitalized surgical patients receive opioid analgesia.[27-29] While postoperative pain control is essential, a significant and growing body of research has questioned the extent to which opioids are used in surgical practice and is elucidating the harms that excessive and indiscriminate prescribing poses to patients and communities.

While opioids are an indispensable tool for the management of acute, severe pain, the human and economic costs of their immediate and long-term adverse effects are enormous. Persistent opioid use after surgery is a widespread, under-recognized complication. More than 80% of patients are prescribed an opioid after low-risk operations, and the vast majority of surgical inpatients receive opioid analgesia, often by multiple routes of administration.[28] Thus the perioperative period is a time of opioid exposure for virtually every surgical patient.[30] Of the 50 million patients who undergo surgery every year, more than two million may transition to persistent opioid use.[30-32] An estimated 5.9% of patients who undergo minor procedures and 6.5% of those who undergo major surgeries become new persistent opioid users.[33] The fact that these rates depend less on the magnitude of the surgical procedure and more on patient factors suggests that careful screening for an elevated risk of developing OUD or chronic postsurgical pain (CPSP) may help protect vulnerable patients.[34] That said, opioids are highly addictive drugs and virtually any patient who is exposed to them—particularly at higher doses and longer duration—is at risk for dependence and addiction.

In addition to the risk of long-term opioid use, ORADEs affect an estimated 10-14% of hospitalized surgical patients and are associated with worse outcomes, including increased inpatient mortality, prolonged length of stay, a greater likelihood of discharge to another care facility, increased health care costs and higher rates of 30-day readmission.[27] Many ORADEs may directly or indirectly impair surgical recovery, including nausea and vomiting, ileus, constipation, respiratory depression, sedation, cognitive impairment and cardiovascular compromise.[27,35-37] Less understood but equally concerning is the evidence that even short-term opioid exposure may contribute to opioid-induced hyperalgesia (OIH), CPSP, immunosuppression and, possibly, cancer growth and metastasis.[38-48]

The extent to which surgeons overprescribe opioids has only recently been investigated. Between 67% and 92% of patients who have undergone a variety of general, orthopedic, thoracic and obstetric-gynecologic surgeries report having unused prescription opioids after their procedures.[49-51] In roughly 75% of cases, opioids were discontinued or never used because the patients' pain was controlled without them. Only 28% of opioid pills prescribed on discharge to general surgical patients are actually taken.[52] Furthermore, fewer than 10% of surgical patients safely dispose of their unused opioids, a factor that contributes significantly to the vast reservoir of pills that are available for diversion.[52] One review found that more than 45% of surgical inpatients from a range of subspecialties were discharged with a prescription for an opioid despite not requiring any opioid analgesia during the final 24 hours of their hospital stay.[53]

In many cases, surgeons overprescribe opioids to ensure that their patients receive adequate and uninterrupted analgesia. Until recently, no guidelines for prescribing opioids at discharge have been available, a deficit that has forced surgeons to rely on the customary prescribing practices they learned in residency. Researchers are now beginning to formulate opioid prescribing guidelines based on what patients actually report needing after common surgical procedures.[54-56] Fortunately, research finds no correlation between patient satisfaction or pain relief and the quantity or duration of opioid prescriptions they receive, suggesting that surgeons may use these newly developed prescribing guidelines to curtail their opioid prescribing without sacrificing analgesia or patient satisfaction.[57]

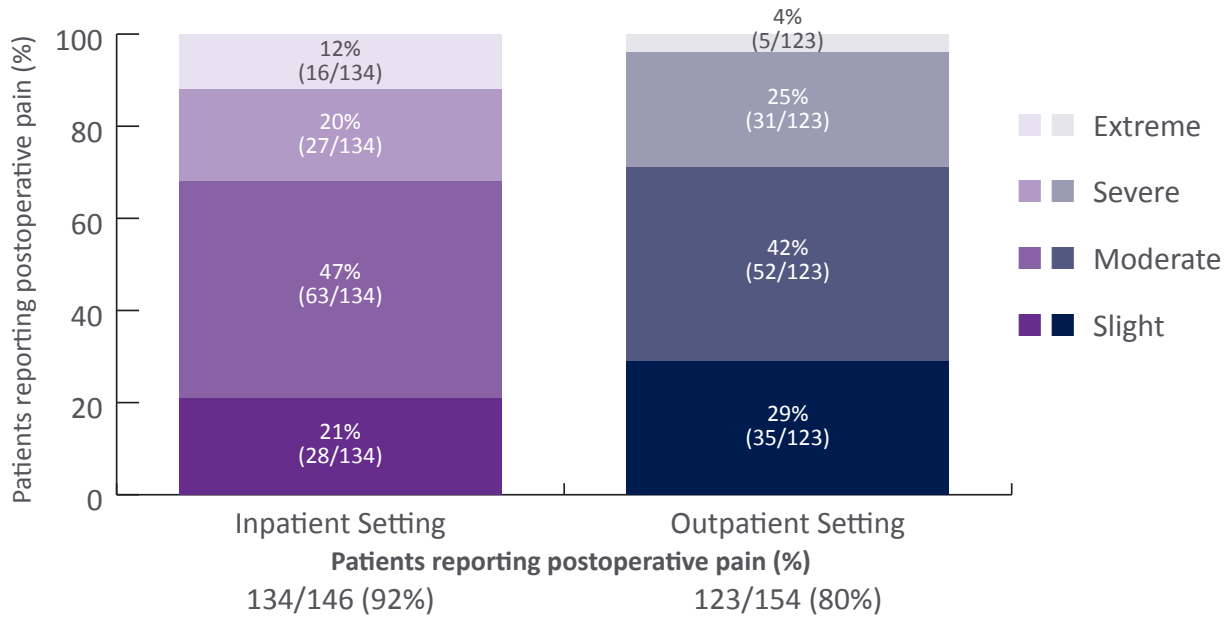
Limiting Opioid Use in Surgical and Anesthesia Practice continued

Surgeons are abundantly aware that poorly controlled pain negatively affects patients' quality of life, function, speed of recovery, risk of surgical complications and the likelihood of developing CPSP.[58-60] Pain causes physiologic stress that may in itself be harmful, but despite the near-universal use of short courses of opioids perioperatively, as many as 80% of patients report moderate to extreme postoperative pain.[61,62] Put simply, increases in perioperative opioid use have not been accompanied by decreases in postoperative pain. Clearly, a new and different approach is warranted, both to improve patient experience and to address the alarming rates of OUD and overdose facing Colorado and the nation.

Close collaboration between surgeons and anesthesiologists and, when appropriate, pain medicine, addiction medicine and behavioral health clinicians may support these efforts. Perioperative care teams best serve their patients and communities by working together to both manage pain and limit patient and community opioid exposure whenever possible. Across all specialties, a common-sense first step to addressing the opioid epidemic is to order and prescribe opioids more judiciously. Perioperative care teams have a vital role to play in ending the crisis by screening patients, prescribing opioids conservatively and providing counsel on the risks of opioid analgesia.

(TABLE 4)

Proportion of Inpatient and Outpatient Patients with Postoperative Pain By Severity[60]



SOURCE: Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and prevention. J Pain Res. 2017;10:2287-2298. doi:10.2147/JPR.S144066

Limiting Opioid Use in Surgical and Anesthesia Practice continued

NOTE: The following practice recommendations may not apply to patients who are dependent on opioids, such as those with active OUD, those on medication for addiction treatment (MAT) and those with chronic pain who are receiving chronic opioid therapy. Special considerations for the care of these patients are addressed below in the Harm Reduction and Treatment of Opioid Use Disorder sections.

Practice Recommendations to Reduce the Risks Associated with Perioperative Opioid Therapy

1. **Opioids are inherently dangerous, highly addictive drugs with significant potential for misuse and addiction, numerous side effects, lethality in overdose, rapid development of tolerance and debilitating withdrawal symptoms. Surgeons are encouraged to reserve opioids for the treatment of pain that has not responded to nonopioid therapy and for patients for whom nonopioid therapy is contraindicated or anticipated to be ineffective.**
   a. Opioids are among the three broad categories of medications with potential for misuse, dependence and addiction, the other two being central nervous system (CNS) depressants and stimulants. Opioids act by attaching to opioid receptors on nerve cells in the brain, spinal cord, gastrointestinal (GI) tract and other organs, triggering a spike in dopamine that not only reduces the perception of pain, but can also manufacture a powerful sense of well-being and pleasure by affecting the brain's limbic reward system.
   b. When used repeatedly, opioids induce tolerance, as exposure to opioids leads to loss of receptor activity and higher doses are required over time to produce the same effect.[63,64] This mechanism also contributes to the high risk of overdose following a period of abstinence.[65] Tolerance can be lost in times of abstinence, leading relapsed users to take a previously "safe" dose with disastrous results.[66]
   c. The effects of opioids are mediated by specific subtype opioid receptors (mu, delta and kappa) that are also activated by endogenous endorphins and enkephalins. The production of endogenous opioids is inhibited by the repeated administration of outside opioids, which accounts for the discomfort that ensues when the drugs are discontinued.
   d. Opioid therapy is associated with a number of common, sometimes serious side effects, including sedation, respiratory depression, constipation, nausea and vomiting **(TABLE 3)**.[25,67] These complications, which often necessitate additional medical care, can prevent patients from performing daily tasks and remaining active in the workforce.
   e. OIH is a paradoxical phenomenon of increased sensitivity to noxious stimuli associated with long-term opioid use. Evidence suggests that even short-term exposures to opioids, particularly to potent agents like remifentanil, may produce OIH.[68,69]
   f. Opioids can impair immune responses, promote angiogenesis and impact NK and T-cell function. In vitro, animal and some human studies suggest a possible association between perioperative opioid use and inferior oncologic outcomes. Research is ongoing to further understand this association.[70-72]
   g. The risk-to-benefit ratio does not support the use of opioids if viable alternatives are available. Nonopioid analgesics, including acetaminophen (APAP) and nonsteroidal anti-inflammatory drugs (NSAIDs), may be equally or more effective than opioids for the management of pain associated with some conditions.[73-77]

(TABLE 3)

Adverse Effects of Opioids[26,55]

Common Side Effects	Serious Side Effect of Chronic Opioid Use
• Nausea/vomiting • Constipation • Pruritus • Euphoria • Respiratory depression, particularly with the simultaneous use of alcohol, benzodiazepines, antihistamines, muscle relaxants or barbiturates • Lightheadedness • Dry mouth	• Cardiac abnormalities, including prolonged QTc and torsades de pointes • Sudden cardiac death with the concomitant use of benzodiazepines and methadone • Hormonal disruptions, including decreased testosterone in males • Decreased luteinizing hormone, follicle-stimulating hormone, and fertility in women • Musculoskeletal compromise, including an increased risk of osteoporosis • Immunosuppression • Inhibition of cellular immunity via delta and kappa receptors • Hyperalgesia (i.e., upregulation of receptors and increased tolerance) • Sleep disturbances (e.g., shortened deep sleep cycle) • Delayed or inhibited gastric emptying, increased sphincter tone, and blockade of peristalsis

SOURCE: Martin PR, Hubbard JR. Substance-related disorders. In: Ebert MH, Loosen PT, Nurcombe B: Current Diagnosis & Treatment in Psychiatry. New York: McGraw Hill; 2000:233-259.

2. When opioids are deemed a necessary part of analgesic therapy, surgeons are encouraged to use the lowest effective opioid dose for the shortest possible duration to manage pain.

a. When managing opioid-naïve patients, it is recommended that the use of perioperative opioids cease as soon as possible after surgery, as every additional day of opioid use may increase the likelihood of chronic opioid use.[78] In a study of 1,294,247 opioid-naïve patients who were prescribed an opioid for acute pain, the rate of long-term opioid use rose with every additional day of use (6% for those who took opioids for at least one day, 13.5% for those who took them for eight days or more and 29.9% for those prescribed opioids for 31 days or more).[78]

b. Higher doses of opioids are associated with a higher incidence of ORADEs, particularly overdose, in both inpatient and outpatient settings.[78,79]

c. Surgeons are advised to consider resetting default opioid doses on computerized provider order entry systems to the lowest available dose and designating the use of these agents for breakthrough pain only.

d. For patients on chronic opioid therapy (COT) prior to surgery, the goal of eliminating opioid use may be unrealistic and inappropriate. In this patient population, a return to baseline opioid use within seven to 14 days after surgery is a reasonable goal.

e. Clinicians are encouraged to frequently reassess their patients' need for opioids and adjust the dosage in accordance with healing, pain improvement and functional improvement.

Limiting Opioid Use in Surgical and Anesthesia Practice continued

3. **Surgeons are encouraged to use immediate-release opioid formulations and to avoid the initiation of long-acting or extended-release formulations for the treatment of perioperative pain.**
   a. Long-acting or extended-release opioids are indicated only for the treatment of chronic pain, OUD or opioid withdrawal. They are not recommended for the treatment of acute or intermittent symptoms.[80]
   b. Long-acting and extended-release agents are especially dangerous in opioid-naïve patients, even at recommended dosages, and are associated with an increased risk of overdose.[81]
   c. Long-acting and extended-release opioids carry a long-term risk of dependence that is nearly 4.5 times higher than that seen with immediate-release formulations.[78]
   d. For patients taking long-acting or extended-release formulations for the treatment of addiction or chronic pain, the discontinuation of these agents is discouraged; opioids are generally necessary to meet the baseline requirements of these patients in the perioperative period. **(SEE MANAGING PERIOPERATIVE PAIN IN PATIENTS ON MEDICATION FOR ADDICTION TREATMENT IN SECTION III, MULTIMODAL ANALGESIA IN SURGICAL AND ANESTHESIA PRACTICE.)**

NOTE: Opioid products with a single ingredient (e.g., oxycodone) are favored over combination formulations (e.g., oxycodone/APAP), as patients are encouraged to take nonopioid analgesics (APAP, NSAID) consistently prior to resorting to an opioid. Use of monoproducts allows APAP or NSAID to be taken preferentially and used as a first-line agent with a lower risk of supratherapeutic dosing or accidental poisoning. Combination products are indicated by asterisk (*) below.

Short-acting opioids include but are not limited to the following agents:[74]

- Hydrocodone – immediate release (IR) (e.g., Vicodin,* Lorcet,* Lortab,* Norco*)
- Hydromorphone – IR (e.g., Dilaudid)
- Morphine – IR
- Oxycodone – IR (e.g., Percocet,* Percodan,* Roxicodone)
- Oxymorphone – IR (e.g., Opana)
- Tramadol – IR (e.g., Ultracet,* Ultram)
- Tapentadol – IR (e.g., Nucynta)

It is recommended that long-acting and extended-release formulations not be newly initiated in the immediate postoperative period. Examples include but are not limited to the following agents:

- Hydrocodone – extended release (e.g., Hysingla ER, Zohydro ER)
- Fentanyl – transdermal (e.g., Duragesic)
- Methadone (e.g., Dolophine)
- Morphine – sustained release (e.g., MS Contin, Avinza, Kadian)
- Oxycodone – sustained release (e.g., OxyContin)
- Oxymorphone – extended release (e.g., Opana ER)
- Tramadol – extended release (e.g., Ultram ER)
- Tapentadol – extended release (e.g., Nucynta ER)

4. **Surgeons are encouraged to use the oral route of administration for opioids whenever possible. Intravenous (IV) opioids are best reserved for patients who cannot take medications by mouth, patients with suspected gastrointestinal malabsorption and patients for whom immediate pain control or rapid dose titration is necessary.**
   a. IV administration is associated with an increased risk of side effects, adverse events and medication errors.[82-84]
   b. In general, rapid onset medications have greater addiction potential. (Onset with IV administration is five to 10 minutes on average compared to 15-30 minutes with oral administration.)[85,86]
   c. Furthermore, the duration of action is greater with oral administration than with IV administration, which may allow for more consistent pain relief and less frequent administration.

5. **When initiating opioid therapy, surgeons are encouraged to use an opioid equivalency table or calculator to understand the relative potency of different medications; this is particularly important when switching to a new drug or changing the route of administration.**
   a. Most of the errors associated with preventable adverse drug events in hospitals occur at the ordering stage.[87]
   b. Clinicians may be unaware of the relative potencies of different opioids and their morphine-equivalent dose; such oversights can lead to inadvertent overdose.
   c. Clinicians are encouraged to use one of many available opioid equivalency tables or calculators—or consult with a pharmacist—to better understand the relative potencies of opioids, inform starting dose calculations, guide conversions between opioids and manage different routes of administration.
   d. When changing from one opioid to another, clinicians are encouraged to reduce the dose of the new opioid by at least 25-50% of the calculated equianalgesic dose to account for interindividual variability in the response to opioids as well as the possibility of incomplete cross-tolerance.
   e. Clinicians are advised to use extreme caution when performing conversions to and from methadone. A consultation with a hospital pharmacist or pain management specialist can help guide conversion decisions and calculations.

6. **When prescribing opioids, surgeons are encouraged to order a bowel regimen to prevent opioid-induced constipation.**
   a. Constipation is a very common adverse effect of opioid therapy due to decreased peristalsis caused by the activation of mu-opioid receptors in the colon.[36]
   b. Surgical patients are already prone to constipation due to their often-limited physical mobility; this risk is amplified by perioperative opioid therapy.
   c. Administration of a bowel regimen is recommended for all surgical patients receiving opioid therapy, unless diarrhea is present.
   d. Stimulant laxatives (e.g., senna, bisacodyl) are suggested as part of the bowel regimen.[36]
   e. Osmotic laxatives (e.g., polyethylene glycol, lactulose) have demonstrated efficacy for the treatment of general (not necessarily opioid-induced) constipation.[88]
   f. Due to the limited and conflicting evidence regarding their use, monotherapy with stool softeners is not suggested for opioid-induced constipation.[88]
   g. Newer agents for opioid-induced constipation, including naloxegol, methylnaltrexone, alvimopan, lubiprostone and naldemedine, are efficacious but significantly more expensive and may be considered for use when conventional therapies have failed. Subcutaneous methylnaltrexone was shown to be more efficacious than lubiprostone, naloxegol and oral methylnaltrexone for opioid-induced constipation.[89]
   h. Surgical teams are encouraged to track bowel movements during hospitalization and, if opioids are continued, upon discharge direct the patient or caregiver to do so; the bowel regimen can be modified accordingly.

7. **Surgeons are encouraged to avoid or limit the coadministration of opioids with benzodiazepines, gabapentinoids, barbiturates and other CNS depressants.[90,91]**
   a. The use of any of the above agents concurrently with opioids increases the risk of ORADEs both in and out of the hospital setting.
   b. Patients taking opioids and benzodiazepines concurrently have 10 times the risk of fatal overdose compared with patients taking opioids alone.[92]
   c. Other medications with CNS-depressant properties may also increase the risk of overdose, including nonbenzodiazepine sedative-hypnotics, muscle relaxants, sedating antidepressants, antipsychotics and antihistamines.[90,93,94]
   d. These combinations are sometimes unavoidable, as the routine discontinuation of long-standing medications is not advised given the risks of withdrawal or the worsening of an underlying condition for which these medications are prescribed. In such cases, clinicians are encouraged to carefully consider the necessity of each medication during hospitalization with input from the patient's outpatient clinicians.
   e. It is advised that new co-prescriptions with CNS depressants be avoided in the perioperative period.

8. **Surgeons are encouraged to monitor the patient's response to opioid therapy, assess for functional improvements and recognize and manage adverse effects.**
   a. A large study of hospitalized postsurgical patients found a rate of ORADEs of 10.6%. Worse outcomes included increased inpatient mortality, a greater likelihood of discharge to another care facility, prolonged lengths of stay, high hospitalization costs and an increased rate of 30-day readmission.[95]
   b. Respiratory depression is the most dangerous ORADE. Surgical teams are encouraged to identify patients for increased risk of opioid-related respiratory depression before initiating opioid therapy and assess for this complication frequently.[96] (See below, practice recommendation 6, for more detail.)
   c. Because sedation typically precedes respiratory depression, it is generally suggested that patients be evaluated after each opioid dose (10-20 minutes for IV administration and 30-60 minutes for oral administration based on the time-to-peak effect).
   d. It is not yet established whether certain patients may benefit from more intensive respiratory monitoring, such as pulse oximetry or capnography.
   e. It is recommended that pain severity and functional status be assessed daily (at minimum) during hospitalization.
   f. An improvement in reported pain severity without an improvement in function after several days of opioid therapy may prompt clinicians to reevaluate the appropriateness of ongoing opioid therapy and reconsider the patient's diagnosis and underlying source of pain.
   g. Surgeons are encouraged to consult anesthesia or pain services when managing patients with increasing opioid requirements for whom multimodal analgesic pharmacologic options have been fully implemented.
      i. Per the Joint Commission, "Access to pain specialists by consultation or referral reflects best practice in addressing patients with complex pain management needs."[96]

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Opioid Stewardship in the Preoperative Period

1. **Surgical teams are encouraged to work with patients, families and caregivers to establish realistic goals and expectations about the course of recovery.**
   a. Patient education can improve health outcomes and the patient experience.[97,98]
   b. Surgical teams are encouraged to provide patients, families and caregivers with educational resources about their surgical procedure and the anesthesia they will receive.
   c. It is suggested that surgical care teams educate patients, families and caregivers on the normal physiology of postoperative healing and emphasize that a period of rest and limited work and social responsibilities may accelerate healing and recovery.
   d. It is essential to discuss expectations with both patients and caregivers at the start of therapy to facilitate a clear understanding of how meaningful improvement will be measured postoperatively and how long opioid therapy may be required.
   e. Clinicians may educate patients, families and caregivers that improvement is best defined by recovery of function rather than scores on numerical pain scales and that improvement in pain without improvement in function is not the goal.
   f. It is recommended that patients be advised that their surgical team aims to keep their pain at a manageable level, not to render them pain-free. Patients, families and caregivers may be advised that mild pain may serve to guide a patient's level of activity. In addition, patients may be advised that overtreatment of pain may mask early indications of a surgical complication.
   g. Reassure patients that acute pain is expected to diminish as the underlying surgical condition resolves and postoperative healing progresses.

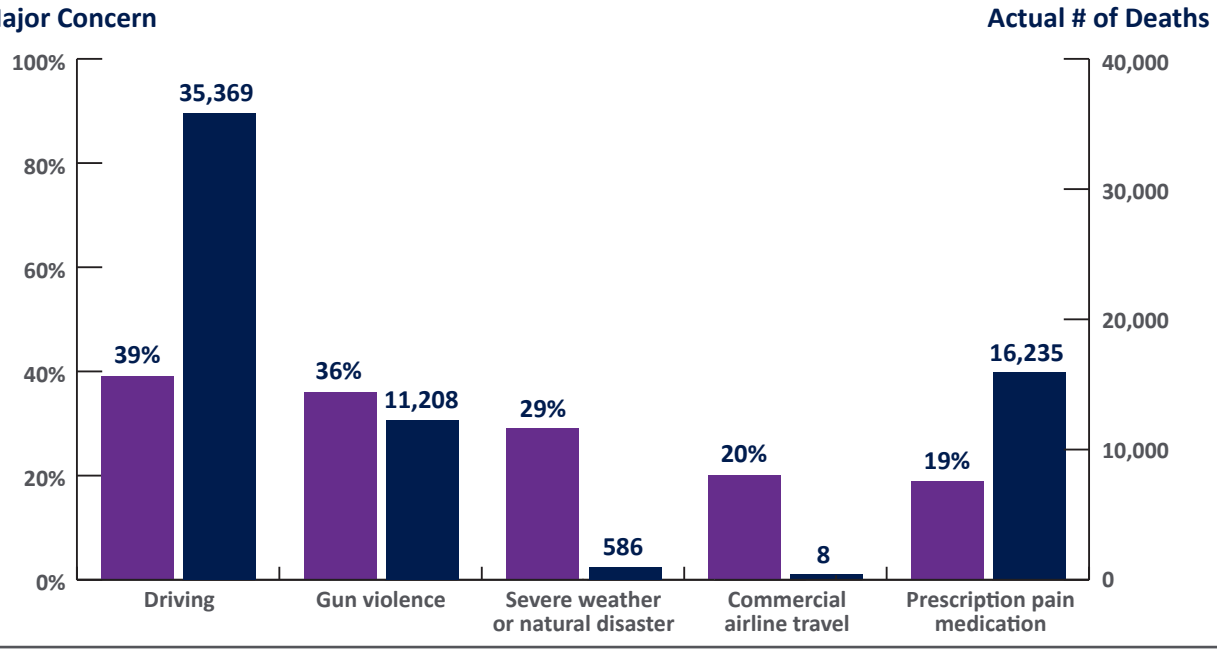
Limiting Opioid Use in Surgical and Anesthesia Practice continued

2. **Prior to surgery, it is important to discuss the role of opioids in postoperative analgesia. Surgical teams are encouraged to educate patients and caregivers about both the potential long-term risks and the immediate adverse effects of opioid therapy.**
   a. Surgical teams are encouraged to provide detailed information about the immediate adverse effects of opioids and their potential impact on surgical recovery, while emphasizing the alternative pharmacologic and nonpharmacologic multimodal analgesic options available.
   b. Patients are often unaware of the short- and long-term risks associated with opioid medications or that there may be equally effective alternatives available for postoperative analgesia.
   c. Fewer than one in five Americans consider prescription pain medication to be a serious safety threat.[99]
   d. It is important for all patients to be aware that they are at risk for opioid dependence and addiction. The National Safety Council estimates that more than half of U.S. patients have at least one risk factor for the development of OUD. A prior or family history of an SUD, current alcohol or tobacco use, chronic pain and behavioral health disorders all increase this potential; however, an opioid-naïve patient with no risk factors can still develop an OUD.[100,101]
   e. Surgical teams are encouraged to inform patients that they may request nonopioid multimodal analgesia in lieu of opioids, even for severe postoperative pain.

(FIGURE 5)

Public Perception of Opioid Risk[99]

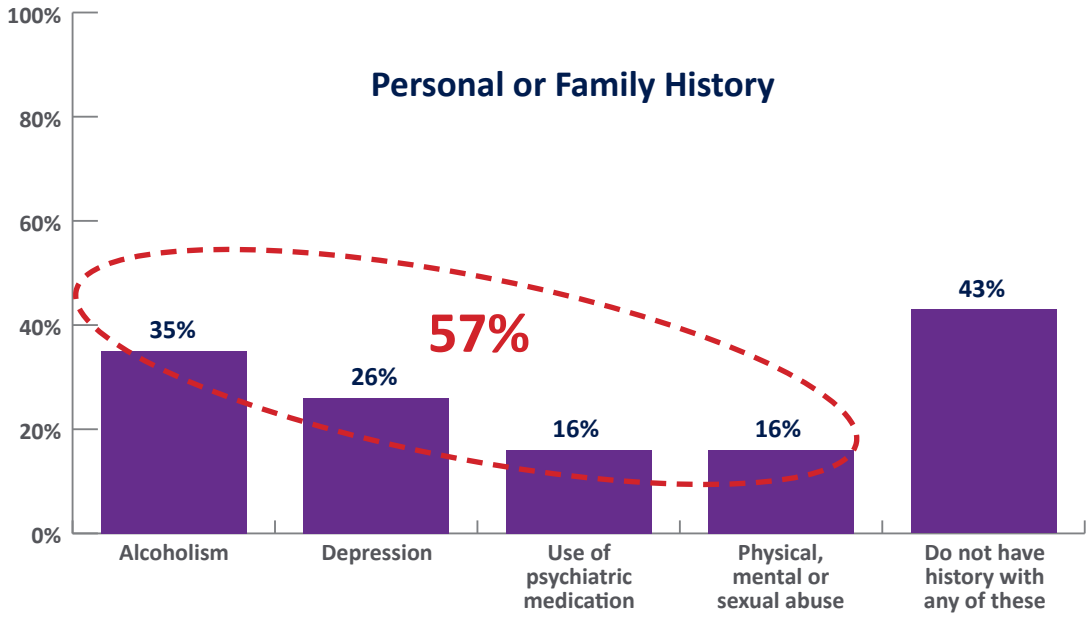
Only 1 in 5 Americans consider prescription pain medication to be a serious safety threat.



SOURCE: What Americans believe about opioid prescription painkiller use. Presented at the National Safety Council – Opioid Painkiller Media Briefing; 2015. https://www.nsc.org/Portals/0/Documents/NewsDocuments/031115-Public-Opinion-Poll.pdf. Accessed Dec. 16, 2019.

(FIGURE 6)

Percentage of U.S. Adults With at Least One Risk Factor for OUD[99]



SOURCE: What Americans believe about opioid prescription painkiller use. Presented at the: National Safety Council – Opioid Painkiller Media Briefing. https://www.nsc.org/Portals/0/Documents/NewsDocuments/031115-Public-Opinion-Poll.pdf. Accessed December 16, 2019.

3. **Surgeons are encouraged to counsel patients on the prehabilitative measures they may take to reduce postoperative pain and to accelerate recovery.[102-104] The concept of surgical prehabilitation is relatively new, and research is needed to determine precisely what medical, nutritional, physical conditioning and/or behavioral health optimization prior to surgery are most beneficial to patients.[105]**
   a. It is recommended that all patients be encouraged to stop smoking. Surgical patients may be additionally advised that smoking cessation may not only improve perioperative outcomes, but also that smoking is associated with greater postoperative pain and opioid requirements.[102,106-108] The mechanism of the association between smoking and postoperative pain is not fully understood.[109]
      i. Nicotine and carbon monoxide are responsible for the immediate perioperative risks of smoking, which include cardiopulmonary complications, wound infection, impaired wound healing and bone fusion and prolonged hospitalization.[110,111] Patients may be educated that even 24-48 hours of smoking cessation may reduce risk.[110]
      ii. Surgical teams are encouraged to prescribe their patients nicotine replacement therapy (NRT) to aid in smoking cessation prior to elective surgery. A Cochrane review found evidence that preoperative NRT and behavioral support did increase short-term smoking cessation and may reduce postoperative morbidity.[112]
      iii. Evidence does not support postoperative benefits of nicotine replacement for surgical patients.[103]

b. Heavy alcohol use (at least five drinks [>60 g ethanol] per day) is associated with poor surgical outcomes and increased postoperative pain and opioid requirements, possibly via changes to NDMA and mu-opioid receptor densities in chronic alcohol users.[113-118]
   i. A study in colorectal patients who were heavy alcohol users (without cirrhosis or clinical evidence of alcohol use) found better outcomes in patients treated disulfiram for one month prior to surgery.[119] A Cochrane review of preoperative alcohol cessation prior to elective surgery also notes lower rates of complications.[120]
      1. Surgical teams may consider referring patients who are heavy alcohol users to addiction medicine and/or behavioral health care for pharmacological strategies for relapse prophylaxis and management of alcohol withdrawal symptoms prior to elective procedures.[120]

c. Surgeons and anesthesiologists frequently encounter patients who are chronic users of dispensary cannabis. Mounting evidence indicates that cannabis is neither safe nor effective as an analgesic. In addition, anesthetic complications are frequent in chronic cannabis users. **(APPENDIX F: CANNABINOIDS: SURGICAL AND ANESTHETIC CONSIDERATIONS)**

d. Limited evidence suggests that preoperative improvements in diet and light exercise may reduce postoperative pain and analgesic requirements.[121-125]
   i. A study in patients undergoing colorectal surgery found that patients who were advised by a dietician and guided in adopting the Mediterranean diet, encouraged to walk >5,000 steps per day and to do core strength exercises, with reminders from a web-based platform, had significantly lower pain scores and half the opioid consumption of the control group.[124]

4. Surgeons are encouraged to avoid prescribing opioids to opioid-naïve patients prior to elective surgery.

a. It is suggested that opioid-naïve patients awaiting surgery who are in pain be managed with opioid-sparing multimodal analgesia whenever possible.

b. Patients who use opioids in the 30-day preoperative period are twice as likely to have persistent postsurgical opioid use.[33]

c. It is recommended that surgical patients who have received a prescription for opioid analgesics from another provider be encouraged to cease or minimize their opioid use and be educated on the risks and benefits of opioids and nonopioid analgesics.

5. When caring for patients receiving COT for pain, surgical teams are encouraged to develop a perioperative pain management plan with the patient's primary opioid prescriber.

a. As many as one in four patients report taking opioids prior to elective surgery.[126] An estimated 33-70% of patients are on COT prior to undergoing spine surgery.[127]

b. COT predisposes patients to OIH, which may significantly complicate pain control after surgery.[128]

c. Patients taking opioids prior to surgery have worse health outcomes, including longer hospital stays, increased costs, a greater need for discharge to rehabilitation facilities and more readmissions than nonopioid users.[129,130]

d. It is suggested that surgeons avoid escalating the preoperative dose of opioids when managing patients on COT.

e. It is advised that patients on COT not be routinely weaned off opioids prior to surgery. This can complicate pain control in the perioperative period.
   i. In the rare case in which a patient must be taken off opioids, it is recommended that the strategy for weaning be individualized to the needs of the patient. It is advised that tapers be gradual enough to minimize withdrawal symptoms.[131]
   ii. Slower tapers (10% per month or slower) are better tolerated, especially by patients who have used opioids for more than one year.[132-135]
   iii. Faster tapers may be appropriate for patients who have used opioids for only weeks to months. A 10% decrease in the original dose per week or slower (until 30% of the original dose is reached) followed by a weekly decrease of 10% in the remaining dose is less likely to trigger withdrawal.[132,134]
   iv. Ultra-rapid detoxification under anesthesia is dangerous and should never be trialed.

f. Surgical teams are encouraged to involve pain medicine as appropriate in the care of surgical patients receiving COT.

Limiting Opioid Use in Surgical and Anesthesia Practice continued

6. **Prior to any surgical procedure, surgical teams are advised to perform a rapid risk assessment to evaluate the patient's risk of developing OUD.[136] Consider obtaining a behavioral health evaluation, a consultation with a pain specialist and/or arranging additional psychosocial support throughout the perioperative period for high-risk patients.**
   a. Surgical clinicians are advised that no validated screening tools exist for the identification of patients at no or low risk for developing OUD. It is important to consider the potential vulnerability of every patient.
   b. Multiple agencies, including the CDC and Colorado Department of Regulatory Agencies, advocate for using an opioid risk screening instrument, such as the Opioid Risk Tool Revised (ORT-R), the Screener and Opioid Assessment for Patients with Pain (SOAPP-R) or the validated shortened version, SOAPP-8, to evaluate for factors that might predispose patients to opioid misuse and addiction **(SEE APPENDIX B)**.[137,138] While these tools have only been validated for patients with chronic pain, such screening instruments may help surgeons identify patients who are at elevated risk for opioid misuse and addiction.[139]
   c. The principles and techniques of motivational interviewing can be effective tools when engaging with patients with SUD. More information about motivational interviewing can be accessed at https://www.integration.samhsa.gov/clinical-practice/motivational-interviewing
   d. Those with a history of SUD, pain disorders and/or non-SUD behavioral health disorders appear to have the highest relative risk for developing OUD. Notably, only the absence of a mood disorder is associated with a reduced risk of developing OUD.[140]
   e. High-risk criteria for persistent opioid use after surgery include:[141,142]
      i. Personal or family history of any SUD (e.g., alcohol, illicit drugs, prescription drugs)[142-144]
      ii. Current tobacco use[34,141]
      iii. History of any pain disorder[33,143,144]
      iv. Preoperative opioid, benzodiazepine or antidepressant therapy[144]
      v. History of a behavioral health disorder, including mood and anxiety disorders, personality disorders, somatoform disorders and psychotic disorders[33,140]
      vi. Lower income[145]
   f. The risk of developing persistent opioid use after a surgical procedure appears to depend on patient characteristics more than on the type or magnitude of the surgical procedure.[37]
   g. Age is not a strong predictor for the later development of OUD. While some research finds that patients aged 16-30 years and those older than 50 years may be at greater risk, others contradict these findings.[37]
   h. No patient should be denied adequate perioperative analgesia due to concerns about their potential for addiction. Opioids may be cautiously administered even to patients determined to be at increased risk for OUD.
      i. Consider maximizing the use of multimodal analgesia to reduce opioid exposure.
      ii. Consider involving pain services and anesthesia to maximize the use of opioid-sparing medications and regional analgesia.

7. **Prior to prescribing an opioid, surgeons are encouraged to perform a risk assessment to screen for factors that may increase the risk of ORADEs.[136]**
   a. Between 10-13% of patients experience ORADEs after surgery.[27] Patients with ORADEs are estimated to have a 55% longer length of stay, 47% higher cost of care, 36% increased risk of 30-day readmission and 3.4 times higher risk of inpatient mortality than those who did not.[35,95]
   b. Opioid-induced respiratory depression (OIRD) and opioid-induced unintended advancing sedation (OIUAS) have been estimated to occur in between 0.003-4.2% of hospitalized patients who receive systemic or neuraxial opioids and may cause hypoxic and anoxic brain injury and/or death.[146]
   c. Surgeons are advised to consider comorbid health conditions and aspects of the procedure and environment that increase risk of OIUAS and OIRD and exercise caution when prescribing opioids to those at increased risk for adverse drug reactions and accidental overdose.[146]
   d. High-risk medical comorbidities include:
      i. Pulmonary comorbidities (e.g., chronic obstructive pulmonary disease, obstructive or central sleep apnea)
      ii. Cardiac comorbidities (e.g., congestive heart failure)
      iii. Organ dysfunction (e.g., renal or hepatic failure)
      iv. Obesity (BMI≥30 kg/m2)
      v. Obesity hypoventilation syndrome

e. Other patient factors include:[1]
   i. Age greater than 65 years
   ii. Male sex
   iii. Current or past smoker and/or preoperative need for supplemental oxygen
   iv. History of difficult-to-control postoperative pain or over-sedation with opioids
   v. Presurgical opioid use, opioid tolerance or high milligram morphine equivalent (MME) requirement
   vi. Current or prior SUD (including alcohol use disorder)[147,148]

f. Procedure- and treatment-related factors include:
   i. Use of general anesthesia, especially longer than six hours
   ii. Operation on the airway, head, neck, thorax or upper abdomen
   iii. Use of continuous opioid infusion (i.e., IV PCA with basal rate)
   iv. Concurrent use of other sedating agents[147,148]
   v. History or current OIUAS or OIRD (i.e., in a post-anesthesia care unit)
   vi. History of previous use of naloxone

8. Surgical teams are encouraged to assess patients for the risk of difficult-to-control postsurgical pain and consider the early involvement of pain and behavioral health services as appropriate. Behavioral health conditions, acute preoperative anxiety, catastrophizing, a history of chronic pain, severe preoperative pain and/or preoperative opioid use may increase the likelihood of difficult-to-control postoperative pain (FIGURE 7).[108,149-151]

a. Patients on COT or MAT are at increased risk of heightened postoperative pain.[152] **(SEE SECTION III, MULTIMODAL ANALGESIA IN SURGICAL AND ANESTHESIA PRACTICE, "MANAGING PERIOPERATIVE PAIN IN PATIENTS ON MEDICATION FOR ADDICTION TREATMENT.")**

b. It is recommended that patients with known or suspected untreated SUDs (including alcohol use disorder and cannabis use disorder) be referred to addiction medicine and/or behavioral health care when available and appropriate, ideally prior to surgery.

c. Patients with a prior diagnosis of chronic pain or significant preoperative pain may benefit from the close involvement of pain and behavioral health services.[106]

d. Preoperative anxiety may be a predictor of heightened postoperative pain and increased opioid consumption.[106] There is conflicting research regarding risk factors that may predispose patients to preoperative anxiety, but experts agree that perioperative anxiety is common.[153-155]
   i. Comprehensive anxiety screening tools like the Spielberger State-Trait Anxiety Inventory are lengthy, time-consuming and may not be appropriate for surgical practice. See **APPENDIX B** for easily administered behavioral health screening instruments, including:
      1. The Amsterdam Preoperative Anxiety and Information Scale[150,151]
      2. The Visual Analogue Scale for Anxiety[156]
      3. The Visual Facial Anxiety Scale
      4. The Surgical Anxiety Questionnaire[157]
   ii. It is recommended that the management of acute preoperative anxiety be tailored to the patient. Surgical teams may ask patients what type of coping assistance might be most helpful. Coping strategies include:[158]
      1. Learning more about their surgery and anesthesia via online and written resources. (Note that some patients may find that information increases their anxiety.)[158]
      2. Distraction techniques.
      3. Calming interactions with surgical team members. Patients report that even brief reassuring conversations with their surgeon or anesthesiologist can help reduce anxiety.[158]
   iii. It is advised that benzodiazepines, long the mainstay of perioperative anxiety management, be an intervention of last resort in this patient population. Other agents have been found to be equally effective and have less impact on general cognitive and psychomotor function.[159-161] Consider using gabapentinoids, clonidine or melatonin for patients with acute perioperative anxiety. (See discussion of anxiolytics below in Section III, Multimodal Analgesia in Surgical and Anesthesia Practice, Nonopioid Pharmacologic Agents for Multimodal Perioperative Pain Management.)

e. Patients who present with a catastrophizing attitude toward their condition or surgical procedure (e.g., displays of excessive worry, ruminations on actual or anticipated pain and a feeling of helplessness) may benefit from behavioral health care.[162]

9. Prior to elective surgery, it is recommended that patients be assessed for the risk of developing CPSP, a common and under-recognized complication that may increase the long-term risk of opioid use and dependence.[163,164]

a. First defined as a clinical entity in 1999,[165] CPSP has been characterized more recently as "pain persisting at least three months after surgery, that was not present before surgery, or that had different characteristics or increased intensity from preoperative pain, localized to the surgical site or a referred area, and other possible causes of the pain were excluded (e.g., cancer recurrence, infection)."[166]

b. Although the rate of CPSP varies widely across procedures, an estimated 500,000 patients experience persistent postsurgical pain every year. More than 50% of those undergoing certain procedures will go on to develop CPSP.[167-169]

c. The etiology of chronic surgical pain is not fully understood, and large-scale prospective studies with detailed pre-, intra- and postoperative multifactorial assessments are needed to elucidate the causes, treatments and prognosis of CPSP.[59]

d. While the benefits of pre-emptive analgesia have not been demonstrated consistently, severe postoperative pain has been identified as a risk factor for CPSP. Although the data is conflicting, other potential risk factors for CPSP include:

i. Duration of surgery[171]
ii. Female sex
iii. Genetic factors
iv. Obesity
v. Preexisting pain in any location
vi. Psychological factors (anxiety or depression)
vii. Younger age
viii. Tobacco use

(TABLE 4)

Incidence of Chronic Postsurgical Pain[170]

Incidence of CPSP, severe CPSP, and proportion of neuropathic pain in CPSP

Type of surgery	Incidence of all CPSP	Incidence of severe CPSP (>5/10 of 10/10)	Proportion of neuropatic pain pain in CPSP
Amputation	30% - 85%	5% - 10%	80%
Caesarean delivery	6% - 55%	5% - 10%	50%
Cholecystectomy	3% - 50%	Not reported	Not reported
Coronary bypass	30% - 50%	5% - 10%	Not reported
Craniotomy	7% - 30%	25%	Not reported
Dental surgery	5% - 13%	Not reported	Not reported
Hip arthroplasty	27%	6%	Not reported
Inguinal herniotomy	5% - 63%	2% - 4%	80%
Knee arthroplasty	13% - 44%	15%	6%
Melanoma resection	9%	Not reported	Not reported
Mastectomy	11% - 57%	5% - 10%	65%
Sternotomy	7% - 17%	Not reported	Not reported
Thoracotomy	5% - 65%	10%	45%

SOURCE: Schug SA, Bruce J. Risk stratification for the development of chronic postsurgical pain. PAIN Rep. 2017;2(6):e627. doi:10.1097/PR9.0000000000000627

e. While no validated screening protocol exists, Appendix B includes a tool that can help identify those at elevated risk of developing CPSP with a reported sensitivity of 60% and a specificity of 83%.
   i. Preventive strategies are encouraged for patients at high risk of developing CPSP, including modified surgical techniques, multimodal pain control throughout the perioperative period, and interventions focused on psychosocial and cognitive behavioral risk factors.[59]
   ii. Limited evidence suggests that use of amine reuptake inhibitors, gabapentinoids, topical lidocaine and/or capsaicin, ketamine, clonidine and/or intraoperative use of lidocaine infusion may reduce the incidence of CPSP.[59] (See Multimodal Analgesia for details.)
   iii. For patients at high risk of CPSP, the early involvement of pain services is optimal.
   iv. Surgeons are encouraged to consider the likelihood a patient will experience CPSP while thoroughly explaining the risks and benefits of elective procedures, including cosmetic surgery. In some cases, it may be prudent to delay surgery until these risk factors have been addressed.

Intraoperative Practice Recommendations

1. Anesthesiologists are encouraged to minimize the intraoperative use of opioids. Where clinically feasible and appropriate, it is recommended that anesthesiologists and surgeons collaborate to maximize the use of opioid-sparing multimodal anesthetic and analgesic agents and techniques.

a. Opioid-sparing or opioid-free anesthesia (OFA) may be feasible and effective for a range of surgical procedures.[172]
   i. Minimizing the patient's exposure to opioids reduces respiratory depression, ileus, nausea, vomiting and sedation in the immediate postoperative period.
   ii. Minimizing the patient's intraoperative opioid exposure spares the μ-receptors for early postoperative analgesia by preventing the occurrence of an acute tolerance phenomenon.[173]

b. Although the intraoperative use of opioids is associated with OIH in the immediate postoperative period, the long-term implications of intraoperative opioid exposure are unknown.[174-176]

c. While there are no large studies comparing outcomes of OFA and anesthetic regimens that include an opioid, OFA has been shown to be safe and feasible in small studies and case reports, where a smoother emergence and lower-immediate postoperative pain have been reported.[177]

d. OFA may be particularly appropriate for patients with chronic obstructive pulmonary disease (COPD), obstructive sleep apnea, obesity hypoventilation syndrome, prior opioid-induced respiratory depression, those with a history of OUD and patients who request OFA.

Limiting Opioid Use in Surgical and Anesthesia Practice continued

2. **Surgeons and anesthesiologists are encouraged to use local infiltration of anesthetic and/or regional anesthesia and analgesia whenever feasible and appropriate to improve pain control and decrease opioid use.** **(SEE SECTION III, MULTIMODAL ANALGESIA IN SURGICAL AND ANESTHESIA PRACTICE, REGIONAL ANESTHESIA.)**
   a. Local and regional anesthesia and analgesia have been shown to reduce postoperative pain and opioid requirements.[178] Carefully selected local and regional techniques can be incorporated into many procedures to improve postoperative pain control.
   b. Use of regional anesthesia may reduce the risk of CPSP after some procedures.[178,179]
   c. Local and regional anesthesia and analgesia encompass a variety of procedures including neuraxial epidural or spinal anesthesia/analgesia, peripheral nerve and plane blocks and single-injection or continuous wound infusion (CWI) with local anesthetic.
      i. When feasible and clinically appropriate, surgical teams are encouraged to perform plane and/or nerve blocks to minimize acute perioperative analgesic requirements.
      ii. Surgeons are encouraged to instill local anesthetic agents prior to incision and/or at the time of closure. Surgeons are encouraged to use adequate volumes of local anesthetic and injection technique that maximizes the efficacy of infiltration. For some procedures, placement of a catheter for CWI may be appropriate.
      iii. For selected procedures and patients, surgeons may consider the instillation of local anesthetic into the peritoneal cavity.
      iv. When a longer duration of action is required, consider using liposomal bupivacaine for wound infiltration and field or regional blocks in those surgical populations with supporting evidence. (See Nonopioid Pharmacologic Agents for Use in Perioperative Multimodal Analgesia for further discussion of the current evidence surrounding use of liposomal bupivacaine.) The cost-benefit ratio of liposomal bupivacaine in comparison to other standard therapies (such as bupivacaine) must be considered.

3. **Surgeons and anesthesiologists are encouraged to follow enhanced recovery protocols (ERP), which have been found to reduce opioid requirements across a range of surgical procedures. Hospitals and surgical facilities may consider the broad adoption of ERPs for common surgical procedures.**
   a. ERPs aim to minimize the physiological stress associated with surgery and hasten postoperative recovery through the use of evidence-based measures.[180] Pioneered in colorectal procedures, these protocols have been shown to improve outcomes in many surgical procedures, reduce opioid requirements, shorten recovery times and reduce complications.[180,181]
   b. The four pillars of enhanced recovery: early mobility, optimized nutrition and early enteral feeding, multimodal nonnarcotic analgesia and goal-directed fluid therapy work synergistically to counteract the physiological impact of surgical interventions.
   c. Comprehensive ERPs result in less painful recoveries and lower opioid requirements due to the reduced physiological stress of surgery they produce.[182]
   d. While ERPs require significant changes to institutional practice patterns and the coordinated involvement of all surgical team disciplines, they have been repeatedly demonstrated to decrease lengths of stay and reduce costs.[180,183-187]
   e. For full enhanced recovery after surgery (ERAS) guidelines for many common procedures, visit:
      i. ERAS Society
      ii. ERAS USA

(TABLE 5)

Key Elements of Enhanced Recovery Protocols[188]

Active Patient Involvement

Pre-operative	Intra-operative	Post-operative
Pre-admission education	Active warming	Early oral nutrition
Early discharge planning	Opioid-sparing technique	Early ambulation
Reduced fasting duration	Surgical techniques	Early catheter removal
Carbohydrate loading	Avoidance of prophylactic NG tubes & drains	Use of chewing gum
No/selective bowel prep		Defined discharge criteria
Venous thromboembolism prophylaxis	Goal directed peri-operative fluid management	
Antibiotic prophylaxis	Pain & nausea management	
Pre-warming		
Audit of compliance & outcomes		
Whole Team Involvement		

SOURCE: Pędziwiatr M, Mavrikis J, Witowski J, et al. Current status of enhanced recovery after surgery (ERAS) protocol in gastrointestinal surgery. Med Oncol. 2018;35(6):95. Published 2018 May 9. doi:10.1007/s12032-018-1153-0

4. **Surgeons are encouraged to employ surgical techniques that minimize tissue damage and inflammation.**
   a. Minimally invasive techniques result in less postoperative pain and lower opioid requirements.
   b. Surgeons are encouraged to preserve nerves whenever possible.
   c. A trial of appropriate conservative measures is recommended prior to considering surgical interventions for the treatment of pain. If surgery is warranted, care must be taken to ensure that the procedure has a high likelihood of success and is well supported in the literature.
   d. Per the American College of Surgeons, "No operation should be performed without suitable justification. It is the surgeon's responsibility to perform a careful evaluation, including consultation with others when appropriate, and to recommend surgery only when it is the best method of treatment for the patient's problem."[189]

(TABLE 6)

Surgical Techniques to Reduce Postoperative Pain[167]

Procedure	Safer Approach
Abdominal Hysterectomy	Laparascopic vaginal approach
Colonic Resection	Gasless laparoscopic technique
Hernia Repair	Laparscopic vs open approach. Lightweight mesh causes less inflammation. International guidelines to prevent postoperative chronic pain recommend identifying and preserving all three inguinal nerves during open inguinal hernia repair to reduce the risk of chronic groin pain. Likewise, elective resection of a suspected injured nerve was recommended.[a]
Laparoscopic Cholecystectomy	Low pressure CO_2 pneumoperitoneum. Laparscopic less pain than open cholecystectomy.
Breast Surgery	Preserve intercostal-brachial nerve. Sentinel lymph node biopsy vs axillary dissection.
Thoracotomy	Intracostal sutures associated with less pain than pericostal sutures. Minimally invasive surgery spares the intercoastal nerve.
Total Hip Arthroplasty	Avoid or minimize drains (more pain, infection).
Total Knee Arthroplasty	Relase tourniquet before sutures and bandages placed at end (decreased VAS pain scores).[b]

VAS, visual analog scale

[a] *Based on Alfieri S, et al.* Hernia. *2011;15(3):239-249.*

[b] *Based on Gray A, et al.* Br J Anaesth. *2005;94(6):710-714.*

SOURCE: Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. The Lancet. 2006;367(9522):1618-1625. doi:10.1016/S0140-6736(06)68700-X

Limiting Opioid Use in Surgical and Anesthesia Practice continued

Postoperative Hospital Pain Management

1. **Surgical teams are encouraged to take advantage of the synergistic benefits of multimodal analgesia to minimize opioid use and improve pain management. It is recommended that opioid monotherapy for the control of postsurgical pain rarely, if ever, be used as it provides suboptimal relief and increases the likelihood of complications.[190]**
   a. It is recommended that multimodal analgesia be offered to every surgical patient who reports pain.
   b. Multimodal analgesia can reduce opioid requirements and provides more effective pain control than opioid monotherapy.[191-193]
   c. Although the perioperative use of multimodal anesthesia is recommended by numerous medical societies, adoption of this practice varies widely among institutions. While virtually every surgical patient in the United States receives opioid analgesia, the likelihood of receiving a single nonopioid analgesic after surgery ranges from 43-99% depending on the institution, and the likelihood of receiving two nonopioid agents ranges from 8-92%.[194]
   d. It is recommended that opioids be ordered pro re nata (PRN) to avoid over-sedation and unnecessary administration.
   e. When opioids are ordered, surgical clinicians are encouraged to pair PRN opioids with scheduled nonopioid analgesics.
   f. Unless clinically contraindicated, it is suggested that all surgical patients receive scheduled doses of APAP and an NSAID, which have been demonstrated to lessen postoperative pain and reduce postoperative opioid use across a wide range of surgical procedures.[195-202]
   g. Clinicians are encouraged to order opioid and nonopioid medications separately so as to avoid exceeding the maximum recommended dose of nonopioid analgesics contained in combination products (e.g., hydrocodone/APAP). **(SEE SECTION III, MULTIMODAL ANALGESIC AGENTS, FOR DESCRIPTIONS OF OTHER PERIOPERATIVE ANALGESIC AGENTS.)**

2. **Nonpharmacologic options can be used concomitantly with pharmacologic options for the treatment of pain. Although few rigorous studies have proven or quantified the benefits of nonpharmacologic, non-procedure-based therapies for the management of surgical pain, such therapies carry little or no risk, may have analgesic benefits, give patients increased control over their perioperative course and can be safely adopted. (See Multimodal Analgesia below.)**
   a. The Joint Commission requires hospitals to offer nonpharmacologic strategies, "including but not limited to: physical modalities (for example, acupuncture therapy, chiropractic therapy, osteopathic manipulative treatment, massage therapy, and physical therapy), relaxation therapy, and cognitive behavioral therapy."[96]
   b. Whenever possible, surgical units are encouraged to offer distraction methods and comfort items, such as books, movies, music, games and massagers.
   c. Simple nonpharmacologic therapies available to patients in nearly any hospital setting include cold and hot packs, therapeutic mobility, positional adjustments, music therapy, chaplain or social worker visits and physical therapy.
   d. Education in mindfulness, guided imagery, relaxation and related psychological techniques may be helpful to receptive patients.[203]
   e. It is suggested that cognitive and behavioral therapies delivered by trained personnel be offered to those at elevated risk for opioid dependence and/or CPSP.

Limiting Opioid Use in Surgical and Anesthesia Practice continued

3. Surgical teams are encouraged to supplement numerical rating scales of pain intensity with functional assessments of pain. It is advised that the dosage and type of opioid prescribed not hinge solely on a patient's numerical estimation of pain intensity.[204]

a. In addition to subjective reports of pain intensity, it is suggested that safe, effective opioid dosing be based on a careful assessment of multiple objective measures, including the patient's age, comorbidities, sedation level, respiratory status, concurrent sedating medications and previous response to opioids.

b. It is recommended that the practice of prescribing specific doses of opioids based solely on a numerical pain intensity scale be avoided.
   i. Compliance with numerical rating scales has not been shown to improve pain control or patient outcomes.[205-209]
   ii. The incidence of over-sedation with opioids more than doubled following the use of an acute pain treatment algorithm guided by a numerical pain rating scale.[210]
   iii. Patient reports of pain intensity are subjective and may be unreliable.[208]
   iv. Administering opioid analgesics based solely on the intensity of a patient's discomfort can result in both the overtreatment and undertreatment of pain.[209,211]

c. There is no correlation between a given pain intensity score and an effective opioid dose.[212]

d. Ideally, pain assessment also takes into consideration the patient's ability to sleep, ambulate, resume the activities of daily life and participate in physical therapy. **TABLE 8** provides two examples of pain assessment tools that incorporate functional parameters.[204,213,214]
   i. Patients prefer assessments that consider the impact of pain on function.[204,213,214]
   ii. While adoption of pain assessments that evaluate function may require additional involvement and education of nursing staff, nurses reported preferring the Functional Pain Scale **(TABLE 8)** to one-dimensional pain intensity rating systems.[204]
   iii. The American Society of Pain Management Nursing finds that pain intensity alone is inadequate to guide therapy.[215]

e. It is advised that pain severity and functional status be assessed regularly, and analgesia adjusted appropriately.[96]
   i. Pain management approaches that are individualized to the patient may decrease pain and reduce opioid exposure.

f. It is recommended that an improvement in pain severity without an improvement in function after several days of opioid therapy prompt an evaluation of ongoing treatment and a reassessment of the patient's underlying etiology.

(TABLE 7)

Sample Pain Assessment Tools: The Clinically Aligned Pain Assessment (CAPA)[204]

Domain	Response
Comfort	Intolerable
	Tolerable with discomfort
	Comfortably manageable
	Negligible pain
Change in pain	Getting worse
	About the same
	Getting better
Pain control	Inadequate pain control
	Partially effective
	Fully effective
Functioning	Cannot do anything because of pain
	Pain keeps me from doing most of what I need to do
	Can do most things, but pain gets in the way of some
	Can do everything I need to
Sleep	Awake with pain most of the night
	Awake with occasional pain
	Normal sleep

CAPA is designed to assess pain more effectively, in a clinically valid way, and to have more dialog with the patient about their pain experience. Printed with permission, University of Utah Hospital and Clinics/Department of Anesthesiology. CAPA, Clinically Aligned Pain Assessment [43].

SOURCE: Gordon DB. Acute pain assessment tools: let us move beyond simple pain ratings. Curr Opin Anesthesiol. 2015;28(5):565-569. doi:10.1097/ACO.0000000000000225

(FIGURE 7)

Funtional Pain Scale

Please answer the following questions to help us better understand your level of comfort.

1. **Do you have pain?** YES NO If YES, circle if it is: NEW (acute) or OLD (chronic)?
2. **Location of your pain:** _____
3. **Words that describe your pain** (circle all that apply):
   Dull Aching Sharp Shooting Stabbing Cramping Burning Pins/Needles
   Throbbing Pulling Tight Tingling Numb Heavy Constant Intermittent
4. **What activities does your pain limit you from doing?** _____
   EXAMPLES: Eating, getting up to the chair, walking to the bathroom, watching TV, reading a book, having a conversation
5. **Think about how your pain limits your activity.**
   Then draw a line (or point) on the thermometer to note your level of discomfort.

YOUR LEVEL OF DISCOMFORT		YOUR ACTIVITY LEVEL
Unbearable		Unable to do any activity
Intense		Pain interferes with most activities
Distressing		
Uncomfortable		Pain interferes with some activities
None		Able to engage in any activity

SOURCE: Halm M, Bailey C, St. Pierre J, et al. Pilot Evaluation of a Functional Pain Assessment Scale. Clin Nurse Spec. 2019;33(1):12-21. doi:10.1097/NUR.0000000000000416

Management of Postoperative Pain After Discharge

1. **Surgical teams are encouraged to educate their patients about the benefits of multimodal analgesia and the risks of opioid use following discharge.**
   a. Opioid-naïve patients who receive an opioid prescription upon hospital discharge are at increased risk for chronic opioid use and/or OUD, and perioperative care teams are encouraged to educate any patient being discharged with a prescription for an opioid on their immediate and long-term adverse effects.[216] **(SEE APPENDIX A FOR PATIENT EDUCATION MATERIALS REGARDING THE SAFE USE OF OPIOIDS.)**
   b. Upon discharge, it is recommended that surgical patients be instructed to manage their pain with scheduled doses of APAP and NSAIDs, except when clinically contraindicated. **(SEE APPENDIX A FOR PATIENT APAP/NSAID SCHEDULING AID.)**
   c. It is suggested that surgeons consider the prescription of additional nonopioid multimodal agents as appropriate. **(SEE MULTIMODAL PHARMACOLOGIC AGENTS.)**

2. **Surgeons are encouraged to prescribe the minimum quantity of opioids anticipated to be necessary upon discharge and to adopt standard prescribing practices for common procedures. TABLE 9 provides procedure-specific guidelines for opioid prescription following common surgeries.**
   a. Recent studies document the over-prescription of opioids across every surgical subspecialty and reveal a wide variability in individual prescribing practices.[52,217]
   b. Pain management plans that are individualized to the patient may reduce opioid exposure. It is recommended that discharge opioid prescribing take into account each patient's:
      i. Inpatient opioid requirements
      ii. Level of pain and function prior to discharge
      iii. Medical comorbidities
      iv. Risk factors for OUD and ORADEs
      v. Preferences surrounding opioid analgesia
   c. It is suggested that patients who required no opioids in the 24 hours prior to discharge not be discharged with a prescription for an opioid.[55]
   d. If breakthrough pain is a concern, surgeons may consider writing a prescription for a small quantity of opioids (i.e., a quantity sufficient to provide coverage for one or two days until the patient can be reasonably evaluated in clinic), with instructions to fill it only if necessary.
   e. Surgical practices and hospitals can consider adopting standardized opioid prescribing ranges as part of their opioid stewardship and quality improvement initiatives.
   f. Outpatient prescriptions of more than 700 MMEs are associated with an increased risk of chronic opioid use.[78]
   g. Prescribing a subsequent fill of an opioid prescription is associated with a one in seven chance of persistent opioid use one year later.[78] Prescribing a subsequent fill of a postoperative opioid prescription is associated with a 44% increase in the likelihood of persistent opioid use.[218]
      i. It is suggested that any subsequent fill of an opioid prescription prompt a discussion of the immediate- and long-term risks of opioid therapy.
      ii. It is recommended that subsequent fills of opioid prescriptions be limited to a short duration.
   h. Colorado Senate Bill (SB) 18-022, Clinical Practice for Opioid Prescribing, limits the duration of first-time opioid prescriptions for acute, noncancer pain to seven days, with the ability to add a discretionary second seven-day fill.[219]
   i. Note that this limit does not apply to patients with "postsurgical pain that, because of the nature of the procedure, is expected to last more than 14 days."[219]

(TABLE 8)

Suggested Ranges For Discharge Quantity of Opioids Following Common Surgical Procedures[54-56]

	Johns Hopkins University	Dartmouth	Michigan OPEN	CO's CURE
Laparoscopic cholecystectomy	0-10*	0-15*	0-10*	0-10*
Open cholecystectomy			0-15	0-15
Laparoscopic inguinal hernia (IH), unilateral	0-15	0-15	0-10	0-10
Open IH, unilateral	0-10	0-15	0-10	0-10
Open umbilical hernia	0-15		0-10	0-10
Appendectomy (open or laparoscopic)			0-10	0-10
Laparoscopic Colectomy			0-10	0-10
Open Colectomy			0-15	0-15
Ileostomy/colostomy creation (re-siting or closure)			0-15	0-15
Open small bowel resection or enterolysis			0-20	0-20
Sleeve gastrectomy			0-10	0-10
Laparoscopic antireflux (Nissen)			0-10	0-10
Laparoscopic Hysterectomy			0-15	0-15
Abdominal Hysterectomy			0-20	0-20
Breast biopsy or lumpectomy			0-5	0-5
Lumpectomy + sentinel node biopsy (SNB)			0-5	0-5
Wide local excision ± SNB			0-20	0-20
Simple mastectomy ± SNB			0-20	0-20
Partial mastectomy without SNB	0-10	0-5		0-10
Partial mastectomy with SNB	0-15	0-10		0-10
Modified radical mastectomy or axillary lymph node dissection			0-30	0-30

*Numbers represent 5-mg tablets of oxycodone. Oxycodone is favored over combination oxycodone/APAP formulations, as it is recommended that patients be encouraged to take APAP independently prior to resorting to an opioid.

SOURCE: Overton HN, Hanna MN, Bruhn WE, et al. Opioid-Prescribing Guidelines for Common Surgical Procedures: An Expert Panel Consensus. J Am Coll Surg. 2018;227(4):411-418. doi:10.1016/j.jamcollsurg.2018.07.659

Hill MV, Stucke RS, Billmeier SE, Kelly JL, Barth RJ. Guideline for Discharge Opioid Prescriptions after Inpatient General Surgical Procedures. J Am Coll Surg. 2018;226(6):996-1003. doi:10.1016/j.jamcollsurg.2017.10.012

mastect\n Opioid Prescribing Engagement Network (Michigan OPEN). Prescribing Recommendations. https://michigan-open.org/prescribing-recommendations/. Published July 1, 2019.

Limiting Opioid Use in Surgical and Anesthesia Practice continued

3. Surgical groups are urged to collect, track and share individual opioid ordering and prescribing patterns among their fellow clinicians to decrease variabilities.

a. There are significant variations in prescribing practices among surgeons, even when performing identical operations **(FIGURE 8)**.[220]

b. A knowledge of current ordering patterns is critical for protocol implementation, clinician education and quality improvement.

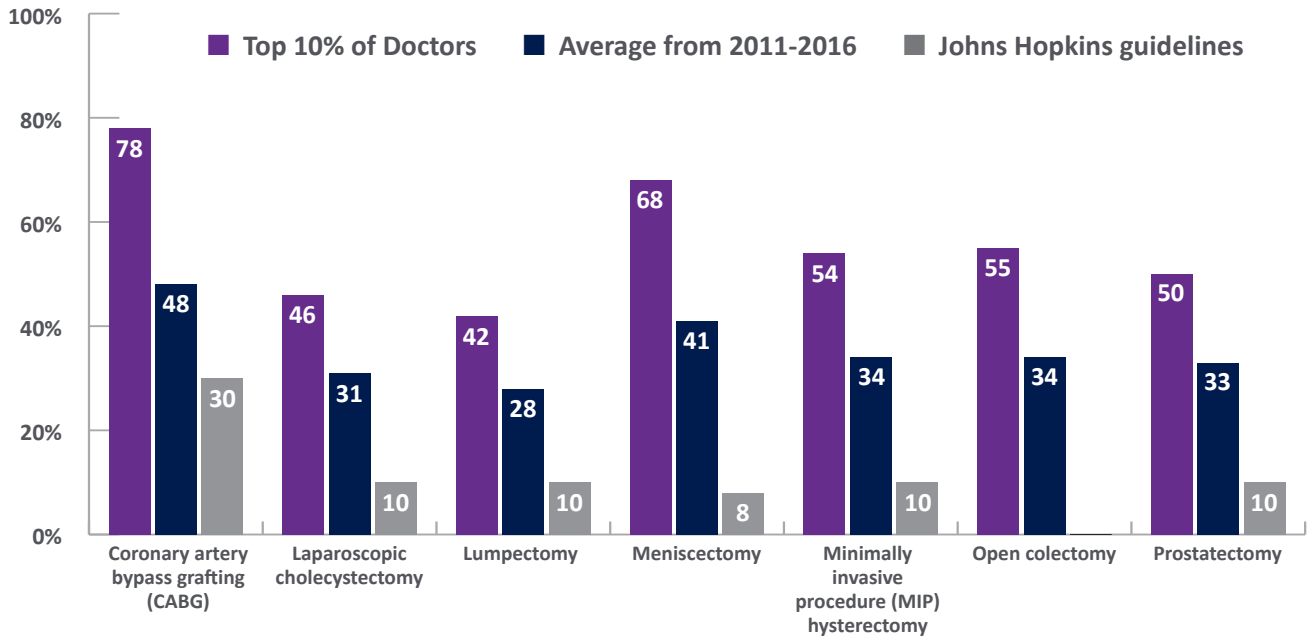
c. Tracking in-hospital opioid ordering patterns and providing comparative data to those within a practice may help reduce discrepancies and identify clinicians who can benefit from further education in multimodal analgesia.

d. It is suggested that this information not be used punitively, but rather to help clinicians understand their own treatment habits and facilitate change.

(FIGURE 8)

Average Number of Pills Prescribed for Seven Common Surgical Procedures[54]

Based on prescriptions filled by Medicare patients within one week of seven common surgical procedures



SOURCE: Overton HN, Hanna MN, Bruhn WE, et al. Opioid-Prescribing Guidelines for Common Surgical Procedures: An Expert Panel Consensus. J Am Coll Surg. 2018;227(4):411-418. doi:10.1016/j.jamcollsurg.2018.07.659

4. Surgical clinicians are encouraged to consult the Prescription Drug Monitoring Program (PDMP) to assess for possible prescription drug misuse or diversion prior to prescribing opioids.

a. The Drug Enforcement Administration (DEA) requires all practicing physicians to create an account with the Colorado PDMP.[221]

i. Colorado SB 18-022, Clinical Practice for Opioid Prescribing, limits first-time opioid prescriptions for acute, noncancer pain to seven days, with the option to add a discretionary second seven-day fill. Prescribers must check the PDMP prior to prescribing a subsequent fill of an opioid.[219]

ii. It is important to understand that 2018 Colorado SB 18-022, Clinical Practice for Opioid Prescribing, outlines exceptions to this seven-day limit, including postsurgical pain that is expected to last more than 14 days.

iii. It is recommended that providers not refuse to provide appropriate care to patients who require opioid analgesia out of misconceptions of Colorado law.

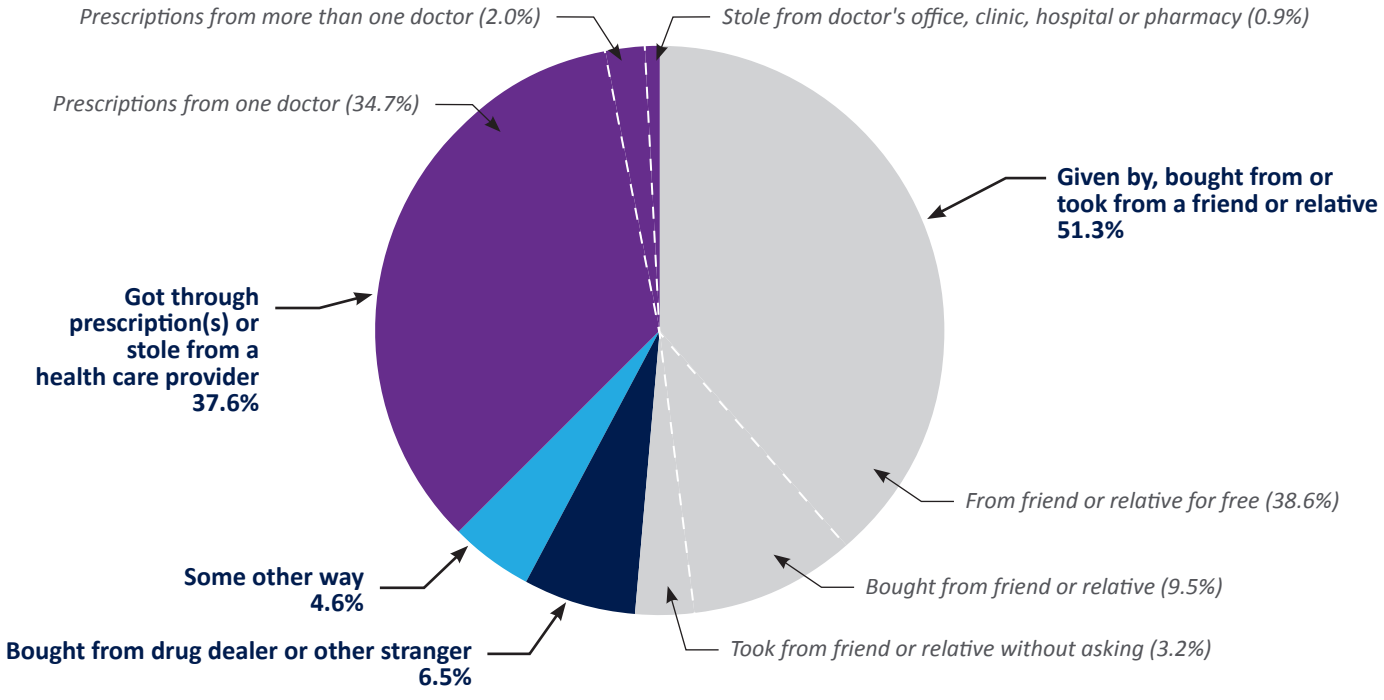
b. Drug monitoring programs have been shown to influence opioid prescribing practices, especially in cases of lost or long-term prescriptions.[222]
c. These programs can help clinicians identify patients with multiple recent prescriptions from various clinicians (i.e., "doctor shopping") and help spot those who are already using other controlled medications on a chronic basis.[223]
d. Although there is limited data to indicate the impact of PDMPs on patient outcomes, these programs can prompt referral to support services, the initiation of MAT and/or consultation with a pain management or addiction specialist.
e. Along with information gathered from PDMPs, it is suggested that concerns about possible misuse of controlled substances or the presence of SUD prompt further conversations between the physician and patient.
f. It is advised that information from PDMPs not preclude the use of opioids for the treatment of perioperative pain, but rather be incorporated into the analysis of the risks and benefits of opioid therapy.

5. It is recommended that all patients who receive prescriptions for opioids be educated on the dangers that unsecured opioids pose to others, safe storage methods and the proper disposal of unused medications.

a. More than 50% of nonmedical opioid users obtain their medication from family members or friends.[224-226]
b. Surgical clinicians are encouraged to inquire about unused opioids at postoperative office visits. Studies show that between 67-92% of patients have unused opioids after surgery, but fewer than 10% actually dispose of their unused medications.[49]

(FIGURE 9)

Where Pain Relievers Were Obtained for Most Recent Misuse among People Aged 12 or Older Who Misused Pain Relievers in the Past Year: 2018[227]



9.9 Million People Aged 12 or Older Who Misused Pain Relievers in the Past Year

NOTE: Respondents with unknown data for the source for most recent misuse or who reported some other way but did not specify a valid way were excluded.

SOURCE: SAMHSA NSDUH 2018[227]

c. The CDC recommends that prescribers discuss the risks that intentionally or unintentionally shared and diverted opioids pose to household members and other individuals. In particular, it is important to emphasize the possibility that others might experience overdose at the same or a lower dosage than was prescribed for the patient.
d. It is recommended that prescriptions be stored safely, ideally in a locked location. The diversion of opioids by adolescents poses a significant risk.
e. It is critical to dispose of unused medication promptly.
f. If disposing of medication at home, it is advised that patients be instructed to:
    i. Remove the medication from its original container and remove any labels and identifying information.
    ii. Mix the pills with something inedible (e.g., kitty litter, coffee grounds, sawdust, home cleanser, etc.).
    iii. Place the mixture in a sealable bag, empty can or other durable container that prevents leakage.
    iv. Wrap the container in newspaper or a plain brown bag to conceal its contents. Place it in a trash can on the day of collection.
    v. The U.S. Food and Drug Administration (FDA) allows opioids to be flushed down the toilet; however, more environmentally friendly disposal methods are encouraged.[228]
g. An increasing number of communities also offer prescription take-back programs. It is advised that patients be encouraged to use one of the preferred disposal locations found on www.takemedsback.org or participate in a national DEA-sponsored take-back event. More than 50% of Colorado counties provide safe disposal sites for controlled substances and the number of these facilities is rapidly increasing.
h. Additional resources include:
    - http://www.takemedsseriously.org
    - http://www.corxconsortium.org/wp-content/uploads/Safe-Disposal-Brochure.pdf
    - http://www.deadiversion.usdoj.gov/drug disposal/takeback/index.html

6. During follow-up visits, surgical teams are advised to inquire about pain control, emphasizing the importance of improvements in function and quality of life over numerical measurements of pain intensity.

a. It is suggested that assessments of postsurgical pain on follow-up clinic visits emphasize functional parameters, including the quality of sleep, ability to participate in the activities of daily life and ability to engage in physical or other therapies.
b. It is recommended that acute pain that persists longer than expected based on the patient's procedure prompt a re-evaluation of the working diagnosis and/or management approach.
c. A prescription renewal request for an opioid is associated with a nearly doubled risk of developing OUD, and it is advised that such a request prompt surgeons to have an in-person discussion with the patient regarding the dangers surrounding aberrant opioid use.[163]
d. Surgeons are encouraged to consider early consultation with and/or referral to pain and/or behavioral health clinicians for patients with postoperative pain not typical for their procedure and in the absence of surgical complications.
e. It is recommended that patients with persistent postsurgical pain without an underlying diagnosis be referred to a pain specialist who is experienced in the management of CPSP. While chronic pain is generally defined as pain that lasts longer than three months, early intervention after surgery may benefit those who are at risk of CPSP and persistent opioid use.[59,229]
    i. When managing patients without the aid of local pain medicine specialists, surgeons should consider establishing consultant relationships with pain experts at referral hospitals or telehealth centers.[230,231]
f. To prescribe additional opioids to the same patient, clinicians are required (per Colorado SB 18-022 Clinical Practice for Opioid Prescribing) to review the PDMP.[219]

7. **Surgical teams are encouraged to prescribe naloxone to patients at elevated risk for opioid overdose.** **(SEE SECTION IV, HARM REDUCTION, FOR DETAILS.)**
   a. The CDC recommends that naloxone be prescribed for any surgical patient who is discharged with an opioid prescription for more than 50 mg MME per day.
   b. CO's CURE recommends that any patient:
      i. On COT be prescribed naloxone.
      ii. With a known or suspected OUD be prescribed naloxone.
      iii. Discharged with a prescription for an opioid and any of the following conditions be prescribed naloxone:
         1. Known or suspected SUD (including alcohol use disorder).
         2. Concurrent use of benzodiazepines or other sedatives.
         3. Have rotated from one opioid to another because of increased tolerance or poor analgesic effects.
         4. A history of tobacco use, COPD, emphysema, asthma, sleep apnea, a respiratory infection or other pulmonary disease.
         5. Renal dysfunction, hepatic disease, cardiac comorbidities or HIV/AIDS.
         6. Known or suspected uncontrolled depression or taking a prescription antidepressant.
         7. Unreliable access to emergency medical services.
   c. Surgical clinicians can direct patients to BringNaloxoneHome.org for education on how to obtain and use naloxone.
   d. It is advised that surgical care teams be familiar with Colorado laws that eliminate the risk of liability when prescribing naloxone and encourage Good Samaritan overdose reporting. Passed in 2013, the Colorado State-Specific Policy Summaries Third-Party Naloxone Bill (Colorado SB 13-014) removes:
      i. Civil liability for prescriber
      ii. Criminal liability for prescriber
      iii. Civil liability for layperson administration
      iv. Criminal liability for layperson administration
   e. Colorado's Good Samaritan laws (Colorado Revised Statutes § 18-1-711 and 2016 House Bill (HB) 16-1390):
      i. Offers immunity for any Good Samaritan acting in good faith
      ii. Eliminates the risk of arrest or prosecution for drug possession
      iii. Eliminates the risk of arrest or prosecution for drug paraphernalia
      iv. Offers protection from other crimes

Policy Recommendations

1. **Improve PDMPs through interoperability and automated integration into electronic health records (EHRs).**
   a. Although the Colorado PDMP is an important tool for reducing inappropriate opioid prescribing, it is cumbersome to use and often incompatible with busy hospital workflows.
   b. Although there is no national data-sharing protocol that crosses state lines, a number of states participate in data-sharing hubs. Without data from surrounding localities, PDMPs cannot provide clinicians with full prescribing information. Access to nationwide data on opioid prescribing practices would enable clinicians to better detect aberrant patterns of opioid prescription and encourage their patients to seek treatment. Legislation is needed to establish a national PDMP and foster the broad exchange of prescribing information.
   c. Providers are required to use two separate logins to access their EHRs and PDMPs, a drawback that can make the use of PDMPs cumbersome and disruptive. Legislation that encourages the direct and automatic integration of PDMP data within EHRs would enable the seamless reconciliation of a patient's opioid prescription history with their current medications and health care needs.
   d. Automatic queries linked to hospital registration significantly increase the use of PDMPs in clinical decision making.[232] Systems that incorporate such technology are overwhelmingly favored by clinicians, 98-100% of whom report improved access.[233]

Limiting Opioid Use in Surgical and Anesthesia Practice continued

2. **Pain should not be considered the "fifth vital sign," and clinical medicine should move to de-emphasize numerical rating scales and incorporate functional assessments into pain management pathways.**
   a. Long promoted as the "fifth vital sign," pain has developed enormous leverage in the American medical lexicon. Medicine has overemphasized pain; as a result, physicians often feel pressured to prescribe opioids to normalize this "vital sign." In response, the American Medical Association (AMA) has issued a statement that pain should not be considered the fifth vital sign.[234]
   b. While a patient's discomfort is an important element of any clinical evaluation, clinicians are advised to consider it simply as one component of a global clinical assessment, along with objective measurements such as heart rate, respiratory rate and blood pressure.
   c. While surgical teams are trained to address pain scores reflexively, pain is a complex biopsychosocial phenomenon that cannot be distilled into a one-dimensional numerical target.
   d. Numerical pain scores have been shown to increase the risk of overtreatment and unintentional overdose in hospital settings.[211]
   e. Functional pain scales, which focus on a patient's ability to perform daily activities, are more clinically relevant than numerical scores and may not reflexively result in the overtreatment of pain.[213,214]

3. **Private and public insurers should provide adequate compensation for the time and expertise required for the universal adoption of appropriate screening measures (e.g., extensive history taking, review of medical records, PDMP queries, urine toxicology screenings, etc.).[235]**
   a. Patients are often reluctant to disclose information about their substance use, particularly on written or quickly administered verbal questionnaires. Obtaining an accurate substance use history may require additional clinical skill and time.
   b. Patients with SUDs may require referrals to primary care clinicians and addiction medicine, pain management and behavioral health specialists. Adequate reimbursement for coordinated care facilitates the comprehensive management of surgical patients with behavioral health needs.

4. **Private and public insurers should provide reimbursement protocols that align with nonopioid pain management initiatives and offer greater flexibility in the design of reimbursement models.[235]**
   a. Pharmacy benefit managers and payers should offer a comprehensive array of nonopioid options in their formularies and be more transparent in communicating the availability of those alternatives to clinicians.
   b. Pharmacy benefit managers and state and federal regulators should ensure that nonopioid analgesics are included on low-cost tiers.
   c. Insurers, hospital systems and government agencies should work together to improve inpatient and outpatient access to nonpharmacologic pain management modalities and evidence-based behavioral health approaches for treating chronic pain and mental health comorbidities (e.g., post-traumatic stress disorder, depression, anxiety, mood disorders, SUDs).
      i. Insurers and regulators are urged to develop reimbursement policies that support multidisciplinary, multimodal psychological and behavioral health interventions via a range of delivery methods (e.g., in-person, telehealth, internet self-management, mobile applications, group therapy, telephone counseling).

5. **State and federal agencies should expand educational outreach to clinicians and the public in safe storage and disposal of excess opioid medication and should increase opportunities for safe drug disposal.[235]**
   a. Provide streamlined processes for clinician offices, pharmacies, hospitals and other public offices to become safe disposal sites.
   b. Support medication safe disposal drop box locations in each county, so that safe disposal sites are easily accessible to Coloradans in both urban and rural areas.
   c. Maintain a database of statewide safe disposal locations to be made available to the public.
   d. Consider providing financial incentives for organizations that participate in safe disposal programs.
   e. Launch targeted statewide public health campaigns to educate the public on the importance of safe disposal and statewide locations of safe drug disposal sites.

Multimodal Analgesia in Surgical and Anesthesia Practice

c|h|a Colorado Hospital Association
COLORADO MEDICAL SOCIETY
COLORADO CONSORTIUM for Prescription Drug Abuse Prevention

Multimodal Analgesia in Surgical and Anesthesia Practice

Most surgical patients experience some degree of pain after surgery. Despite the near-universal use of short courses of opioids perioperatively, as many as 80% of patients report moderate to extreme postoperative pain.[61,62] Surgical pain is multifactorial and, depending on the procedure, may involve nociceptive pain associated with incision and surgical injury, visceral pain associated with disruption of visceral structures, neuropathic pain secondary to nerve damage or transection and the systemic inflammatory response to tissue damage. Compounding pain caused by surgery itself, many patients present with conditions that are acutely painful or have a history of chronic pain. Thus, perioperative pain is often complex and multifactorial. Despite the ubiquity of pain in surgical practice, pain is poorly understood by many medical professionals and seldom taught in medical schools, 96% of which have no dedicated pain medicine module.[236] A better understanding of pain and the interventions that can be therapeutically applied to alleviate it is among the most important aspects of better opioid stewardship and safer, effective analgesia. **APPENDIX C: UNDERSTANDING PAIN: A COMPLEX BIOPSYCHOSOCIAL PHENOMENON**, provides a brief overview of how clinicians may conceptualize pain.

Pain is best addressed by simultaneously intervening at multiple points in the physiological pathways involved in the transmission of pain signals. By selecting pharmacological agents that act on different channels, enzymes and receptors, surgeons can leverage the additive and synergistic mechanisms of analgesia provided by complementary medications to treat pain more comprehensively. At the same time, surgeons and anesthesiologists also have a powerful array of regional anesthetic and analgesic interventions at their disposal which, if used widely and consistently, have the potential to provide anatomically selective anesthesia and analgesia, further reducing the need for systemic analgesics. Evidence supporting the concomitant use of regional and nonopioid pharmacologic analgesia for acute perioperative pain is strong, and the possibility that such multimodal approaches may reduce the incidence of CPSP may additionally motivate surgical care teams to use multiple modes of pain control for all their patients.[59,167-171,179]

An obvious, common-sense approach to reducing our national reliance on opioids is to ensure that every surgical patient is offered nonopioid analgesics. Despite evidence in support of alternatives to opioids, physicians and hospitals frequently fail to offer surgical patients more than one mode of pain control. While virtually every surgical patient in the U.S. receives opioid analgesia, the likelihood of receiving a single nonopioid analgesic after surgery ranges from 43% to 99% depending on the institution, while the likelihood of receiving two nonopioid agents ranges from 8% to 92%.[194] The consistent delivery of multimodal analgesia remains an area of opportunity for reducing perioperative opioid use.

Opioid monotherapy often fails to achieve adequate analgesia and exposes patients to both increased immediate risk of ORADEs and long-term risk of dependence and addiction. For some surgical patients, scheduled APAP and an NSAID provides adequate analgesia. For others, the addition of one or more of the nonopioid therapies may reduce or eliminate perioperative opioid requirements while simultaneously improving pain control and the speed of recovery.[191-193] Appropriate use of the nonopioid therapies described below may significantly improve perioperative pain management. Surgeons and anesthesiologists who modify their clinical practices to employ more multimodal pharmacologic and nonpharmacologic approaches may deliver better, safer patient care while simultaneously protecting their communities from the harms associated with unused opioid medications.

When selecting multimodal analgesic medications and interventions, surgeons and anesthesiologists must contend with the lack of high-quality, procedure-specific evidence for many of the suggestions outlined in the pathways below.[237] Further research is urgently needed to determine the quality of evidence and strength of recommendations for many elements in these pathways. That said, the absence of conclusive findings must be weighed against the incontrovertible evidence of the immediate and long-term harms caused by an overreliance on opioid analgesia, and clinicians are encouraged to consider the relatively safe risk profiles of the many nonopioid options available. It is imperative that surgeons and anesthesiologists partner with researchers, pharmacists and nurses to define and implement safe and effective analgesic protocols that incorporate available and evolving evidence in a way that is compatible with their unique practice settings.

Multimodal Analgesia in Surgical and Anesthesia Practice continued

Practice Recommendations

1. **Surgeons and anesthesiologists are encouraged to use multimodal analgesia and adopt the following principles when managing perioperative pain:**
   a. Use nonopioid approaches as first-line therapies.
   b. Use several pharmacological agents and/or regional anesthetic/analgesic interventions for pain control rather than relying on opioid monotherapy.
   c. Use opioids primarily as rescue medications.
   d. Emphasize realistic, functional pain management goals with patients.
   e. Use empathic language when discussing pain.

2. **Prior to every surgery, surgeons and anesthesiologists are encouraged to discuss the neuraxial and regional anesthetic techniques that may be applicable to each case and the risks and benefits of each.**
   a. Surgical teams are encouraged to work together to select the modes of neuraxial anesthesia, peripheral nerve or plane blocks, single-shot blocks and/or catheter placement for CWI that are safe, effective and best suited to each patient in an effort to reduce postoperative pain and opioid consumption.
   b. Surgeons may wish to consider wound infiltration with amide anesthetics and/or, in appropriate patients, installation of intraperitoneal local anesthetic (IPLA).
   c. Collaboration between surgeons and anesthesiologists may require the restructuring of operative workflows to efficiently facilitate the wider use of regional anesthetic interventions.
   d. Ideally, a plan for altering the approach to regional anesthesia/analgesia will be in place prior to surgery in the event that a laparoscopic procedure must be converted to an open procedure.
   e. It is advised that patients be informed of the risks and benefits of regional anesthesia/analgesia and patient consent be obtained prior to surgery for the use of any appropriate regional anesthesia/analgesia in the case that such an approach becomes indicated if not initially planned.
      i. It is recommended that standard preoperative consent forms be amended to facilitate the use of any appropriate regional anesthetic and analgesic interventions.
   f. Surgical and anesthesiology teams can work with hospitals to ensure that they are credentialed and have the equipment necessary to perform these opioid-sparing procedures.

3. **Anesthesiologists are encouraged to consider the use of opioid-sparing or opioid-free anesthesia protocols when clinically appropriate.**

4. **Surgical clinicians are encouraged to consider the use of preoperative and intraoperative medications that may contribute to reduced postoperative pain and analgesic requirements and are encouraged to use nonopioid analgesics in the postoperative period.**
   a. Strongly consider concomitantly prescribing scheduled APAP and an NSAID for the treatment of perioperative pain.
      i. It is suggested that APAP be used both pre- and postoperatively for any surgical patient in whom it is not contraindicated. For lengthy procedures (> 6 hours), consider use of IV APAP to maintain schedule in patients under anesthesia or unable to take medication per os (PO) or per rectum (PR).
      ii. It is recommended that NSAIDs be strongly considered for pre- and postoperative pain management, unless contraindicated. Although NSAIDs have in the past been avoided out of surgical, renal and bleeding concerns, more recent research supports the perioperative benefits of these medications for the majority of surgical procedures.
   b. Low-dose, sub-dissociative ketamine is an effective analgesic that can be opioid-sparing during and following many different surgeries. It may be particularly beneficial for patients with chronic pain or opioid dependence.

c. IV lidocaine is an effective analgesic; it is recommended that its routine intra- and postoperative administration be supported by appropriate education and hospital policies.
d. Alpha-agonists (dexmedetomidine, clonidine), N-methyl-D-aspartate receptor (NMDA) antagonists in addition to ketamine (magnesium, dextromethorphan) and esmolol are agents that may have analgesic benefit for some patients.
e. Consider using an amine-reuptake inhibitor (e.g., duloxetine, venlafaxine) or a gabapentinoid when CPSP is anticipated or when managing patients with pre-existing chronic pain conditions. Consider coordinating with primary care or pain clinicians who can manage the ongoing use of these agents.
f. Consider the use of topical medications for pain control, including topical lidocaine and diclofenac.
g. Consider advocating for or conducting further research into pharmacological agents that have limited evidence or pre-clinical evidence supporting their potential use as analgesics.

5. **For patients whose pain may be exacerbated by significant perioperative anxiety, it may be helpful to consider prescribing an anxiolytic agent in the perioperative period, such as:**
   a. Oral or sublingual (SL) melatonin
   b. Oral clonidine
   c. Oral gabapentin
   d. The routine use of benzodiazepines in the perioperative period is NOT recommended, and surgeons are advised against discharging patients on concomitant benzodiazepines and opioids. For select patients, low and limited doses of benzodiazepines may be appropriate.

6. **Surgical clinicians are encouraged to familiarize themselves with the identification and targeted treatment of different types of perioperative pain and comorbid pain conditions.**
   a. Consider NSAIDs, APAP and glucocorticoids for somatic pain or pain with an inflammatory component.
   b. For pain with a tension or spastic component, consider muscle relaxants or antispasmodics.
   c. For pain with a neuropathic component, consider gabapentinoids and/or topical and IV lidocaine.
   d. For chronic neuropathic, musculoskeletal, or abdominal pain, consider an amine-reuptake inhibitor (e.g., duloxetine, venlafaxine).

7. **Opioids are best reserved for pain that is severe or limits function despite the use of nonopioid treatments.**
   a. When opioid analgesia is used, the concurrent receipt of opioids and nonopioid analgesics can reduce the patient's total opioid requirements and improve pain management.[152]
   b. Monoproducts of opioids, including oxycodone, hydromorphone and morphine sulfate, are preferred over combination products that contain APAP. This allows APAP to be taken preferentially and used as a first-line agent with a lower risk of supratherapeutic dosing or accidental poisoning.
   c. It is advised that opioids be tapered or discontinued as soon as possible.
   d. It is recommended that surgical patients who received no opioid analgesia in the last 24 hours of hospitalization not be discharged with a prescription for an opioid.

8. **Surgical teams are encouraged to integrate multimodal treatment strategies and pathways into their computerized physician order entry systems to facilitate the seamless adoption and safe delivery of novel medications.**

9. **Nonpharmacologic options can be used concomitantly with medications and regional anesthesia for the treatment of all types of pain.**

Multimodal Analgesia in Surgical and Anesthesia Practice continued

10. With the legalization of cannabis in Colorado, surgical patients increasingly present who are chronic cannabis users and/or who have used cannabis in the immediate preoperative period. (SEE APPENDIX F: CANNABINOIDS: SURGICAL AND ANESTHETIC CONSIDERATIONS for a detailed examination of this topic.)

a. Both recent and chronic cannabis use may alter anesthetic and analgesic requirements and effectiveness.
b. Patients may mistakenly believe that cannabinoids are effective analgesics.
c. Clinicians and patients must also be aware of the possibility of cannabis withdrawal syndrome in hospitalized patients.

11. Surgical teams are encouraged to consider the use of opioid-sparing multimodal perioperative pain management as suggested in the pain management options outlined below for:

a. Colorectal
b. Cholecystectomy
c. Appendectomy
d. Ventral abdominal wall repair
e. Inguinal herniorrhaphy
f. Mastectomy
g. Breast Biopsy, Lumpectomy +/-SLNB
h. Thoracotomy

NOTE: The principles of enhanced recovery pathways and the analgesic interventions suggested in these sample pain management pathways can be applied to surgical procedures beyond those addressed here.

Opioid-Sparing Multimodal Perioperative Pain Pathways For Common Surgical Procedures

The following recommendations are derived from existing enhanced recovery pathways, a comprehensive literature review and expert opinion, and have been reviewed by the CO's CURE editors. The clinical judgment of surgeons and anesthesiologists must always supersede suggested clinical care pathways.

The following pathways offer comprehensive lists of interventions that may be useful for improving perioperative pain management and limiting patient opioid exposure. Surgical teams are encouraged to select from these options the pharmacological and regional anesthetic interventions that are best suited to each patient and procedure. It is in no way intended that most or all of the interventions listed below be used for any one patient or procedure. For **every** patient, the risks and benefits of **every** intervention and combination of interventions must be carefully weighed in consultation with the patient and the entire surgical team. Patients undergoing minimally invasive procedures will generally require fewer, low-risk multimodal analgesic options; patients undergoing major surgeries may benefit from more extensive, possibly higher-risk, multimodal analgesic interventions. For the vast majority of patients, it is recommended that multimodal analgesic interventions be carefully selected from the sample pain pathways below in order to address pain at multiple anatomic and physiological junctures.

The interventions included in the procedure-specific lists of possible multimodal pharmacological agents and regional anesthetic and analgesic techniques below are divided into the preoperative, intraoperative, immediate postoperative and discharge time periods. They are further loosely organized into the following categories:

1. Interventions that are recommended for the majority of patients appear under the heading "Recommend" for the relevant perioperative period.
2. Interventions that may be useful additions to an opioid-sparing multimodal analgesic regimen in patients without contraindications appear under the heading "Consider."
3. Beneath the "Recommend" and "Consider" categories are additional "Consider" pain management interventions that may be relevant to patients undergoing major and/or open procedures that are anticipated to produce moderate-to-severe postoperative pain. Consider also for patients who may benefit from more comprehensive pain management regimens, including those receiving chronic opioid therapy for pain, those receiving naltrexone, buprenorphine or methadone for addiction treatment, those with a history of refractory or difficult-to-control postoperative pain and patients who request opioid-free surgery.

The pathways below are limited to considerations of pain and analgesia. Many of the recommendations for nonopioid anesthesia and analgesia presented below are derived from existing ERPs. Surgeries conducted using comprehensive enhanced recovery protocols have been demonstrated to result in reduced postoperative pain and analgesic requirements, and surgeons and anesthesiologists may consider developing and implementing full ERPs at their institutions where feasible and clinically appropriate. (**SEE LIMITING OPIOID USE IN SURGICAL AND ANESTHESIA PRACTICE** for more information on ERP.)

It is recommended that multimodal analgesic regimens be tailored to safely meet the needs of individual patients. It is also recommended that medication selection and dosages be adjusted based on patient-specific factors, including organ function, comorbidities, home medication regimens and previous medication intolerances. Several of these drugs and blocks when administered together or in combination with anesthetic drugs or opioids can contribute to perioperative bradycardia, dysrhythmias, hypotension, local anesthetic systemic toxicity, renal disease, respiratory depression, somnolence and other adverse effects. The risk of these adverse effects can be decreased by eliminating certain drug-drug combinations, giving a single dose and/or reduced dosages of certain drugs and timing the administration of certain drugs so that they do not reach peak levels simultaneously. Anesthesiologists and surgeons must understand the administration instructions, benefits and risks of each block, drug and block/drug combination, and are encouraged to consult a pharmacist for guidance regarding the use of the agents in these pathways as needed. Evidence supporting the medications recommendations below is available in Descriptions of Pharmacologic Agents Used in Multimodal Surgical Analgesia. For descriptions of the regional anesthetic blocks included in these pathways, see **TABLE 14**. Peripheral Nerve Blocks for Common Surgical Procedures.

Multimodal Analgesia in Surgical and Anesthesia Practice continued

At Preoperative Consultation:

1. Educate all patients and caregivers on reasonable postoperative expectations. It is important to emphasize that some pain following surgery is normal and that the elimination of pain can conceal valuable clinical information. Patients and caregivers may be further counseled that mild pain can be a helpful tool for moderating patient activity.
2. Families and caregivers are encouraged to take measures to ensure that the patient has adequate rest and respite from work and family obligations following surgery in order to facilitate optimal postoperative healing.
3. It is advised that patients and caregivers be educated that improvements in function are as important as improvements in pain intensity. It is important to stress that some limitations in function are to be expected following surgery and will resolve as healing progresses.
4. Involve patients and family or caregivers in the development of a pain management plan, emphasizing both the immediate and long-term risks of opioid use and the benefits of multimodal analgesia, including nonpharmacologic modalities.
5. Screen patients for elevated risk of developing OUD. Consider providing a behavioral health referral and additional psychosocial support for high-risk patients.
6. Identify and provide appropriate care for patients receiving COT or MAT and those with untreated OUD.
7. Screen patients for an elevated risk of developing CPSP. Consider the early involvement of pain medicine service and/or additional psychosocial support systems.
8. Advise patients that prehabilitation with smoking cessation, daily physical activity, increased protein intake in the week prior to surgery and a protein drink prior to surgery may speed recovery and indirectly reduce the duration and intensity of postoperative pain.

Opioid-sparing Multimodal Analgesic Pathways for Common Surgical Procedures

I. Opioid-sparing Multimodal Analgesic Pathway for Colorectal Surgeries

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO once	• COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once) • Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction[238] • Gabapentin 300-600 mg PO once OR pregabalin 75-150 mg PO once (adjust the dose for age, renal function)[239,240] • Melatonin 6 mg PO once[241-244] • Clonidine 0.1 mg PO once[245-247] • Dextromethorphan 90 mg PO once[248-250]

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.

Intraoperative Recommendations	Consider for Intraoperative Use
Operative technique: • Laparoscopic repair is associated with less postoperative pain[251-256] Operative anesthesia: • Minimize or avoid induction opioids and minimize intraoperative maintenance opioids • Infiltration of local amide anesthetic at the surgical sites[257] Pharmacologic agents: • APAP 1000 mg IV if more than 6 hours since last dose and patient cannot take PO, with a goal of administering a dose every 6 hours • Ketorolac 15 mg IV at closure, unless contraindicated or an NSAID was administered preoperatively	Operative anesthesia: • Opioid-free total intravenous anesthesia (TIVA) (e.g., propofol, dexmedetomidine, lidocaine and ketamine)[285] Regional anesthesia, consider[258-260] • Transversus abdominis plane (TAP) block (single shot or continuous infusion) • Quadratus lumborum (QL2 or TQL) block[261] • Erector spinae block[262] • Rectus sheath block[263] • Consider the use of liposomal bupivacaine for incisional and/or regional analgesia[264,265] • Consider instillation of intraperitoneal local anesthetic (IPLA)[266,267] Pharmacologic agents: • Lidocaine 1.5 mg/kg IV bolus (max dose 150 mg) +/- 1-3 mg/kg/hr IV infusion[268-271] • It is recommended that infusion be stopped if and when liposomal bupivacaine is administered • Esmolol loading dose of 0.5 mg/kg IV bolus over one minute followed by 0.01-0.05 mg/kg/min IV infusion[272,273] • Magnesium sulfate 30-50 mg/kg IV bolus followed by 6-20 mg/kg/hr IV infusion OR 4 gm IV given over 30-60 minutes at the close of case[274-277]

I. Opioid-sparing Multimodal Analgesic Pathway for Colorectal Surgeries *continued*

Consider for Intraoperative Use

For major open colorectal surgeries or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:
- Ketamine 0.1-0.3 mg/kg IV bolus once pre-incision +/- ketamine 0.1-0.3 mg/kg/hr IV infusion[278-281]
- Dexmedetomidine 0.8-1 mcg/kg IV bolus + 0.2-0.8 mcg/kg/hr IV infusion[245,282-286]
- Catheter placement for continuous wound infusions with amide anesthetic

Regional analgesia:
- Neuraxial analgesia: spinal, thoracic epidural anesthesia (TEA) or combined spinal and epidural anesthesia (CSEA)[287]
- For patients with thoracic epidural, consider administering a bolus prior to incision and/or running an infusion intraoperatively

Postoperative Recommendations	Consider for Postoperative Use

• APAP 1 g PO every 6-8 hours until pain is resolved. Use IV APAP only for patients in whom oral and PR administration are contraindicated ***PLUS***
• Nonpharmacological interventions
	• Ketorolac 15 mg IV every 6 hours for 24-48 hours followed by
	  - NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR***
	  - COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved
	• Gabapentin 300-600 mg PO 1 to 3 times daily ***OR*** pregabalin 75-150 mg PO 1 to 2 times daily (adjust for age, renal function)[288]
	• Lidocaine 1-2 mg/kg/hr IV infusion[268-271]
	  - Avoid if liposomal bupivacaine used or continuous wound infusion continued
	• Dextromethorphan 40 mg PO 3 times per day for 2 days[248-250]
	• Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches)

For major open colorectal procedures or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:
- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion for 24-48 hours[278-281]
- Dexmedetomidine 0.2-0.8 mcg/kg/hr IV infusion for up to 24 hours[245,282-284]
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if liposomal bupivacaine or other forms of wound infusion or epidural amide anesthetic are continued)

Regional analgesia:
- Continuous wound infusion with amide anesthetic
- Continued epidural adjunctive analgesia

I. Opioid-sparing Multimodal Analgesic Pathway for Colorectal Surgeries *continued*

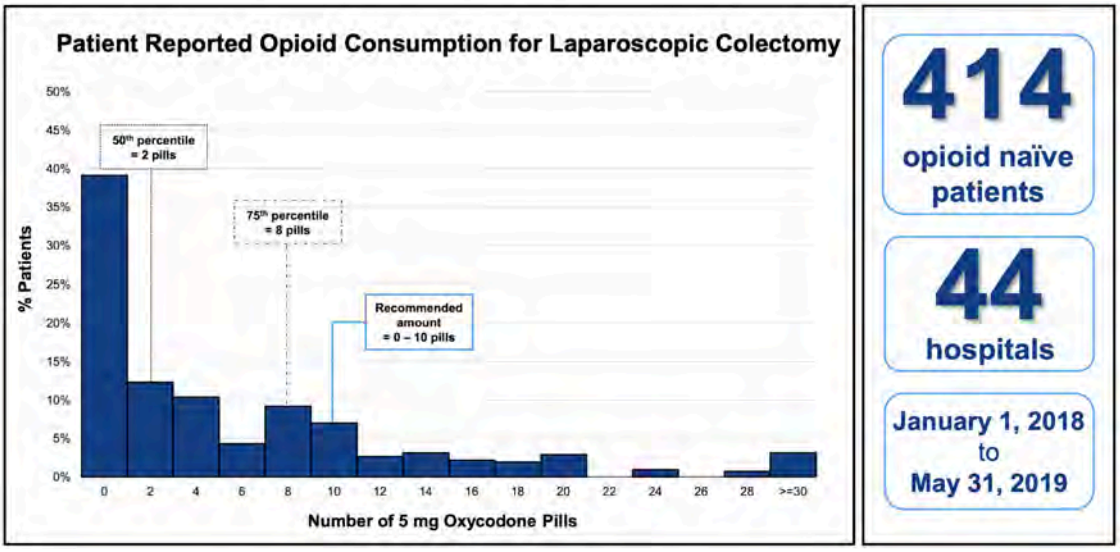
It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia, that patients receiving opioid therapy be maintained on multimodal analgesic agents as clinically appropriate and that opioid monotherapy be avoided.

Initiate opioid treatment with:
- Oxycodone IR 2.5-10 mg PO every 4 to 6 hours as needed ***OR***
- Morphine IR 5-20 mg PO every 4 to 6 hours as needed

For pain not controlled with above opioid options, consider:
- Tapentadol IR 50-100 mg PO every 6 hours as needed
- Hydromorphone IR 2-6 mg PO every 6 hours as needed

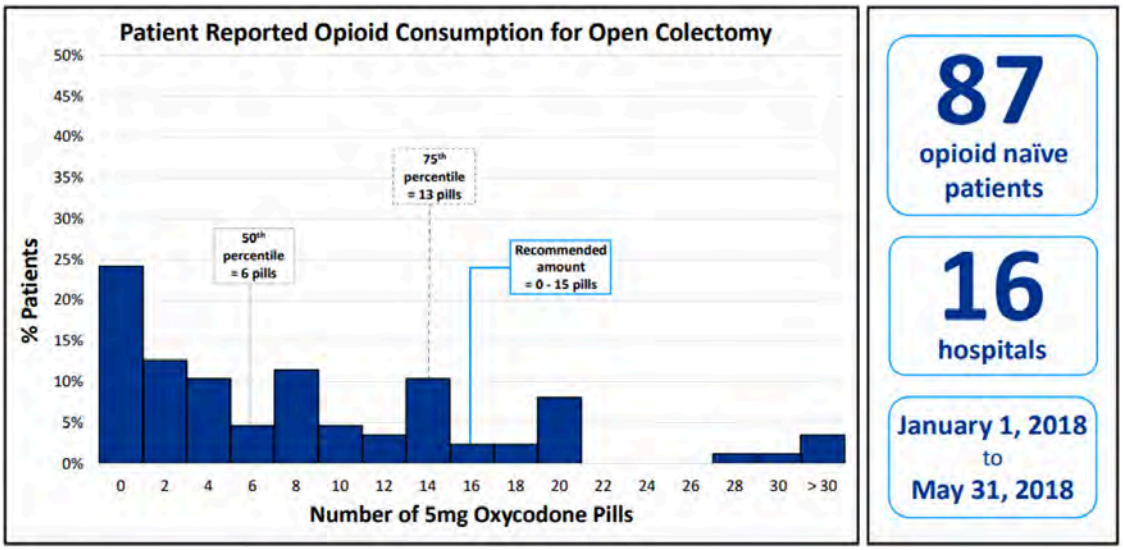
For pain not controlled by oral opioids, if patient strict NPO or for severe breakthrough pain, consider:
- Morphine 1-4 mg IV every 4 hours as needed ***OR***
- Hydromorphone 0.25-1 mg IV every 3 to 4 hours as needed

Discharge Recommendations	Consider for Prescription on Discharge
• APAP 1 g PO every 6 to 8 hours until pain is resolved • Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches) • For opioid-naïve patients, prescribe between 0 and 15 tablets of oxycodone 5 mg (or other opioid monoproduct equivalent) for open, or between 0 and 10 tablets for laparoscopic colectomy.	• NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • Dextromethorphan 40 mg PO 3 times per day for 2 days[248-250] • For patients who benefitted from gabapentinoid therapy while hospitalized, consider prescribing a 5- to 10-day course of a gabapentinoids upon discharge. - It is suggested that the discharge dosing regimen match the inpatient dosing regimen. - It is recommended that concurrent use of gabapentinoids and opioids in the outpatient setting be avoided as it increases the risk of respiratory depression.



SOURCE: Michigan Opioid Prescribing Engagement Network[56]

I. Opioid-sparing Multimodal Analgesic Pathway for Colorectal Surgeries *continued*



SOURCE: Michigan Opioid Prescribing Engagement Network[56]

II. Opioid-sparing Multimodal Analgesic Pathway for Cholecystectomy

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO once • COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)	• Gabapentin 300-600 mg PO once ***OR*** pregabalin 75-150 mg PO once (adjust dose for age, renal function)[239,240,289,290] • Melatonin 6 mg PO once[241,242,244] • Clonidine 0.1 mg PO once[245-247] • Tizanidine 4 mg PO once[291,292] • Dextromethorphan 90 mg PO once[248-250,293]

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.

Intraoperative Recommendations	Consider for Intraoperative Use
Operative technique:[294] • Laparoscopic surgery is associated with less postoperative pain • Low-pressure (10-12 mm Hg) peritoneum if surgically feasible • Saline lavage and suction after removal of gallbladder if there is spillage of bile • Aspiration of pneumoperitoneum gas Operative anesthesia: • Minimize or avoid induction opioids, and minimize intraoperative maintenance opioids • Infiltration of local amide anesthetic at the surgical sites[295] Pharmacologic agents: • Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction[238,295,296] • Ketorolac 15 mg IV, unless contraindicated or an NSAID was administered preoperatively	Operative anesthesia: • Opioid-free/sparing total intravenous anesthesia (TIVA) (e.g., propofol, dexmedetomidine, lidocaine and ketamine)[285] • Instillation of IPLA[297-303] Regional anesthesia, consider: • Rectus sheath block[304] Pharmacologic agents: • Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion[268-270,285,305-307] • Esmolol loading dose of 0.5 mg/kg IV bolus over one minute followed by 0.01-0.05 mg/kg/min IV infusion[272,273,308] • Magnesium sulfate 30-50 mg/kg IV bolus followed by 6-20 mg/kg/hr IV infusion ***OR*** 4 gm IV given over 30-60 minutes at the close of case[274-277]

Consider for Intraoperative Use

For open cholecystectomy or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:
- Ketamine 0.1-0.3 mg/kg IV bolus once pre-incision +/- 0.1-0.3 mg/kg/hr IV infusion[278-281,309]
- Dexmedetomidine 0.8-1 mcg/kg/hr IV bolus +/- 0.2-0.8 mcg/kg/hr IV infusion[286,310,311]

Regional anesthesia:
- Neuraxial analgesia: spinal, TEA or CSE[305,312-314]
- TAP block[315]
- Quadratus lumborum block[261]
- Subcostal TAP blocks[316]
- Bilateral T6 erector spinae plane (ESP) single-shot blocks[262,317]
- Catheter placement for continuous wound infusions with local anesthetic

II. Opioid-sparing Multimodal Analgesic Pathway for Cholecystectomy *continued*

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** • NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • Nonpharmacological interventions	• Lidocaine 5% patch once daily, applied adjacent to incision (up to three patches) • Dextromethorphan 40 mg PO 3 times per day for 2 days[248-250]

For open cholecystectomy or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, use the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:
- Gabapentin scheduled 300-600 mg PO 1 to 3 times daily OR pregabalin 50-150 mg PO 1 to 2 times daily[290]
- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion for 24-48 hrs[278-281,309]
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if other forms of wound infusion or epidural amide anesthetic are continued)[268-271]

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia. Clinicians are encouraged to maintain patients receiving opioid therapy on multimodal analgesic agents as clinically appropriate; it is advised that opioid monotherapy be avoided.

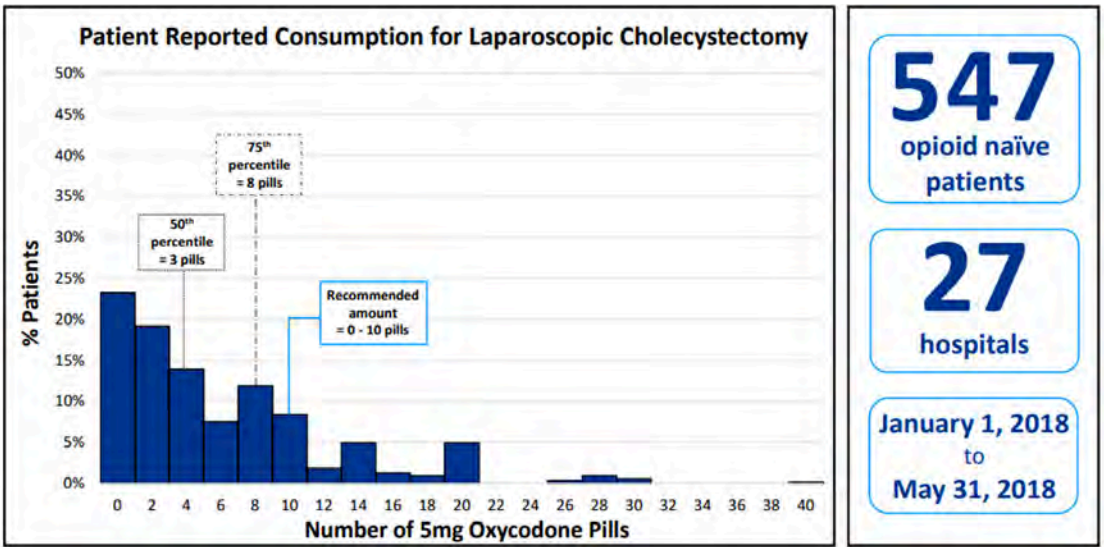
Initiate opioid treatment with:
- Oxycodone IR 2.5-10 mg PO every 4 to 6 hours as needed ***OR***
- Morphine IR 5-20 mg PO every 4 to 6 hours as needed

For pain not controlled with above opioid options, consider:
- Tapentadol IR 50-100 mg PO every 6 hours as needed ***OR***
- Hydromorphone IR 2-6 mg PO every 6 hours as needed

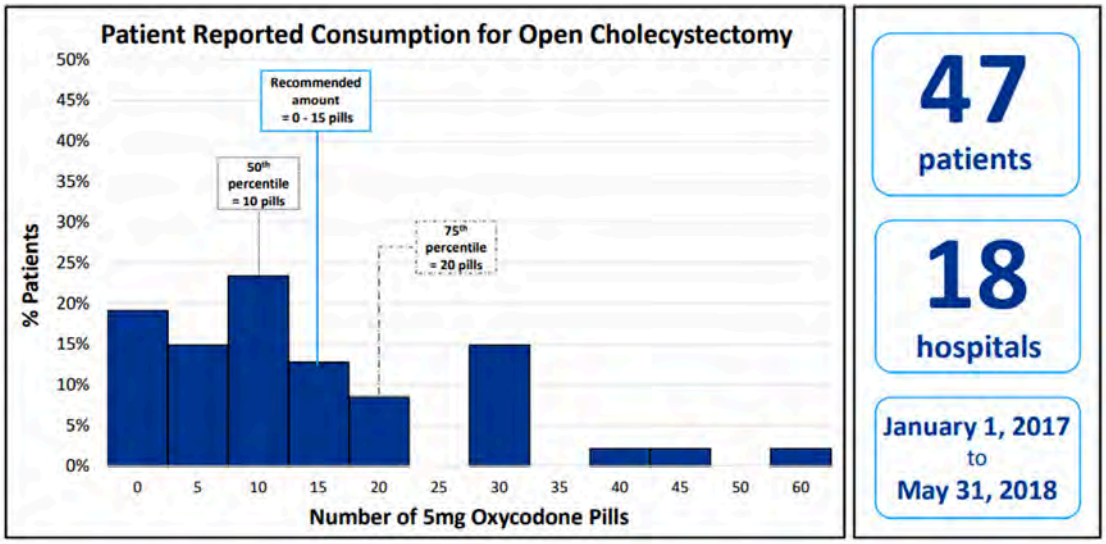
For pain not controlled by oral opioids, if patient strict NPO or for severe breakthrough pain, consider:
- Morphine 1-4 mg IV every 4 hours as needed ***OR***
- Hydromorphone 0.25-1 mg IV every 3 to 4 hours as needed

Discharge Recommendations	Consider for Prescription on Discharge
• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** • NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • For opioid-naïve patients, prescribe between 0 and 10 tablets of oxycodone 5 mg (or other opioid monoproduct equivalent) for laparoscopic cholecystectomy and between 0 and 15 tablets for open cholecystectomy.	• Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches) • Dextromethorphan 40 mg PO 3 times per day for 2 days[248-250] • For patients who benefitted from gabapentinoid therapy while hospitalized, consider prescribing a 5- to 10-day course of a gabapentinoid upon discharge. - It is recommended that the discharge dosing regimen match the inpatient regimen. - It is recommended that concurrent use of gabapentinoids and opioids in the outpatient setting be avoided as it increases the risk of respiratory depression.

II. Opioid-sparing Multimodal Analgesic Pathway for Cholecystectomy *continued*



SOURCE: Michigan Opioid Prescribing Engagement Network[56]



SOURCE: Michigan Opioid Prescribing Engagement Network[56]

III. Opioid-sparing Multimodal Analgesic Pathway for Appendectomy

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO once • COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)	• Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction[238] • Gabapentin 300-600 mg PO once ***OR*** Pregabalin 75-150 mg PO once (adjust dose for age, renal function)[239,240,289] • Melatonin 6 mg PO once[241-244] • Clonidine 0.1 mg PO once[245-247] • Dextromethorphan 90 mg PO once[248-250]

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.

Intraoperative Recommendations	Consider for Intraoperative Use
Operative technique: • Laparoscopic repair is associated with less postoperative pain[318,319] Operative anesthesia: • Minimize or avoid induction opioids and minimize intraoperative maintenance opioids. • Infiltration of local amide anesthetic at surgical sites[267,320]	Operative technique: • Single-port technique Operative anesthesia: • Opioid-free/sparing TIVA (e.g., propofol, dexmedetomidine, lidocaine and ketamine)[285] • Instillation of IPLA[321,322] Pharmacologic agents: • Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion[268-271] • Esmolol loading dose of 0.5 mg/kg IV bolus over 1 minute followed by 0.01-0.05 mg/kg/min IV infusion[272,273,323,324] • Magnesium sulfate 30-50 mg/kg IV bolus followed by 6-20 mg/kg/hr IV infusion ***OR*** 4 gm IV given over 30-60 minutes at the close of case[274-277] Regional anesthesia, consider: • TAP block[259,325] • Quadratus lumborum block[261]

Consider for Intraoperative Use

For open appendectomy or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:
- Ketamine 0.1-0.3 mg/kg IV bolus once pre-incision +/- 0.1-0.3 mg/kg/hr IV infusion[278-281]
- Dexmedetomidine 0.8-1 mcg/kg/hr IV bolus +/- 0.2-0.8 mcg/kg/hr IV infusion[245,283,28]

Regional Anesthesia:
- Consider epidural/spinal/CSEA as sole mode of anesthesia or as adjunctive analgesia[326,327]
  - Consider preoperative TEA placement
  - For patients with a thoracic epidural, consider providing a bolus prior to incision and/or running infusion intraoperatively
- Consider placing a catheter for continuous wound infusion with amide anesthetic

III. Opioid-sparing Multimodal Analgesic Pathway for Appendectomy continued

Postoperative Recommendations	Consider for Postoperative Use

• APAP 1 g PO every 6 to 8 hours ***PLUS***
• Ketorolac 15 mg IV every 6 hours for 24-48 hours followed by
  - NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR***
  - COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved
• Lidocaine 5% patch topically once daily, applied adjacent to incision (up to 3 patches)[328]
• Nonpharmacological interventions
	• Dextromethorphan 40 mg PO 3 times per day for two days[248-250]
	• Gabapentin 300-600 mg PO 1 to 3 times daily ***OR*** pregabalin 75-150 mg PO once or twice daily (adjust dose for age, renal function)

For open appendectomy or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic agents:
- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion for 24-48 hours[278-281]
- Dexmedetomidine 0.2-0.8 mcg/kg/hr IV infusion for up to 24 hours[283]
- Gabapentin 300-600 mg PO 1 to 3 times daily ***OR*** pregabalin 75-150 mg PO once or twice daily
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if other forms of wound infusion or epidural amide anesthetic are continued)[268-271]

Regional anesthesia:
- Continuous wound infusion with amide anesthetic[288]

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia. Clinicians are encouraged to maintain patients receiving opioid therapy on multimodal analgesic agents as clinically appropriate; it is advised that opioid monotherapy be avoided.

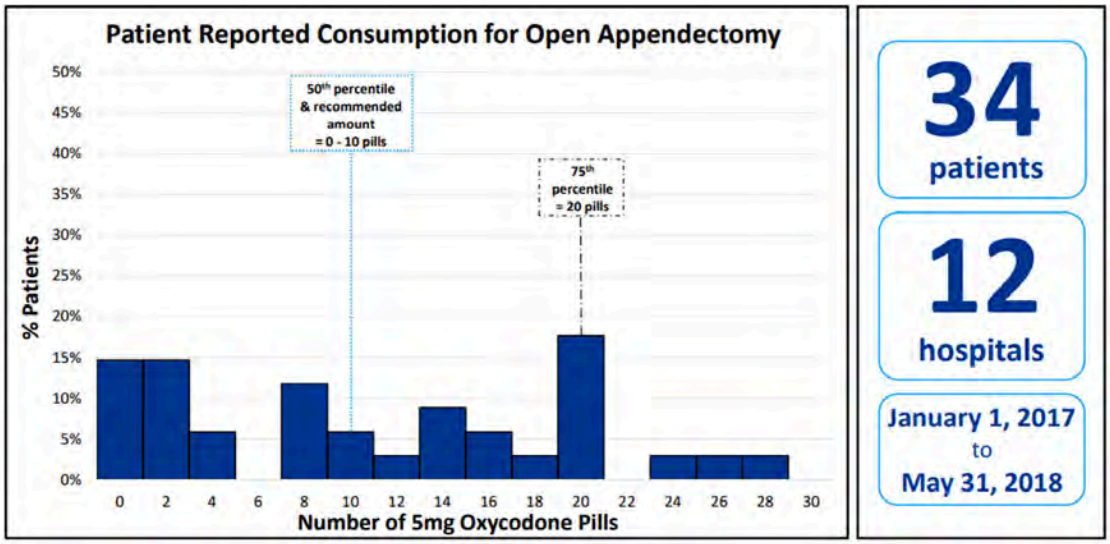
Initiate opioid treatment with:
- Oxycodone IR 2.5-10 mg PO every 4 to 6 hours as needed ***OR***
- Morphine IR 5-20 mg PO every 4 to 6 hours as needed

For pain not controlled with above opioid options, consider:
- Tapentadol IR 50-100 mg PO every 6 hours as needed
- Hydromorphone IR 2-6 mg PO every 6 hours as needed

For pain not controlled by oral opioids, if patient strict NPO, or for severe breakthrough pain, consider:
- Morphine 1-4 mg IV every 4 hours as needed ***OR***
- Hydromorphone 0.25-1 mg IV every 3 to 4 hours as needed

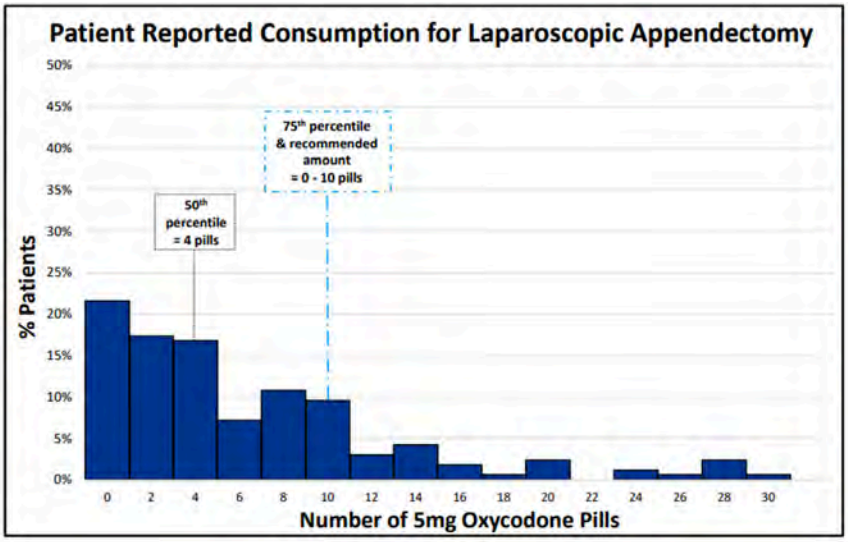
III. Opioid-sparing Multimodal Analgesic Pathway for Appendectomy continued

Discharge Recommendations	Consider for Prescription on Discharge
• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** • NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • Lidocaine 5% patch once daily, applied adjacent to incision (up to three patches) • For opioid-naïve patients, prescribe between zero and 10 tablets of oxycodone 5 mg (or other opioid monoproduct equivalent) for open or laparoscopic appendectomy.[151]	• Dextromethorphan 40 mg PO 3 times per day for 2 days[248-250] • For patients who benefitted from gabapentinoid therapy while hospitalized, consider prescribing a 5- to 10-day course of a gabapentinoids upon discharge. - It is recommended that the discharge dosing regimen match the inpatient regimen. - It is recommended that concurrent use of gabapentinoids and opioids in the outpatient setting be avoided as it increases the risk of respiratory depression.



SOURCE: Michigan Opioid Prescribing Engagement Network[56]

III. Opioid-sparing Multimodal Analgesic Pathway for Appendectomy continued



167 opioid naïve patients

23 hospitals

January 1, 2018 to May 31, 2018

SOURCE: Michigan Opioid Prescribing Engagement Network[56]

IV. Opioid-Sparing Multimodal Analgesic Pathway for Ventral Abdominal Wall Repair

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO once • COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)	• Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction[238] • Gabapentin 300-600 mg PO once ***OR*** pregabalin 75-150 mg PO once (adjust dose for age, renal function)[239,240,329] • Melatonin 6 mg PO once[241-244] • Clonidine 0.1 mg PO once[245-247] • Dextromethorphan 90 mg PO once[248-250]

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.

Intraoperative Recommendations	Consider for Intraoperative Use
Operative technique: • A laparoscopic approach is associated with less postoperative pain[330] • When feasible, use mesh for all ventral hernia repairs • Use of sutureless, self-gripping mesh may result in lower analgesic requirements than the use of transfascially sutured mesh[331-333] Operative anesthesia: • Minimize or avoid induction opioids, and minimize the use of intraoperative maintenance opioids • For large defects, consider preoperative placement of thoracic epidural, bolus and/or running basal dose during procedure[334,335] • Local anesthetic infiltration into the peritoneal, musculofascial and subdermal tissue planes at incision sites[336] Regional analgesia, consider: • TAP block[315,329,337-339] • Quadratus lumborum block[261] • Oblique subcostal TAP block[316] • Rectus sheath block[263] Pharmacologic agents: • Ketorolac 15 mg IV at closure, unless contraindicated or an NSAID was administered preoperatively[340]	Operative technique: • Opioid-free/sparing TIVA (e.g., propofol, dexmedetomidine, lidocaine and ketamine)[285] • For minor procedures, consider anesthesia with local or regional anesthesia only[266] • Instillation of IPLA[266] Pharmacologic agents: • Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion[268-271] • Esmolol loading dose of 0.5 mg/kg IV bolus over 1 minute followed by 0.01-0.05 mg/kg/min IV infusion[272,273] • Magnesium sulfate 30-50 mg/kg IV bolus followed by 6-20 mg/kg/hr IV infusion ***OR*** 4 gm IV given over 30-60 minutes at the close of case[274-277]

IV. Opioid-Sparing Multimodal Analgesic Pathway for Ventral Abdominal Wall Repair continued

Consider for Intraoperative Use

For large defects or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic Agents:
- Ketamine 0.1-0.3 mg/kg IV bolus once pre-incision +/- ketamine 0.1-0.3 mg/kg/hr IV infusion[278-281]
- Dexmedetomidine 0.8-1 mcg/kg IV bolus +/- 0.2-0.8 mcg/kg/hr IV infusion[245,283,284]

Regional Anesthesia:
- Catheter placement for continuous wound infusion with amide anesthetic[341,342]
- Neuraxial anesthesia: spinal, TEA, or CSEA[340,343]

Postoperative Recommendations

- APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS***
- NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR***
- COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved
- Nonpharmacological interventions

Consider for Postoperative Use

- Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches)
- Cyclobenzaprine 5-10 mg PO 3 times daily as needed ***OR*** metaxalone 800 mg PO 3 to 4 times daily as needed for pain caused by muscle spasms
- Dextromethorphan 40 mg PO 3 times daily for 2 days[248-250]
- Gabapentin 300-600 mg PO 1 to 3 times daily ***OR*** pregabalin 75-150 mg PO once or twice daily (dose adjusted for renal function, age)[288]

For major defects or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Regional Anesthesia:
- Continuous wound infusion with amide anesthetic
- Continued epidural adjunctive analgesia[344]

Pharmacologic Agents:
- Ketamine 0.1-0.3 mg/kg IV bolus +/- ketamine 0.1-0.3 mg/kg/hr IV infusion for 24-48 hours[278-281]
- Dexmedetomidine 0.2-0.8 mcg/kg/hr IV infusion for up to 24 hours[283]
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if other forms of wound infusion or epidural amide anesthetic are continued)[268-271]

IV. Opioid-Sparing Multimodal Analgesic Pathway for Ventral Abdominal Wall Repair continued

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia. Clinicians are encouraged to maintain patients receiving opioid therapy on multimodal analgesic agents as clinically appropriate; it is advised that opioid monotherapy be avoided.

Initiate opioid treatment with:
- Oxycodone IR 2.5-10 mg PO every 4 to 6 hours as needed ***OR***
- Morphine IR 5-20 mg PO every 4 to 6 hours as needed

For pain not controlled with above opioid options, consider:
- Tapentadol IR 50-100 mg PO every 6 hours as needed
- Hydromorphone IR 2-6 mg PO every 6 hours as needed

For pain not controlled by oral opioids, if patient strict NPO or for severe breakthrough pain, consider:
- Morphine 1-4 mg IV every 4 hours as needed ***OR***
- Hydromorphone 0.25-1 mg IV every 3 to 4 hours as needed

Discharge Recommendations	Consider for Prescription on Discharge
• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** • NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • For opioid-naïve patients, prescribe between 0 and 10 tablets of oxycodone 5 mg (or other opioid monoproduct equivalent).	• Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches) • Dextromethorphan 40 mg PO 3 times per day for 2 days[248-250] • For patients who benefited from gabapentinoid therapy while hospitalized, consider prescribing a 5- to 10-day course of a gabapentinoids upon discharge. - It is suggested that the discharge dosing regimen match the inpatient dosing regimen. - It is recommended that concurrent use of gabapentinoids and opioids in the outpatient setting be avoided as it increases the risk of respiratory depression.

V. Opioid-sparing Multimodal Analgesic Pathway for Inguinal Herniorrhaphy

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO once • COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)	• Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction[238] • Gabapentin 300-600 mg PO once ***OR*** pregabalin 75-150 mg PO once (adjust dose for age, renal function)[239,240] • Melatonin 6 mg PO once[241-244] • Clonidine 0.1 mg PO once[245-247] • Tizanidine 4 mg PO once[291,292] • Dextromethorphan 90 mg PO once[248-250]

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.

Intraoperative Recommendations	Consider for Intraoperative Use
Operative technique: • Laparoscopic repair is associated with less postoperative pain.[331] • There are no recommendations for one particular open mesh technique, prosthesis type, or mesh fixation technique over another due to limited available pain data.[345] Operative anesthesia: • Minimize or avoid induction opioids, and minimize intraoperative maintenance opioids. Pharmacologic agents: • Ketorolac 15 mg IV at closure, unless contraindicated or an NSAID was administered preoperatively[346]	Operative anesthetic technique: • Opioid-free/sparing total intravenous anesthesia (TIVA) with propofol, dexmedetomidine, lidocaine and ketamine[285,347] • Local anesthetic infiltration at surgical sites[348,349] - Consider the use of liposomal bupivacaine for incisional and/or regional analgesia[264,265] Regional anesthesia, consider: • IL/IH block Inguinal nerve block[350] • TAP block[351] • "Double TAP": (IL/IH and TAP block)[352,353] • Paravertebral blocks[348,354,355] • Erector spinae plane block[313] Pharmacologic agents: • Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion[268,269,356] • Esmolol loading dose 0.5 mg/kg IV bolus over 1 min followed by 0.01-0.05 mg/kg/min IV infusion[272,273] • Magnesium sulfate 30-50 mg/kg IV bolus followed by 6-20 mg/kg/hr IV infusion OR 4 gm IV given over 30-60 minutes at the close of case[274-277]

Consider for Intraoperative Use

For open inguinal hernia repair or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic Agents:
- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion[278-281]
- Dexmedetomidine 0.8-1 mcg/kg IV bolus +/- 0.2-0.8 mcg/kg/hr IV infusion[245,283,284,347]

Regional Anesthesia:
- Catheter placement for continuous wound infusions with amide anesthetic[357-359]

V. Opioid-sparing Multimodal Analgesic Pathway for Inguinal Herniorrhaphy continued

Postoperative Recommendations	Consider for Postoperative Use
• APAP 1 g PO every six to eight hours until pain has resolved ***PLUS*** • NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • Nonpharmacological interventions	• Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches) • Tizanidine 4 mg PO twice daily[291,292] • Dextromethorphan 40 mg PO three times a day for two days[248-250]

For open herniorrhaphy or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain, and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic Agents:
- Gabapentin 300-600 mg PO one to three times daily OR pregabalin 75-150 mg PO once or twice daily[288]
- Ketamine 0.1-0.3 mg/kg IV bolus +/- ketamine 0.1-0.3 mg/kg/hr IV infusion for 24-48 hours[278-281]
- Dexmedetomidine 0.2-0.8 mcg/kg/hr IV infusion for up to 24 hours[283]
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if other forms of wound infusion or epidural amide anesthetic are continued)[268,269,356]

Regional Analgesia:
- Continuous wound infusion with amide anesthetic

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia. Clinicians are encouraged to maintain patients receiving opioid therapy on multimodal analgesic agents as clinically appropriate; it is advised that opioid monotherapy be avoided.

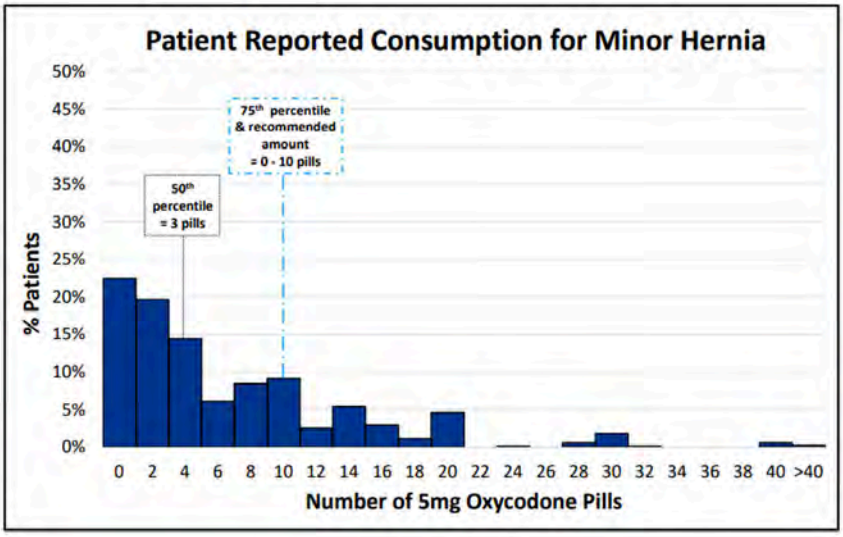
Initiate opioid treatment with:
- Oxycodone IR 2.5-10 mg PO every four to six hours as needed ***OR***
- Morphine IR 5-20 mg PO every four to six hours as needed

For pain not controlled with above opioid options, consider:
- Tapentadol IR 50-100 mg PO every six hours as needed
- Hydromorphone IR 2-6 mg PO every six hours as needed

For pain not controlled by oral opioids, if patient strict NPO, or for severe breakthrough pain, consider:
- Morphine 1-4 mg IV every four hours as needed ***OR***
- Hydromorphone 0.25-1 mg IV every three to four hours as needed

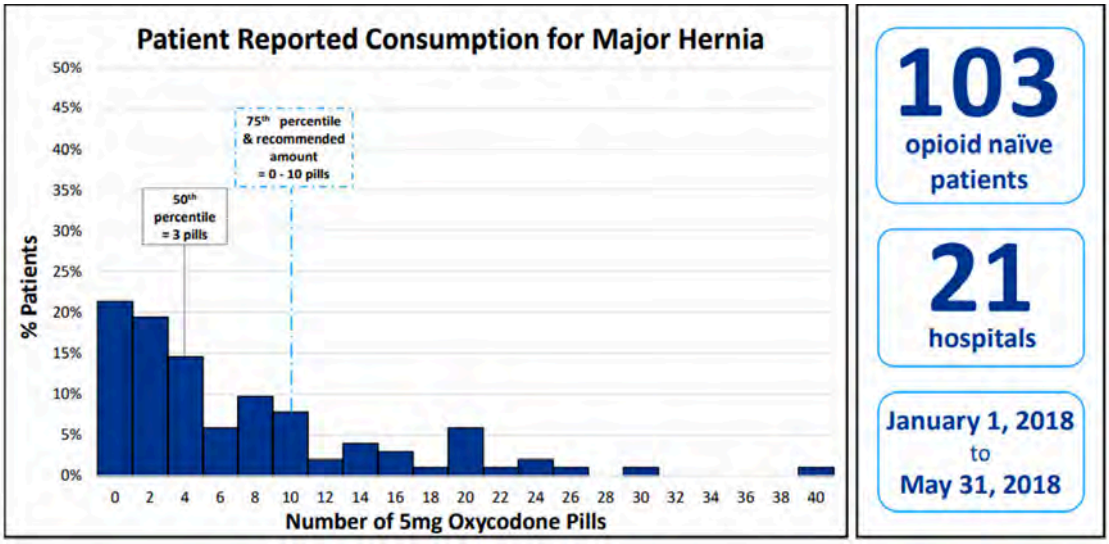
V. Opioid-sparing Multimodal Analgesic Pathway for Inguinal Herniorrhaphy continued

Discharge Recommendations	Consider for Prescription on Discharge
• APAP 1 g PO every six to eight hours until pain has resolved PLUS • NSAID (ibuprofen 600 mg PO every 6 hours OR naproxen 500 mg PO every 12 hours) OR • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours OR meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved[1-3] • For opioid-naïve patients, prescribe zero to 10 tablets of oxycodone 5 mg (or equivalent opioid monoproduct)	• Lidocaine 5% patch once daily, applied adjacent to incision (up to three patches) • Tizanidine 4 mg PO twice daily for seven days[291,292] • Dextromethorphan 40 mg PO three times a day for two days[248-250] • For patients who benefited from gabapentinoid therapy while hospitalized, consider prescribing a 5- to 10-day course of a gabapentinoids upon discharge. - It is suggested that the discharge dosing regimen match the inpatient regimen. - It is recommended that concurrent use of gabapentinoids and opioids in the outpatient setting be avoided as it increases the risk of respiratory depression.



SOURCE: Michigan Opioid Prescribing Engagement Network[56]

V. Opioid-sparing Multimodal Analgesic Pathway for Inguinal Herniorrhaphy continued



SOURCE: Michigan Opioid Prescribing Engagement Network[56]

VI. Opioid-Sparing Multimodal Analgesic Pathway for Mastectomy With or Without Implant-Based or Flap Reconstruction

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO • COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)	• Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction[360] • Gabapentin 300-600 mg PO once ***OR*** Pregabalin 75-150 mg PO once (adjust dose for age, renal function)[239,240,361] • Melatonin 6 mg PO once[241-244] • Clonidine 0.1 mg PO once[245-247] • Venlafaxine 37.5 mg PO daily for 2 weeks, beginning the day prior to procedure for the prevention of chronic post-mastectomy pain (CPMP)[362] (caution with the concomitant use of methylene blue) • EMLA cream 5 g on the sternal area 5 minutes before surgery, and 15 g on the supraclavicular area and axilla at the end of the operation and daily for 4 days for the prevention of CPMP[363] • Dextromethorphan 90 mg PO once[248-250]

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.

VI. Opioid-Sparing Multimodal Analgesic Pathway for Mastectomy With or Without Implant-Based or Flap Reconstruction continued

Intraoperative Recommendations

Operative technique:
- Preserve axillary nerves whenever possible

Operative anesthesia:
- Minimize or avoid induction opioids and minimize intraoperative maintenance opioids

Regional anesthesia, consider:
- Paravertebral nerve block[364]
- Pectoral nerve block (Pecs)[365,366]
  - Pecs I and II block after induction prior to incision
- Serratus plane blocks
- ESP block
  - Consider adding dexamethasone or dexmedetomidine to PVB to enhance the quality and duration of peripheral nerve blocks

Pharmacologic agents:
- Ketorolac 15 mg IV, unless contraindicated or an NSAID was administered preoperatively[45,46,367]

Consider for Intraoperative Use

Operative anesthesia:
- Opioid-free/sparing TIVA (e.g., propofol, dexmedetomidine, lidocaine and ketamine)[285, 368, 369]
- Administer local anesthetic at incision sites before making the incision, and infiltrate into skin, subcutaneous tissue and the chest wall (+/- axilla, drain site) prior to closure[370,371]
  - For large incisions, surgeons must be mindful of limits on total quantity of local anesthetic injected and may opt to defer infiltration until after removal of the breast
- Liposomal bupivacaine infiltrated prior to incision and prior to closure[264,265]
  - 1:1 mixture of 1.3% liposomal bupivacaine suspension and 0.5% bupivacaine injected prior to incision
  - At least 20 mL of liposomal bupivacaine mixture infiltrated into skin, subcutaneous tissue, chest wall (+/- axilla, drain site) prior to closure
    - As above, for large incisions, consider reserving liposomal bupivacaine for use after removal of the breast

Pharmacologic agents:
- Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion (stop if and when liposomal bupivacaine is administered)[269,271,372-376]
- Esmolol loading dose of 0.5 mg/kg IV bolus over 1 minute followed by 0.01-0.05 mg/kg/min IV infusion[272,273]
- Magnesium sulfate 30-50 mg/kg followed by 6-20 mg/kg/hr IV infusion OR 4 gm IV given over 30-60 minutes at the close of case[274-277]

Consider for Intraoperative Use

For patients undergoing flap-based reconstruction or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic Agents:
- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion[278-281]
- Dexmedetomidine 0.8-1 mcg/kg IV bolus +/- 0.2-0.8 mcg/kg/hr IV infusion[283]

Regional Anesthesia:
- Catheter placement for continuous wound infusion of amide anesthetic
- Epidural placement for adjunctive analgesia

VI. Opioid-Sparing Multimodal Analgesic Pathway for Mastectomy With or Without Implant-Based or Flap Reconstruction continued

Postoperative Recommendations	Consider for Postoperative Use
• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** • Nonpharmacological interventions	• NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) OR • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours may reduce incidence of CMPS (avoid if liposomal bupivacaine used or wound infusion of amide anesthetic continued)[271,372,373,375,376] • Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches) • Gabapentin 300 mg PO daily, titrated to 300 mg PO 3 times daily[377] • Dextromethorphan 40 mg PO 3 times per day for 2 days[248-250] • Cyclobenzaprine 5-10 mg PO 3 times daily as needed ***OR*** methocarbamol 750 mg PO 4 times daily as needed for pain caused by muscle spasms • Melatonin 6 mg PO once or QHS as needed for anxiety[241-244]

For patients undergoing flap-based reconstruction or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic Agents:
- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion for 24-48 hours[278-281]
- Dexmedetomidine 0.2-0.8 mcg/kg/hr IV infusion for up to 24 hours
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if liposomal bupivacaine or other forms of wound infusion or epidural amide anesthetic are continued)[269,271,372,373,375,376]

Regional Anesthesia:
- Continuous wound infusion with amide anesthetic
- Continued epidural or paravertebral adjunctive analgesia

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia. Clinicians are encouraged to maintain patients receiving opioid therapy on multimodal analgesic agents as clinically appropriate; it is advised that opioid monotherapy be avoided.

Initiate opioid treatment with:
- Oxycodone IR 2.5-10 mg PO every 4 to 6 hours as needed ***OR***
- Morphine IR 5-20 mg PO every 4 to 6 hours as needed

For pain not controlled with above opioid options, consider:
- Tapentadol IR 50-100 mg PO every 6 hours as needed
- Hydromorphone IR 2-6 mg PO every 6 hours as needed

For pain not controlled by oral opioids, if patient strict NPO, or for severe breakthrough pain, consider:
- Morphine 1-4 mg IV every 4 hours as needed ***OR***
- Hydromorphone 0.25-1 mg IV every 3 to 4 hours as needed

VI. Opioid-Sparing Multimodal Analgesic Pathway for Mastectomy With or Without Implant-Based or Flap Reconstruction continued

Discharge Recommendations

- APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS***
- NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR***
- COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved
- Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches)
- For opioid-naïve patients, prescribe between 0 and 20 tablets of oxycodone 5 mg (or equivalent opioid monoproduct) for simple mastectomy +/- SLND or between 0 and 30 tablets for MRM or ALND

Consider for Prescription on Discharge

- Venlafaxine 37.5 mg PO daily for up to 10 days may reduce risk of chronic post-mastectomy pain[362]
- Topical diclofenac 1% gel, apply 2 g around surgical site 4 times daily
- Melatonin 6 mg PO QHS[378-380]
- Consider dextromethorphan 40 mg PO 3 times per day for 2 days[248-250,381]

Post-Mastectomy Pain Syndrome

- It is recommended that assessment for post-mastectomy pain syndrome (PMPS) be a component of long-term follow-up of breast surgery patients and that management of PMPS be initiated upon diagnosis.
- It is suggested that surgeons consider early referral of patients with persisting pain to a pain specialist.
- Therapies may include:
  - Lidocaine 5% transdermal patch, apply up to 3 patches around incision site daily
  - Topical diclofenac 1% gel, apply 2 g around surgical site 4 times daily
  - Gabapentin 300 mg PO once daily, titrated to 300 mg PO 3 times daily[377]
  - Surgical excision of neuroma (for non-resectable neuromas, consider infiltration of area with liposomal bupivacaine)[264,265]
  - Treatment of PMPS with regional nerve blocks
    - Intercostal nerve blockade[382]
    - Stellate ganglion blockade
    - Paravertebral blockade
    - Thoracic plane blocks
    - Superficial or deep serratus plane block[383,384]
- Physical therapy
- Acupuncture or other nonpharmacologic interventions

VII. Opioid-Sparing Multimodal Analgesic Pathway for Breast Biopsy, Lumpectomy, Lumpectomy and SLNB and SNLB only

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO once • COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)	• Gabapentin 300-600 mg PO once ***OR*** Pregabalin 75-150 mg PO once (adjust dose for age, renal function)[239,240] • Melatonin 6 mg PO once[241-244] • Clonidine 0.1 mg PO once[245–247] • Dextromethorphan 90 mg PO once[248,249,381]

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.

Intraoperative Recommendations

Operative analgesia:

- For procedures under general anesthesia, minimize or avoid induction opioids and minimize intraoperative maintenance opioids
- Long-acting local anesthetic at incision sites before incision and infiltrated into skin and subcutaneous tissue prior to closure[370,371]
  - 0.25% or 0.5% bupivacaine hydrochloride (HCl) alone ***OR***
  - Consider use of liposomal bupivacaine with 0.25% or 0.5% bupivacaine HCl[264,265]
  - NOTE: do not mix liposomal bupivacaine with lidocaine

Pharmacologic agents:

- Ketorolac 15 mg IV, unless contraindicated or an NSAID was administered preoperatively[45,46,367]

Consider for Intraoperative Use

For patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

- Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion (if liposomal bupivacaine not used)[269,271,373,375,376]
- Esmolol loading dose 0.5 mg/kg IV bolus over 1 minute followed by 0.01-0.05 mg/kg/min IV infusion[272,273]
- Magnesium sulfate 30-50 mg/kg IV given over 30-60 minutes[274–277]

VII. Opioid-Sparing Multimodal Analgesic Pathway for Breast Biopsy, Lumpectomy, Lumpectomy and SLNB and SNLB only continued

Postoperative/Discharge Recommendations	Consider for Postoperative/Discharge Use
• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** • NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • For opioid-naïve patients, prescribe between 0 and 5 tablets of oxycodone 5 mg (or opioid monoproduct equivalent) following breast biopsy, lumpectomy, lumpectomy and SLNB or SNLB only • Nonpharmacological interventions	• Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches) • Diclofenac 1% gel, apply 2 g around surgical site 4 times daily • Dextromethorphan 40 mg PO 3 times a day for 2 days[248-250 ,381] • Gabapentin 300-600 mg PO 1 to 3 times daily ***OR*** pregabalin 75-150 mg PO once or twice daily (adjust dose for age, renal function)[377]

For patients who are anticipated to have difficult-to-manage pain following minor breast procedures, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free pain management, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

- Gabapentin 300 mg PO daily, titrated over 3-5 days to 300 mg PO 3 times daily until pain resolved[377]
- Dextromethorphan 40 mg PO 3 times daily for 2 days[248–250,381]

VIII. Opioid-sparing Multimodal Analgesic Pathway for Thoracotomy

Preoperative Recommendations	Consider for Preoperative Use
• APAP 1000 mg PO once • Dexamethasone 0.1-0.2 mg/kg IV given slowly preoperatively or at induction OR methylprednisolone 125 PO once[238,385]	• COX-2 NSAID (celecoxib 200-400 mg PO once ***OR*** meloxicam 7.5-15 mg PO once)[386] • Gabapentin 300-600 mg PO once ***OR*** pregabalin 75-150 mg PO once (adjust dose for age, renal function)[239,240] • Melatonin 6 mg PO once[241–244] • Clonidine 3 mcg/kg IV over 30 minutes preoperatively[245–247] • Dextromethorphan 90 mg PO once[248–250,387]

It is recommended that preoperative oral agents listed be administered 30-90 minutes prior to procedure.

VIII. Opioid-sparing Multimodal Analgesic Pathway for Thoracotomy continued

Intraoperative Recommendations

Operative technique:

- Minimally-invasive technique with video-assisted thoracotomy (VATS) is associated with less postoperative pain and a lower risk of persistent opioid use than with open thoracotomy[388,389]
- Robotic-assisted procedures have not been demonstrated to reduce postoperative pain or analgesic requirements
- Minimize the number of interspaces used. Placing multiple incisions on one interspace reduces the number of dermatomes affected and, thus, reduces postoperative incisional pain
- Use the fewest possible number of ports or a single-port procedure as feasible[390]

Operative anesthesia:

- Minimize or avoid induction opioids and minimize intraoperative maintenance opioids
- Infiltration of incisional sites with long-acting local anesthetic[391]
- Neuraxial
  - Thoracic epidural analgesia (TEA)[389]
    - Adjuvant dexmedetomidine[392]
- Regional anesthesia/analgesia
  - Paravertebral block with amide anesthetic (may be a first-line mode of anesthesia, as evidence suggests this approach may be as effective as TEA with fewer complications)[391,393]
    - Consider placement of catheter for continuous amide anesthetic infusion following paravertebral block[394,395]
    - It is recommended that placement of catheters for CWI be done under direct visualization where feasible[394]
  - Consider using alternative regional anesthetic blocks:[178]
    - ESP block[262,396–398]
    - Intercostal nerve block[386,399–402]
    - PECs block
    - Intrapleural block/infusion
    - Serratus anterior plane block[403–405]

Pharmacologic agents:

- Dexamethasone 0.1-0.2 mg/kg IV ***OR*** methylprednisolone 125 IV once, if not administered preoperatively[385]
- Ketorolac 15 mg IV at close of case, unless contraindicated or an NSAID was administered preoperatively

Consider for Intraoperative Use

Operative technique:

- Utilize muscle-sparing technique as feasible (e.g. when dividing latissimus dorsi and serratus)
- When performing open thoracotomy, consider use of anterolateral approach as alternative to posterolateral[389]

Operative anesthesia:

- Opioid-free/sparing TIVA (e.g., propofol, dexmedetomidine, lidocaine and ketamine)[285,403,406–409]
- Catheter placement for continuous infusion of amide anesthetic following procedure[403,410–412]
- Liposomal bupivacaine for incisional infiltration[386,399–401,403,413]
  - 30 mL 0.25% bupivacaine (w/epi) + 20 mL liposomal bupivacaine: 5 mL injected per intercostal space (total 30 mL) and 20 mL injected into incision
- Cryoanalgesia is not recommended, as it appears to potentiate chronic pain[386,403,408]

Pharmacologic agents:

- Lidocaine 1.5 mg/kg IV bolus (max 150 mg) followed by 1-3 mg/kg/hr IV infusion, particularly for patients who are not candidates for regional anesthesia (stop if and when liposomal bupivacaine is administered)[269,271,414]
- Esmolol loading dose of 0.5 mg/kg IV bolus over 1 minute followed by 0.01-0.05 mg/kg/min IV infusion[272,273]
- Magnesium sulfate 40 mg/kg IV over 10 minutes during the induction of anesthesia followed by an infusion over 24 hours (10 mg/kg/hr)[274–277,415]
- Methadone 10-40 mg IV for its opioid-sparing potential[416,417]

VIII. Opioid-sparing Multimodal Analgesic Pathway for Thoracotomy continued

Consider for Intraoperative Use

For open thoracotomy (retraction, fracture or dislocation of ribs, injury to the intercostal nerves or irritation of the pleura or intercostal bundles by chest tubes) or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Regional anesthesia as above.
Pharmacologic Agents:

- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion.[278–281,386,395,408,418,419]
- Dexmedetomidine 0.8-1 mcg/kg IV bolus +/- 0.2-0.8 mcg/kg/hr IV infusion[245,283,284]

Postoperative Recommendations

- APAP 1 g PO every 6 to 8 hours until pain is resolved ***PLUS***
- Ketorolac 15 mg IV every 6 hours for 24-48 hours, ***FOLLOWED BY***
  - NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR***
  - COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved
- Lidocaine 5% patch once daily, applied adjacent to incision (up to 3 patches)
- Nonpharmacological interventions

Consider for Postoperative Use

- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if liposomal bupivacaine used)[269,271,414]
- Gabapentin scheduled 300-600 mg PO every eight hours or QHS ***OR*** Pregabalin 75-150 mg PO every 12 hours or QHS[386]
- Dextromethorphan 40 mg PO 3 times a day for two days[248–250]

For open thoracotomy (retraction, fracture or dislocation of ribs, injury to the intercostal nerves or irritation of the pleura or intercostal bundles from chest tubes)or as adjunctive analgesia for patients who are anticipated to have difficult-to-manage postoperative pain, including opioid-dependent patients, patients with chronic pain, patients with a history of severe or refractory postoperative pain and patients who request opioid-free surgery, consider use of the above multimodal agents and one or more of the following as clinically appropriate:

Pharmacologic Agents:

- Ketamine 0.1-0.3 mg/kg IV bolus +/- 0.1-0.3 mg/kg/hr IV infusion for 24-48 hours[278–281,386,395,408,418,419]
- Dexmedetomidine 0.2-0.8 mcg/kg/hr IV infusion for up to 24 hours[245,283,284]
- Lidocaine 1-2 mg/kg/hr IV infusion for 24-48 hours (avoid if liposomal bupivacaine or wound infusion or epidural amide anesthetic are continued)[269,271,414]

Regional anesthesia:

- Continued regional amide anesthetic infusion via catheter
- Continued epidural analgesia

VIII. Opioid-sparing Multimodal Analgesic Pathway for Thoracotomy continued

It is recommended that opioids be reserved for patients whose pain is not well controlled with nonopioid analgesia. Clinicians are encouraged to maintain patients receiving opioid therapy on multimodal analgesic agents as clinically appropriate; it is advised that opioid monotherapy be avoided.

Initiate opioid treatment with:
- Oxycodone IR 2.5-10 mg PO every 4 to 6 hours as needed ***OR***
- Morphine IR 5-20 mg PO every 4 to 6 hours as needed

For pain not controlled with above opioid options, consider:
- Tapentadol IR 50-100 mg PO every 6 hours as needed
- Hydromorphone IR 2-6 mg PO every 6 hours as needed

For pain not controlled by oral opioids, if patient is strict NPO, or for severe breakthrough pain, consider:
- Morphine 1-4 mg IV every four hours as needed ***OR***
- Hydromorphone 0.25-1 mg IV every 3 to 4 hours as needed

Discharge Recommendations	Consider for Prescription on Discharge
• APAP 1 g PO every 6 to 8 hours until pain has resolved ***PLUS*** • NSAID (ibuprofen 600 mg PO every 6 hours ***OR*** naproxen 500 mg PO every 12 hours) ***OR*** • COX-2 NSAID (celecoxib 100-200 mg PO every 12 hours ***OR*** meloxicam 7.5-15 mg PO once daily) scheduled until pain is resolved • Lidocaine 5% patch (up to three), once daily, applied adjacent to affected area • For opioid-naïve patients, prescribe between 0 and 20 tablets of oxycodone 5 mg (or other opioid monoproduct equivalent) for VATS and between 0 and 30 tablets for thoracotomy	• For patients who benefited from gabapentinoid therapy while hospitalized, consider prescribing a 5- to 10-day course of a gabapentinoids on discharge[386] - It is recommended that dosing and regimen match that used while inpatient. - It is recommended that concurrent use of gabapentinoids and opioids in the outpatient setting be avoided as it increases the risk of respiratory depression. • Dextromethorphan 40 mg PO 3 times a day for 2 days[248–250] • Duloxetine 60 mg PO daily or venlafaxine 37.5 mg PO daily for those at high risk of CPSP; must have follow-up for appropriate continuation vs taper discontinuation

Managing Perioperative Pain in Patients Receiving Medication for Addiction Treatment

- The use of methadone, buprenorphine or naltrexone for the treatment of OUD may complicate perioperative pain management.
- It is recommended that analgesia be offered to all patients receiving MAT who are in pain. A patient's usual dose of buprenorphine or methadone is generally inadequate to provide adequate pain control.
  - Splitting home doses of buprenorphine or methadone three times per day leverages the early analgesic effects of these medications; however, the analgesic effect is inadequate to address moderate or severe pain.[420,421]
- It is advised that the use of pharmacologic and procedural alternatives to opioids be maximized in patients receiving MAT.
- Strongly consider consulting anesthesia or pain medicine for the use of neuraxial or regional anesthetic techniques in patients with difficult-to-manage perioperative pain.
- The following agents may be of particular value for the treatment of patients receiving MAT.
  - It is recommended that any patient in pain receive scheduled APAP and an NSAID, except when clinically contraindicated.
  - Gabapentinoids: Gabapentin (300-600 mg PO three times per day) OR pregabalin (75-150 mg PO twice daily) can reduce pain and opioid consumption in hospitalized patients; careful monitoring for over-sedation and respiratory depression is required.
  - Alpha-2 agonists: Clonidine and dexmedetomidine are anxiolytic and analgesic with significant opioid-sparing effects (e.g., clonidine 0.1-0.3 mg PO every six to eight hours as needed for pain or anxiety [max 1.2 mg/day, hold if blood pressure <100/70]).
  - NMDA antagonists: Ketamine is the most potent nonopioid analgesic for opioid-tolerant patients. A brief infusion of 0.1-0.3 mg/kg IV over 15 minutes is followed by 0.1-.3 mg/kg/hr IV infusion. In addition, magnesium is an NMDA receptor antagonist with analgesic and opioid-sparing effects (e.g., 30-50 mg/kg IV bolus followed by 6-20 mg/kg/hr IV infusion).
  - IV lidocaine: A bolus of 1.5 mg/kg is followed by 1-3 mg/kg/hr infusion. Contraindications include cardiac dysrhythmias.
- It is recommended that patients on MAT whose pain is not controlled with nonopioid approaches be offered opioid analgesia and that no patient be denied adequate pain relief. Due to cross-tolerance and increased pain sensitivity, it is advised that higher-than-typical doses of opioids be anticipated.
  - As with any patient receiving opioids, close monitoring is advised.
  - For patients receiving buprenorphine for addiction treatment, consider treating acute pain with additional buprenorphine doses.
    - There is no clinical ceiling on buprenorphine for analgesia. SL buprenorphine can be given as frequently as every two hours. IV buprenorphine is a potent analgesic. Start at 0.3 mg IV and titrate as needed. Respiratory depression does occur at higher doses, but it has a ceiling effect that reduces the baseline by about 50%.[82]
    - Buprenorphine is a partial agonist with a high affinity for the mu-opioid receptor. Thus, for patients receiving buprenorphine with severe acute pain for whom additional opioids are required, clinicians are advised to select agents with affinity for the mu-opioid receptor sufficient to displace buprenorphine, such as fentanyl, sufentanil or hydromorphone.
- As a full opioid antagonist, naltrexone blocks the analgesic effects of most opioids. If naltrexone is still present and opioids are necessary, high-dose, high-potency opioids can be used to out-compete naltrexone at the opioid receptor. Patients must be closely monitored, at minimum with pulse oximetry and telemetry, to prevent over-sedation and unintentional overdose.

SOURCE: Adapted from Project Shout. For complete guide visit www.ColoradoMAT.org

Nonopioid Pharmacologic Agents for Multimodal Perioperative Analgesia

(TABLE 9)
Multimodal Analgesic Medications

Type	Example
Alpha-2 adrenergic agonists	Clonidine, dexmedetomidine, tizanidine
Amide anesthetics	Lidocaine, bupivacaine, ropivacaine, liposomal bupivacaine
Amine reuptake inhibitors	Duloxetine, venlafaxine
Anxiolytics	Benzodiazepines, clonidine, gabapentin, melatonin
Central prostaglandin synthesis inhibitor	Acetaminophen
Beta blockers	Esmolol
Gabapentinoids	Gabapentin, pregabalin
Glucocorticoids	Dexamethasone, prednisone
Muscle relaxants/antispasmodics	Cyclobenzaprine, methocarbamol, metaxalone,
N-methyl D-aspartate receptor antagonists	Dextromethorphan, ketamine, magnesium
NSAID	(Cox-1, 2, 3 inhibitors) ibuprofen, ketorolac, celecoxib, meloxicam
Other/Novel Agents	Antipsychotics (haloperidol, droperidol, olanzapine), ascorbic acid, caffeine, capsaicin, memantine, nicotine, oxytocin

SOURCE: Colorado Opioid Profile[12]

Alpha-2 Adrenergic Agonists

CLONIDINE

EVIDENCE: A meta-analysis of nearly 1800 surgical patients receiving either clonidine or dexmedetomidine perioperatively found that clonidine reduced opioid requirements 12-24 hours postoperatively, with an overall decrease in opioid requirements of 25%.[245] Premedication with both oral and IV clonidine prolongs the duration of effect of bupivacaine spinal anesthesia, can significantly decrease cumulative MME 12 and 24 hours after surgery and decrease the incidence of early postoperative nausea and vomiting (PONV).[245,422–424] Epidural and spinal clonidine also enhance the quality and duration of neuraxial anesthesia and reduce the required dose of local anesthetic and other neuraxial additives, including opioids.[246] In fact, a study of colonic surgery patients found that intrathecal (IT) clonidine had better short-acting analgesic and long-term antihyperalgesic effects than bupivacaine.[425] Oral clonidine also helps alleviate opioid withdrawal symptoms in patients with difficult-to-manage pain who are receiving MAT or COT.

MECHANISM OF ACTION: Stimulates alpha 2-adrenergic receptors in the brain, resulting in reduced sympathetic outflow from the CNS. It is less selective for alpha-2 adrenoreceptors than dexmedetomidine, which may account for the less pronounced opioid-sparing effect when the two drugs are compared.

DOSING: IT dosing typically starts at 15 mcg, alone or in combination with other agents, and may be increased up to 150 mcg. IV dosing is 3 mcg/kg over 10 minutes immediately following the spinal block; dose may be repeated 50 minutes later. Dosing for adjunct agents in opioid withdrawal is 0.1-0.3 mg PO every six to eight hours; may transition to equivalent dose of a transdermal patch once a stable oral dose is established.

CONTRAINDICATIONS AND CAUTIONS: Epidural clonidine is not recommended for patients with severe cardiovascular disease or hemodynamic instability.

MONITORING: Monitor for bradycardia and hypotension. Abrupt discontinuation after prolonged use may result in withdrawal symptoms, including agitation, headache and rebound hypertension.

DEXMEDETOMIDINE

EVIDENCE: The meta-analysis cited above found that dexmedetomidine produced a statistically significant decrease in opioid consumption and postoperative pain intensity at 24 hours, as well as early PONV.[245] While no large-scale clinical trials have been conducted, the current body of evidence suggests that dexmedetomidine is suitable for use as an adjuvant analgesic at all perioperative stages, via multiple administration routes (IV, intranasal (IN), IT), particularly in conjunction with regional anesthetics and for patients who are on COT or MAT.[426] One small study in laparoscopic cholecystectomy patients showed less postoperative ketorolac needed in the treatment group, suggesting dexmedetomidine might be helpful for postoperative pain after laparoscopic cholecystectomy with multimodal analgesia.[286] IV dexmedetomidine, when combined with ketamine, has also demonstrated the ability to enhance analgesic effects while reducing the incidence of ketamine-related adverse effects, including emergence reactions and nausea and vomiting.[427] Dexmedetomidine, along with supplemental IV ketamine (0.5 mg/kg), has also been used successfully for analgesia in laparoscopic appendectomy patients.[428] Overall, studies have demonstrated that dexmedetomidine elicits opioid-sparing effects, improves pain control and minimizes opioid-related side effects, most notably when used in the inpatient perioperative setting.[283,284] In conjunction with regional anesthetics, dexmedetomidine increases the anesthetic's duration of effect and prolongs analgesia.[428–430] While no studies have tested clonidine and dexmedetomidine head-to-head, dexmedetomidine appears to have a greater effect on postoperative morphine consumption and postoperative pain.

MECHANISM OF ACTION: Relatively selective alpha-2 adrenergic agonist with anesthetic and sedative properties, which are thought to be due to the activation of G-proteins by $alpha_{2a}$-adrenoceptors in the brainstem, resulting in inhibition of norepinephrine release.

DOSING: Dexmedetomidine 0.2-0.8 mcg/kg/hr continuous IV infusion, though dose may be increased further based on the level of sedation and side effects. A loading IV infusion of 0.8-1 mcg/kg over 10 minutes may be considered but is typically avoided due to the risk of bradycardia; use additional caution if administering dexmedetomidine bolus with other medication boluses that may affect hemodynamics (i.e. ketamine, esmolol, lidocaine). Dexmedetomidine 2-10 mcg IT added to spinal anesthesia.

CONTRAINDICATIONS AND CAUTIONS: Use dexmedetomidine with caution in patients with advanced heart block or severe ventricular dysfunction. Bradycardia and hypotension may be more pronounced in the elderly and in those with hypovolemia; dosage reduction is recommended. Caution when co-administering multiple bolus medications at induction, particularly those that affect hemodynamics.

SPECIAL CONSIDERATIONS: Clinicians are advised to monitor for potential adverse effects, such as hypotension and bradycardia. While a dexmedetomidine infusion may be continued postoperatively, regardless of the patient's extubation status, most hospital policies require patients on infusions to be monitored in an intensive care setting.

MONITORING: Assess the patient's level of sedation, heart rate and blood pressure.

TIZANIDINE

EVIDENCE: Tizanidine is a centrally-acting α2-agonist with muscle-relaxant properties. One study in patients undergoing laparoscopic cholecystectomy found that tizanidine 4 mg administered prior to surgery reduced pain scores, analgesic use and the duration of stay in a recovery room.[292] Another study of patients undergoing inguinal hernia repair found that tizanidine 4 mg administered one hour prior to surgery, and twice daily for one week following the procedure, decreased postoperative pain and analgesic requirements and resulted in a quicker recovery.[291]

MECHANISM OF ACTION: Relatively selective alpha-2 adrenergic agonist with analgesic effects. Also thought to have some activity at the imidazoline receptors, reducing the facilitation of spinal motor neurons. Preferred in patients with spastic disorders due to central activity.

DOSING: Perioperative dosing = 4 mg orally once prior to surgery; has also been studied as 4 mg orally twice daily for one week following surgery. Typical maintenance dose: initial dose = 2 mg orally; may repeat every six to eight hours as needed; increase by 2 to 4 mg per dose at one- to four-day intervals (max 36 mg/day).

CONTRAINDICATIONS AND CAUTIONS: Do not use with potent cytochrome P450 1A2 (CYP1A2) inhibitors (e.g., fluvoxamine, ciprofloxacin). Use caution with concomitant CNS depressants.

SPECIAL CONSIDERATIONS: If stopping prolonged use of the medication, tizanidine must be discontinued gradually by slowly decreasing the dose by 2 mg to 4 mg per day to minimize side effects.
MONITORING: Evaluate for sedation and hepatic (metabolized) and renal (eliminated) function.

Amide Anesthetics

LIDOCAINE IV INFUSIONS

EVIDENCE: IV lidocaine appears to pose a lower risk of postoperative ileus than opioids, offers better analgesia than placebo, and has been shown to reduce the quantity of opioids administered after laparoscopic cholecystectomies.[306,307] The only study of colectomy patients revealed lidocaine to have a salutary effect on pain control, pulmonary function and ileus. However, the study did not include patients who received epidural catheters, so it is unclear if IV or epidural amide anesthetics offer a differential benefit.[431] Given the dramatic difference in the cost of IV lidocaine (<$3) and the cost, time commitment and procedural risk of epidural catheters, this topic warrants further study. It is advised that the use of IV lidocaine be strongly considered for patients without epidural catheters.

In one review, a perioperative lidocaine infusion (1.5-3 mg/kg/hr following a bolus of 0-1.5 mg/kg) consistently improved postoperative pain scores in patients undergoing open or laparoscopic surgery.[271] Visual Analogue Scale (VAS) pain scores, as well as early (24-hour) and late (up to 72-hour) opioid consumption were decreased. In addition to improving analgesia, a perioperative lidocaine infusion shortened the duration of postoperative ileus by an average of eight hours and decreased the incidence of PONV by 10-20%. Perioperative lidocaine infusions also reduced the length of hospital stay by eight to 24 hours. Other studies have found IV lidocaine effective for reducing the incidence and intensity of chronic pain following mastectomy.[372,375] Another review found the treatment to be most effective in the abdominal surgery population.[270]
MECHANISM OF ACTION: Blocks the conduction of nerve impulses through the inhibition of sodium channels.
DOSING: Optimal dosing is unknown, but studies suggest IV lidocaine can be given as a bolus (usually 1-2 mg/kg infused over 10 minutes) followed by a continuous infusion of 1-3 mg/kg/hr, continued for 24-72 hours postoperatively. The continuous IV infusion may be used for up to 72 hours if it is effective and no adverse effects are noted.
CONTRAINDICATIONS: Avoid IV lidocaine in patients with unstable coronary disease, a recent MI, heart failure, severe electrolyte disturbances, cirrhosis, arrhythmias and seizure disorders.
MONITORING: It is recommended that patients should undergo telemetry monitoring.
ADVERSE REACTIONS/CAUTIONS: Local anesthetic systemic toxicity (LAST) is a life-threatening adverse reaction evidenced by circumoral numbness, a metallic taste in the mouth, dizziness, light-headedness and tinnitus. Later signs of toxicity include confusion, slurred speech, blurred vision, myoclonic jerking and seizures. If undetected or untreated, toxicity can progress to coma, respiratory arrest and cardiovascular effects (hypotension, pulse rate <50 or >120, cardiac arrest). If toxicity is suspected, stop the lidocaine and consider a poison center consultation and treatment with lipid emulsion. It is suggested that a lipid rescue kit (i.e., 20% lipid emulsion infusion and appropriate dosing recommendations) be readily available in any practice that uses local anesthetic agents.

INTRAPERITONEAL INSTILLATION OF LOCAL ANESTHETIC (IPLA)

EVIDENCE: A meta-analysis of nine systematic reviews of IPLA which included 76 randomized controlled trials (RCTs) and 4000 patients over a range of surgeries found that IPLA may be of analgesic benefit in the early postoperative period. (The authors note that IPLA may be even more effective for general abdominal and gynecology procedures other than laparoscopic cholecystectomy and that further research in abdominal procedures beyond laparoscopic cholecystectomy is warranted).[266] The practice of instilling or nebulizing the peritoneum with local anesthetic was first reported in the 1950s but is not widely used in the United States.[66] The peritoneum is highly innervated and is known to respond to surgical injuries with local and systemic immune and inflammatory changes via nociceptors that contribute to visceral pain.[432–434] IPLA has been the subject of numerous RCTs, primarily in laparoscopic cholecystectomy, but also in other open and laparoscopic abdominal and gynecologic operations.[266] A meta-analysis of 7 RCTs of IPLA in laparoscopic appendectomy found

decreased pain (both surgical site and shoulder pain), reduced opioid use and resulted in a shorter length of stay. A Cochrane review of IPLA in laparoscopic cholecystectomy found evidence of reduced pain in the four to 24 hours following surgery compared with the control group, but notes that the heterogeneity of study type and quality, agent used and quantity and method of IPLA used precludes a definitive conclusion on efficacy of IPLA and warrants further study. The authors note that adverse effects were rare.[435] In one RCT of patients undergoing laparoscopic cholecystectomy, the intraperitoneal nebulization of ropivacaine 1% (3 mL) significantly reduced postoperative pain, referred shoulder pain (absolute reduction 98%) and morphine requirements.[436] A study of patients undergoing abdominal hysterectomy found significant opioid-sparing effects with patient-controlled intraperitoneal infusions of levobupivacaine.[437] A similar study comparing IV lidocaine and IP lidocaine found IP lidocaine reduced morphine requirements slightly, with significantly lower serum lidocaine levels. The authors conclude that the effects of local anesthetics are "likely to be predominant via local intraperitoneal receptors or anti-inflammatory effects and not via central mechanisms alone".[438] Further studies are required to determine the efficacy of IPLA. The risk of local anesthetic systemic toxicity is presumed to be lower with IPLA than with IV use, as serum levels of LA are lower.

DOSING: The authors of one review recommended a dose of bupivacaine of 2 mg/kg, noting that bupivacaine was the agent used most often in the studies included in their analysis.[435] A review of systemic levels of local anesthetic following IPLA reported no cases of clinical toxicity, though in 2.7% cases patients had systemic local anesthetic levels above or close to a safe threshold; the authors note that the addition of adrenaline to IPLA almost halves systemic levels and prolongs effect.[439]

LIPOSOMAL BUPIVACAINE

EVIDENCE: Available clinical trial evidence includes investigation of the intraoperative use of liposomal bupivacaine (LB) in colorectal, hysterectomy, Cesarean section, urologic, breast, knee and shoulder surgeries. Decreased opioid use has been reported from some of the clinical trials in breast, colorectal, thoracic and hysterectomy procedures. However, the benefits of better pain control and/or decreased opioid consumption with LB compared to standard therapy is considered equivocal at this point. In a pooled analysis from nine studies representing five different surgical procedures, LB administered at doses ≤266 mg in a multimodal analgesic approach was associated with statistically significant and clinically meaningful lower cumulative pain score at 72 hours, delayed and less consumption of opioids, and fewer ORADEs than bupivacaine HCl.[265] Another meta-analysis found that LB at the surgical site appears to reduce postoperative pain compared to placebo, however, found that evidence did not demonstrate superiority to bupivacaine hydrochloride.[264]

In a study of local infiltration of LB in patients undergoing mastectomy with immediate tissue expander reconstruction decreases narcotic requirements in the recovery room, shortens preoperative anesthesiology time and provides similar—if not better—perioperative pain control compared with paravertebral block.[440] In another study done in a similar breast reconstruction population, use of LB was associated with decreased patient VAS pain scores in the immediate postoperative period compared with bupivacaine pain pump and IV/oral narcotic pain management and reduced inpatient length of stay.[441] In one study, patients treated with LB vs bupivacaine undergoing laparoscopic colectomy needed less opioids, had earlier bowel function and shorter lengths of stay.[258] Another retrospective review found that a TAP block with LB versus other local anesthetic in elective colorectal patients was found to significantly lower pain scores for the first 24-36 postoperative hours and reduce post-op opioid use by one-third.[260] In the thoracic surgery population, there are three small, retrospective studies that have compared experience with LB to that of similar patients receiving thoracic epidural analgesia (TEA); the results are mixed, with one study finding TEA to be more effective,[442] one finding LB more effective,[443] and the other finding the two interventions comparable.[400] The only direct comparison of LB to plan bupivacaine (with epinephrine) is also a retrospective review looking at just over 100 patients total. Use of LB was associated with significantly less postoperative opioid consumption and a comparable length of stay.[444] As the literature seems mixed on the clinical and cost benefits of liposomal bupivacaine, especially compared to administration of bupivacaine, it is currently recommended in these guidelines for

consideration in breast, colorectal and thoracic cases only. Many institutions find it cost-prohibitive to stock liposomal bupivacaine and/or have a very restricted use agreement with surgeons. These guidelines recognize the inherent barriers with this medication and therefore do not routinely recommend its use at this point until further literature can provide more robust support.
MECHANISM OF ACTION: Blocks conduction of nerve impulses through inhibition of sodium channels.
DOSING: Liposomal bupivacaine local infiltration of up to 266 mg (20 mL) injected slowly; max dose = 266 mg; dose based on size of surgical site and individual patient factors. Liposomal bupivacaine should be injected 1-1.5 cm apart with 1-2 mL volumes through a 25 gauge or larger needle to maintain the structural integrity of the liposomes. When injecting surgical incisions, liposomal bupivacaine should be injected above and below fascial planes and into the subcutaneous tissues.
CONTRAINDICATIONS: It is advised that liposomal bupivacaine not be used in obstetrical paracervical block anesthesia—fetal bradycardia and death have been reported.
MONITORING: It is recommended that liposomal bupivacaine be administered in areas where treatments for neurologic or cardiac toxicity are available (i.e. lipid-rescue kit).
ADVERSE REACTIONS/CAUTIONS: LAST is a life-threatening adverse reaction. It is recommended that a lipid rescue kit (i.e. lipid emulsion 20% infusion and appropriate dosing recommendations) be made readily available in any area of practice that utilizes any local anesthetic agent. It is advised that liposomal bupivacaine NOT be directly mixed (in the same syringe or vial) with lidocaine agents; it may be mixed with bupivacaine agents.
SPECIAL CONSIDERATIONS: The main concern of routinely using a relatively high-cost item such as liposomal bupivacaine is the lack of overwhelming literature to support efficacy and cost-avoidance when compared to bupivacaine alone. Liposomal bupivacaine is available as a 266 mg in 20 mL or 133 mg in 10 mL vial, which cost approximately $175 and $325 per vial, respectively.[445] Compared to plain bupivacaine, this is approximately a 100-fold cost difference in dose. The dose needed is based on size of surgical site and neuroanatomy, volume needed to cover the width and depth of site and patient factors impacting safety of an amide local anesthetic. One suggestion to optimize use of the 10 mL vial of liposomal bupivacaine is volume expansion, which is a procedure that recommends dilution with plain bupivacaine in a 1:2 ratio of bupivacaine equivalence (i.e. a 133 mg/10 mL vial can be mixed with up to 15 mL of 0.5% bupivacaine or 30 mL 0.25% bupivacaine) to provide 250 mg bupivacaine equivalence.[446] The manufacturer of liposomal bupivacaine also provide a volume expansion method via the package insert involving dilution with sterile normal saline of up to 100 mL with a 133 mg/10 mL vial.

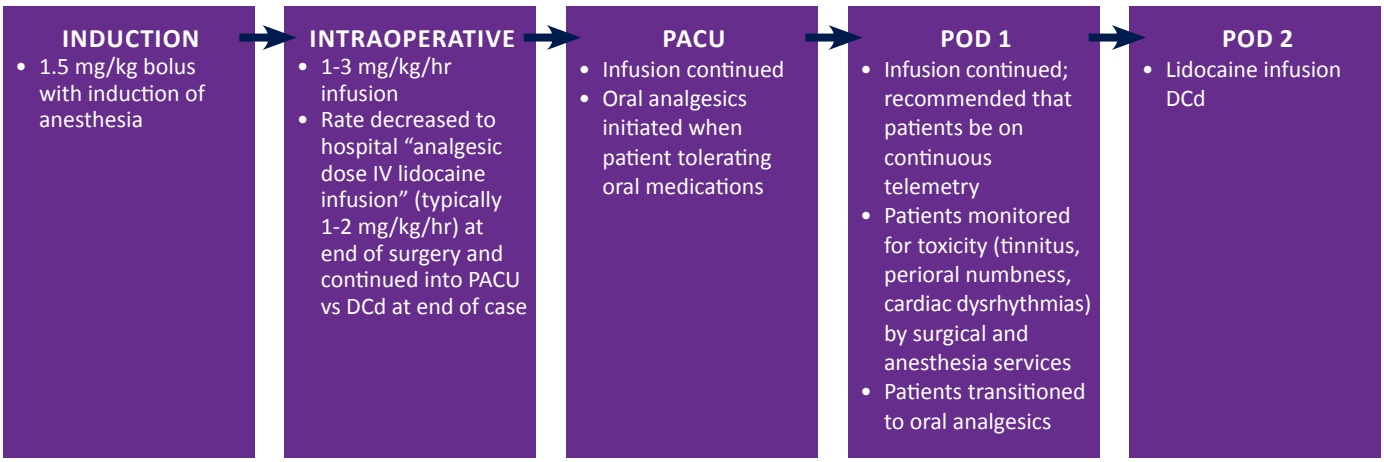
LIDOCAINE TOPICAL (transdermal patches, gel and aerosolized topicals, EMLA cream)
EVIDENCE: While the evidence is somewhat limited and mixed, several small studies support the use of lidocaine transdermal patches for the control of postoperative pain. Studies have found lidocaine transdermal patches effective for patients undergoing thoracotomy, laparoscopic appendectomy and gynecologic surgeries.[328,447,448] Eutectic mixture of local anesthetics (EMLA) cream is another topical option backed by limited evidence. One small study in patients undergoing laparoscopic hysterectomy found EMLA, along with trigger-point injections, effective for managing postoperative shoulder pain.[449] Another small study in patients undergoing breast surgery also found benefit.[363] EMLA cream is just one of many topical local anesthetic formulations that can be considered. Lidocaine topical agents come in spray, cream, ointment and gel solutions ranging from 1-5%, many of which can be purchased without a prescription. Aerosolized lidocaine has been found to be an effective pain adjunct in some wound sites without conveying any adverse reactions.[450,451] Topical local anesthetics also appear to convey a mild antimicrobial effect, an added benefit of using these agents in the postoperative period.[452,453] Due to the relatively low risk associated with topical medications, the ability to transition these treatments to the outpatient setting and the availability of over-the-counter products, topical lidocaine transdermal patches and EMLA cream (or similar local anesthetic topicals) can be a reasonable option in most perioperative and discharge analgesic plans.
MECHANISM OF ACTION: Blocks the conduction of nerve impulses through the inhibition of sodium channels.
DOSING: *Lidocaine patches:* Apply one to three patches to the site of pain once daily. It is advised that patches only be applied to intact skin. While the manufacturer

recommends removing the patch after 12 hours, several small studies have validated the safety of wearing lidocaine patches for up to 24 hours prior to replacement. *EMLA topical:* Apply 2 g of cream topically per 10 cm^2 of skin and cover with an occlusive dressing for at least two hours.

MONITORING: Watch for skin irritation and burning.
DISCHARGE: Patches may be prescribed upon discharge. If the prescription-strength patches (lidocaine 5%) are cost prohibitive or not covered by insurance, counsel patients regarding the over-the-counter availability of lidocaine 4% patches.

(FIGURE 10)

Perioperative Use of IV Lidocaine



Adapted from Lauren K. Dunn, Marcel E. Durieux; Perioperative Use of Intravenous Lidocaine. Anesthesiology *2017;126(4):729-737)*

Local anesthetic systemic toxicity caution:[454,455]

Local anesthetic systemic toxicity (LAST) is a concern when any of the amide anesthetics discussed above are used, and clinicians are encouraged to know suggested dosage limits, cautions and signs of systemic toxicity. For a generally healthy patient, pharmacologic data suggest that the maximum recommended dose of lidocaine is 4.5 mg/kg and bupivacaine is 3 mg/kg, though it is advised that clinicians take into account the varying degree of absorption based on route of administration. It is recommended that caution be exercised when using multiple routes of administration and when using more than one amide anesthetic agent. LAST manifests in organs of the body that depend upon sodium channels for proper functioning, most critically the cardiovascular and central nervous systems. LAST is a life-threatening adverse reaction evidenced by circumoral numbness, a metallic taste in the mouth, dizziness, light-headedness and tinnitus. Later signs of toxicity include confusion, slurred speech, blurred vision, myoclonic jerking and seizures. If undetected or untreated, toxicity can progress to coma, respiratory arrest and cardiovascular effects (hypotension, pulse rate <50 or >120, cardiac arrest). If toxicity is suspected, stop further administration of the anesthetic and consider a poison center consultation and treatment with lipid emulsion. It is recommended that a lipid rescue kit (i.e., 20% lipid emulsion infusion and appropriate dosing recommendations) be readily available in any practice that uses local anesthetic agents.

Amine Reuptake Inhibitors

The Department of Health and Human Services 2019 Report on Pain Management and Best Practices states, "Overall, the analgesic actions of antidepressants occur even in patients who are not clinically depressed, and their analgesic effect typically occurs sooner and at lower doses than those required for the treatment of depression."[235]

DULOXETINE

EVIDENCE: Although the evidence is inconclusive, one meta-analysis of more than 500 patients found that duloxetine was associated with a significant reduction in pain scores as early as four hours postoperatively and up to 48 hours.[456] In addition, duloxetine was associated with a significant reduction in postoperative opioid use and PONV. Duloxetine has been demonstrated to significantly reduce opioid consumption after knee replacement and spine surgery.[457,458] Duloxetine 60 mg given prior to and 24 hours after abdominal hysterectomy has also been shown to significantly reduce postoperative opioid consumption.[459] While additional research is warranted to further determine duloxetine's effect on postoperative pain and analgesic use, duloxetine may be considered in the immediate pre- and postoperative periods for appropriate patients, particularly those undergoing abdominal surgeries.[460]

MECHANISM OF ACTION: Exerts influence on affective components of pain. As a selective serotonin and norepinephrine reuptake inhibitor, duloxetine exerts pain inhibitory actions by potentiating the serotonergic and noradrenergic activity in the CNS. SNRIs increase spinal cord concentrations of norepinephrine, which inhibits neuropathic pain through α2-adrenergic receptors.

DOSING: Duloxetine 60 mg once preoperatively and once 24 hours postoperatively. Typical maintenance dosage for continued use is 60 mg orally once daily.

CONTRAINDICATIONS AND CAUTIONS: SNRIs may increase the risk of suicide in patients aged 18 to 25 years. Do not use within 14 days of an MAOI due to the risk of serotonin syndrome. Use caution in elderly patients with a history of falls (meets Beers criteria).

MONITORING: Monitor for serotonin syndrome and interactions with other medications. Do not discontinue abruptly if the patient has been taking the drug for an extended period of time; gradual dose reduction is recommended.

VENLAFAXINE

EVIDENCE: In one study, venlafaxine 37.5 mg/day for 10 days starting the night prior to surgery was found equivalent to gabapentin 300 mg/day in reducing postoperative analgesic requirements in patients undergoing mastectomy. Venlafaxine significantly decreased the incidence of postmastectomy pain syndrome at six months.[362] It is recommended that venlafaxine be considered for appropriate patients undergoing mastectomy.

MECHANISM OF ACTION: Venlafaxine potentiates neurotransmitter activity in the CNS and neuronal serotonin, norepinephrine and dopamine reuptake.

DOSING: Venlafaxine 75 mg one daily for two weeks, starting the night before breast surgery.

CONTRAINDICATIONS AND CAUTIONS: SNRIs may increase the risk of suicide in patients aged 18 to 25 years. Do not use within 14 days of an MAOI due to the risk of serotonin syndrome. Use caution in elderly patients with a history of falls (meets Beers Criteria). The concomitant use of methylene blue can increase the risk of fatal serotonin syndrome (see breast surgery pathways).[461]

MONITORING: Monitor for serotonin syndrome and interactions with other medications. Do not discontinue abruptly if the patient has been taking the drug for an extended period of time; gradual dose reduction is recommended.

ANTIPSYCHOTICS

EVIDENCE: While agents like haloperidol and droperidol can reduce PONV, there is less evidence to suggest a correlation between pain and opioid consumption.[462–464] One study of gastric sleeve surgery patients did, however, find that haloperidol, when combined with ondansetron and dexamethasone, not only reduced PONV but also decreased morphine consumption.[465] The chronic use of the atypical antipsychotics (e.g., olanzapine, aripiprazole, risperidone) in patients undergoing elective noncardiac surgeries is also associated with a reduced risk of PONV.[466] Olanzapine is also validated for the prevention and treatment of chemotherapy-induced nausea.[467–471] In general, it seems reasonable in appropriate patients to consider adding a low-dose antipsychotic as part of the perioperative plan to reduce PONV, which may possibly attenuate pain.

MECHANISM OF ACTION: Haloperidol and droperidol are butyrophenone antipsychotics. Their antiemetic effect stems from the blockade of dopamine stimulation of the chemoreceptor trigger zone. Second-generation or atypical antipsychotics (most commonly olanzapine) display antagonism of serotonin 5-HT, dopamine, histamine and alpha1-adrenergic receptors.

OPTIONS AND DOSING: Haloperidol 2-5 mg PO/IM/IV, olanzapine 5 mg PO/IM/IV, droperidol 0.625-1.25 mg IV,[472] all may be given during the perioperative period.
CONTRAINDICATIONS AND CAUTIONS: Haloperidol has a black box warning for increased mortality in elderly patients with dementia-related psychosis; droperidol has a black box warning for QT prolongation, serious arrhythmias and torsades de pointes. It is recommended that both agents be used with extreme caution or avoided altogether in patients at risk. Olanzapine can also cause QT prolongation but to a lesser extent. Of note, all agents are recommended at low doses that should convey less risk of side effects.
MONITORING: Monitor for QT prolongation and conduction abnormalities, dystonic reactions and neuroleptic malignant syndrome.

Anxiolytics

BENZODIAZEPINES

EVIDENCE: Multiple studies have shown the preoperative administration of benzodiazepines to be ineffective for reducing postoperative anxiety and pain; some studies show negative effects, including increased time to extubation and recovery.[473–476] However, it may be appropriate to consider a low-dose benzodiazepine for select patients with extreme preoperative anxiety, as significant anxiety may contribute to pain.[477,478]
MECHANISM OF ACTION: Binds to benzodiazepine receptors linked to the GABA-A receptors, enhancing the inhibitory effects of GABA on neuronal excitability.
OPTIONS AND DOSING: Lorazepam 1-2 mg PO/IV once preoperatively and every six hours as needed postoperatively; diazepam 5-10 mg PO/IV once preoperatively and every six hours as needed postoperatively. Midazolam 1-2 mg once preoperatively may be considered, but is typically not recommended for routine use outside of the operative setting.
CONTRAINDICATIONS AND CAUTIONS: Use caution when used concomitantly with other potential CNS depressants. Black box warning: Concomitant use with opioids or other CNS depressants can result in profound sedation, respiratory depression, coma and death.
MONITORING: Monitor for CNS and respiratory depression, and evaluate hepatic function.

CLONIDINE

EVIDENCE: Small oral doses of preoperative clonidine have been found to be effective for attenuating preoperative anxiety and reduce postoperative pain and opioid consumption. One study in abdominal hysterectomy patients found clonidine 0.1 mg administered orally as effective as oral melatonin at reducing preoperative anxiety, postoperative pain and postoperative opioid consumption.[479] Another study in abdominal hysterectomy patients found preoperative oral clonidine 0.1 mg to have a clinically relevant anxiolytic effect and may be a suitable alternative to other preoperative sedatives.[480] A preoperative oral clonidine 0.2 mg dose has also been found to be as effective as gabapentin in producing preoperative sedation.[481] A study comparing temazepam, clonidine and timolol as preanesthetic medications in patients undergoing minor orthopedic surgery found all three lowered preoperative anxiety and clonidine and temazepam reduced postoperative pain.[424] Overall, it is reasonable to consider a preoperative dose of oral clonidine 0.1 mg to reduce anxiety in patients undergoing surgery, and it may also reduce postoperative pain and opioid consumption. **(SEE ALPHA-2 AGONIST SECTION ABOVE FOR MORE INFORMATION.)**

GABAPENTIN

EVIDENCE: Premedicating highly anxious patients with gabapentin (1200 mg) may reduce preoperative anxiety and pain catastrophizing.[482] Premedication with gabapentin (1200 mg) appears to be more effective than hydroxyzine and placebo for the reduction of preoperative anxiety and may lead to greater patient satisfaction.[483] Gabapentin (typically 300-600 mg/dose) is part of many surgical pathways due to its opioid-sparing and pain-attenuating effects. It may be reasonable to give highly anxious patients a higher preoperative dose (e.g., 1200 mg). **(SEE THE GABAPENTINOID SECTION BELOW FOR MORE INFORMATION.)**

MELATONIN

EVIDENCE: Premedication with melatonin may reduce preoperative anxiety in adult patients and is as effective as standard treatment with midazolam.[241-244] One study in patients undergoing hysterectomy found that preoperative melatonin also reduced morphine requirements, suggesting that administration may attenuate pain too.[479] Additional in vitro, animal and preclinical evidence further

suggests that melatonin may have analgesic potential, but further research is needed.[241-244,484] Due to the overwhelming safety profile of melatonin and emerging supportive literature, premedication can be considered for highly anxious patients.

MECHANISM OF ACTION: Binds to the MT1, MT2 and MT3 receptors, which may contribute to the agent's sleep-promoting properties. Its ability to reduce anxiety is thought to be due to its effects on the pineal gland, which impair contextual fear conditioning.[485]

DOSING: 6 mg PO once 60-90 minutes prior to surgery.

MONITORING: Melatonin, particularly as a single dose, is exceedingly safe.

APAP

EVIDENCE: Acetaminophen has been demonstrated in clinical trials and systematic reviews to reduce postoperative opioid use by as much as 30% four hours after some surgical procedures.[195-201] In five randomized controlled trials, APAP significantly lowered pain compared to placebo without increased adverse events. Number needed to treat to achieve pain relief is four.[486] The American Society of Anesthesiologists' 2012 *Practice Guidelines for Acute Pain Management in the Perioperative Setting* recommends including APAP in an around-the-clock, multimodal regimen for the management of postoperative pain (unless contraindicated).[192]

MECHANISM OF ACTION: Although not completely understood, it is theorized to be due to an inhibition of central prostaglandin synthesis (specifically COX-2) and an elevation of the pain threshold.

DOSING: APAP 1000 mg by mouth once prior to surgery. APAP 650-1000 mg per dose, can be given three to four times daily.

CONTRAINDICATIONS AND CAUTIONS: Life-threatening cases of acute hepatic failure leading to liver transplant or death have been linked with APAP use. In most cases of hepatic injury, APAP doses exceeded maximum daily limits and often involved the use of more than one APAP-containing product.

HEPATIC DOSING: For patients with cirrhosis with stable liver function tests (LFTs), reduce the total daily dose to 2 g (expert opinion).[487]

MONITORING: Check LFTs, especially in patients with pre-existing liver disease.

SPECIAL CONSIDERATIONS: APAP has a high bioavailability when administered orally and rectally. It is recommended that IV APAP not be used unless the drug cannot be administered via oral or rectal routes; a 2015 systematic review concluded that there is little evidence for using IV acetaminophen over oral acetaminophen in patients that are able to take medications by mouth perioperatively.[488] While IV APAP may be of utility in surgeries lasting more than six hours, a dose of 1000 mg IV APAP costs approximately $40, compared to pennies for a dose of oral or rectal APAP.

DISCHARGE INSTRUCTIONS: Instruct the patient to avoid other over-the-counter products that contain APAP and to limit the total daily dose to less than 4,000 milligrams.

Atypical Opioids

TAPENTADOL

EVIDENCE: A meta-analysis of three randomized, multicenter trials found that patients who received immediate-release tapentadol had similar improvements in pain scores in the first 24-48 hours following surgery and better tolerability than those taking immediate-release oxycodone and morphine.[489]

MECHANISM OF ACTION: Tapentadol is a combination mixed opioid agonist with norepinephrine reuptake inhibition that works on descending (norepinephrine) and ascending (opioid) pain pathways.

SPECIAL CONSIDERATIONS: Among its many FDA-approved indications, tapentadol is the only "opioid" endorsed for the treatment of diabetic peripheral neuropathy; it is also approved for the management of acute postoperative pain.[490,491] Tapentadol is associated with a 65% lower risk of abuse than oxycodone.[492] Diversion rates based on drug availability are an estimated 0.03 (immediate-release formulations) per 1,000 prescriptions dispensed; other Schedule II opioids are diverted almost six to 10 times more frequently at 0.172 per 1,000 prescriptions.[493] In addition, fewer than 5% of patients experience withdrawal symptoms when abruptly stopping tapentadol.[491]

RECOMMENDATION: Tapentadol is available in both immediate- and extended-release formulations. A dose of 50-100 mg can reduce pain with the same efficacy as approximately 10-20 mg of oxycodone.[494] For patients undergoing surgical procedures that are expected to result in moderate-to-severe postsurgical pain requiring

more than 48 hours of postoperative opioids, immediate-release tapentadol may be considered to replace typical opioid choices (e.g., immediate-release oxycodone, hydromorphone or morphine) due to its better safety profile.[491,494,495]

CONTRAINDICATIONS AND CAUTIONS: Do not use in patients with significant respiratory depression, asthma or hypercarbia and known or suspected GI obstruction or ileus and those who use monoamine oxidase inhibitors (MAOIs) or have taken them within the last 14 days.

TRAMADOL

EVIDENCE: A systematic review and meta-analysis of adult surgical patients did not find significant clinical benefits from the combination of IV tramadol and morphine after surgery. (Note: Tramadol is only available as an oral formulation in the Unites States.)[496]

MECHANISM OF ACTION: Tramadol is a weak opioid mu-receptor agonist that also has nonopioid-receptor actions. In addition to its actions at the opioid receptors, the drug provides analgesia by inhibiting the reuptake of serotonin and norepinephrine.

SPECIAL CONSIDERATIONS: Prescribing tramadol requires an understanding of its unique nuances to ensure patient safety. The response to tramadol varies widely due to individual genetic polymorphisms, specifically at CYP2D6. At recommended doses, the drug is less effective in patients who are deemed "poor metabolizers" of CYP2D6.[497] In addition, the CYP2D6 enzymes are responsible for the metabolism of many other medications, including serotonin antagonists (e.g., ondansetron) used to treat postoperative nausea and vomiting, serotonin receptor antagonists (SSRIs) and serotonin norepinephrine receptor antagonists (SNRIs [such as venlafaxine and duloxetine]), tricyclic antidepressants (TCAs), MAOIs, antipsychotics (e.g., haloperidol), migraine medications (e.g., "triptans") and antiarrhythmics. Interactions between tramadol and other medications, such as serotonergic antidepressants, may decrease the efficacy of the drugs and increase the risk of serotonin syndrome.[498] Even at subtherapeutic concentrations, tramadol also lowers the seizure threshold, even in those without a prior history of seizures.[498] If stopped abruptly, tramadol may induce withdrawal symptoms due to its actions on the opioid, norepinephrine and serotonin receptors.[498] Contrary to prior assumptions, tramadol carries a risk of abuse and dependence.[498] In fact, the World Health Organization (WHO) published a 2014 report highlighting the medication's addiction potential and the growing incidence of abuse in some African and West Asian countries.[499]

RECOMMENDATION: Prescribing tramadol for postoperative pain requires an understanding of the drug's unique characteristics, including interpatient variability due to known genetic polymorphisms, drug-drug interactions leading to serotonin syndrome, the potential for seizures, the risk of dependence or abuse and the likelihood of withdrawal symptoms with the abrupt cessation of therapy. Due to these concerns the perioperative use of tramadol is not recommended.

Beta Blockers

ESMOLOL

EVIDENCE: Two randomized controlled trials have shown comparable or even favorable outcomes when esmolol is used in lieu of opioids for the control of sympathetic nervous system responses to noxious stimuli under general anesthesia.[308,500] A recent meta-analysis of intraoperative esmolol showed that its use reduced intraoperative and postoperative opioid use but had no effect on postoperative pain scores.[273] Another review found that perioperative esmolol reduced postoperative pain intensity, opioid consumption and rates of nausea and vomiting.[272]

MECHANISM OF ACTION: Recent studies suggest that esmolol may have antinociceptive and postoperative opioid-sparing effects, though exact mechanism is unknown; both pharmacokinetic and pharmacodynamic interaction with other anesthetic agents have been proposed.

DOSING: 0.01-0.05 mg/kg/min continuous infusion throughout surgery. May consider an initial bolus of 0.5 mg/kg given over 60 seconds.

CONTRAINDICATIONS AND CAUTIONS: Avoid use in patients with decompensated heart failure, pulmonary hypertension, second- or third-degree atrioventricular block, severe sinus bradycardia and sick sinus syndrome.

MONITORING: Monitor blood pressure and heart rate to assess clinical response.

Gabapentinoids

GABAPENTIN

EVIDENCE: Use of gabapentin in the perioperative period may improve pain outcomes and has been shown to reduce postoperative opioid requirements and promote opioid cessation after surgery.[30,239,288,501-508] Two large meta-analyses demonstrated lowered pain scores and/or opioid requirements with preoperative gabapentin treatment for the first 24 hours following surgery.[239,509] Dosing regimens vary widely among studies included in these meta-analyses, and no concrete determination can be made of optimal gabapentin dosing.[510,511] Several meta-analyses of total knee and hip arthroplasty patients have also found an opioid-sparing effect with the use of gabapentin.[512-514] It is suggested the drug be considered as part of perioperative multimodal pain management regimen per the American Society of Anesthesiologists' 2012 *Practice Guidelines for Acute Pain Management in the Perioperative Setting*.[192]

MECHANISM OF ACTION: Structurally related to the neurotransmitter GABA. Thought to inhibit alpha 2-delta subunit of voltage-gated calcium channels, which are believed to decrease the conduction of neuropathic pain sensations.

DOSING: Dosing varies widely in studies, but typically a starting dose of 300-600 mg preoperatively, followed by 300-600 mg PO one to three times daily. Dosing recommendations are influenced by renal function.

CONTRAINDICATIONS AND CAUTIONS: Avoid gabapentin in older adults with a history of falls, as it may cause syncope, impaired psychomotor function, dizziness and ataxia. Gabapentin has shown to increase risk of respiratory depression.[515] A number of studies show an increased risk of ORADEs and overdose death when gabapentin and opioids are used concurrently.[516,517] In December 2019 the FDA issued a black box warning for concurrent use of gabapentinoids and opioids or other CNS depressants.[91]

MONITORING: Evaluate serum creatinine levels, watch for sedation.

PREGABALIN

EVIDENCE: A meta-analysis of 43 studies reported a modest reduction in analgesic requirements and postoperative pain with perioperative pregabalin use.[508] An earlier meta-analysis found reductions in postoperative opioid requirements and ORADEs.[518] Meta-analyses of total knee and hip arthroplasty patients have found an opioid-sparing effect with the use of pregabalin.[513,519] A placebo-controlled trial showed equivalent analgesic benefit of preoperative pregabalin and gabapentin for shoulder pain in the 48 hours following laparoscopic cholecystectomy.[520] A RCT comparing pregabalin and gabapentin found a greater decrease in pain and opioid consumption after laparoscopic cholecystectomy in the pregabalin group compared to gabapentin group, with both gabapentinoids showing superiority to placebo.[521] It is suggested that the drug be considered as part of a perioperative multimodal pain management regimen per the American Society of Anesthesiologists' 2012 *Practice Guidelines for Acute Pain Management in the Perioperative Setting*.[192]

MECHANISM OF ACTION: GABA analog that strongly binds to the alpha (2)-delta site (a subunit of voltage-gated calcium channels) in CNS tissues, reducing pronociceptive neurotransmitters. May also interact with descending noradrenergic and serotonergic pathways in the brainstem that modulate pain transmission in the spinal cord.

DOSING: Pregabalin has better oral bioavailability and a faster onset of action (one hour versus three hours with gabapentin). Dosing recommendations vary widely (50-300 mg) in the perioperative period. A reasonable preoperative starting dose is 150 mg for healthy patients; for patients with renal dysfunction and those older than 65 years, reduce to 50-75 mg, then followed by the same dose one to two times daily.[518] Dosing recommendations are influenced by renal function.

CONTRAINDICATIONS AND CAUTIONS: Avoid pregabalin in older adults with a history of falls, as it may cause syncope, impaired psychomotor function, dizziness and ataxia. In December 2019, the FDA issued a black box warning for concurrent use of gabapentinoids and opioids or other CNS depressants.[91]

MONITORING: Assess serum creatinine levels and monitor for signs of peripheral edema.

DISCHARGE: Pregabalin poses a risk of misuse and abuse, requires a DEA waiver (as it is a schedule V controlled substance), and may be cost prohibitive.

GLUCOCORTICOIDS

EVIDENCE: Dexamethasone given perioperatively at doses greater than 0.1 mg/kg may produce a dose-dependent reduction in postoperative pain and an opioid-sparing effect.[522] The preoperative administration of the drug produces more consistent pain outcomes. A single dose of preoperative dexamethasone has been associated with reduced opioid use and a small but statistically significant analgesic benefit at two and 24 hours postoperatively.[523] Dexamethasone produces a dose-dependent opioid-sparing effect in the general surgical setting and is particularly effective for reducing pain scores with dynamic movement; these effects have been produced with a single dose of dexamethasone between 10-40 mg with few serious side effects.[524-526] A recent trial showed that preoperative high-dose methylprednisolone reduces postoperative pain, nausea and fatigue without increasing the risk of complications in patients undergoing VATS lobectomy.[385] Low- to moderate-quality evidence suggests that dexamethasone used in the perioperative period may reduce pain scores and opioid consumption at 12, 24 and 48 hours in patients undergoing total joint arthroplasty.[527]

MECHANISM OF ACTION: Glucocorticoids (e.g., dexamethasone and methylprednisolone) have analgesic, antiemetic, antipyretic and anti-inflammatory effects.

DOSING: Doses of greater than or equal to 0.1 mg/kg are most effective, though minimal additional benefit is seen in doses greater than 0.2 mg/kg. It is recommended that the initial dose be given pre- or perioperatively; therapy may be continued postoperatively for up to 24 hours.

COMPLICATIONS: Risks of glucocorticoid use include gastric irritation, impaired wound healing, impaired glucose homeostasis and sodium retention.

SURGICAL-SPECIFIC COMPLICATIONS AND CONCERNS: Data regarding the relationship between perioperative corticosteroid use and the risk of anastomotic leaks is inconsistent. However, a systematic review of 12 studies demonstrated a significantly higher rate of anastomotic leaks in patients who received corticosteroids in the preoperative period compared with those who did not (6.8% vs 3.3%).[528]

CONTRAINDICATIONS AND CAUTIONS: Due to the abbreviated nature of glucocorticoid therapy, relative contraindications are of lesser concern; these include adrenal suppression, immunosuppression, myopathy and psychiatric disturbances.

MONITORING: Due to </= 24 hours of therapy, blood glucose monitoring is the only consideration in high-risk patients.

DISCHARGE: Prolonged treatment with glucocorticoids is not recommended due to complications and side effects, and it is suggested that most surgical patients discontinue therapy after 24 hours.

MUSCLE RELAXANTS (e.g., cyclobenzaprine, metaxalone, methocarbamol)

EVIDENCE: While there is little evidence to support the use of muscle relaxants for analgesia in the perioperative period, surgeons may encounter patients with painful muscle spasms associated with laparoscopies, laparotomy incisions, rib fractures, thoracotomies or trauma. Providers may also treat patients already taking muscle relaxants for lower back pain or other musculoskeletal conditions. Although there is no evidence to support the superiority of one muscle relaxant over another, cyclobenzaprine has been shown to be effective for the treatment of various musculoskeletal conditions.[529,530] It is recommended that the appropriate agent be chosen according to its pharmacokinetic profile, side-effect profile, abuse potential and possible interactions.

MECHANISM OF ACTION: Cyclobenzaprine is structurally related to tricyclic antidepressants (TCAs); it acts at the brain stem within the CNS to influence both gamma and alpha motor systems by reducing tonic somatic motor activity. The effects of metaxalone and methocarbamol may be associated with general CNS depression.

DOSING: Cyclobenzaprine 5-10 mg PO three times daily. Metaxalone 800 mg PO three to four times daily. Methocarbamol 750-1500 mg PO three to four times daily. Agents are typically given on an as-needed basis.

CONTRAINDICATIONS AND CAUTIONS: Do not use cyclobenzaprine in the acute recovery period following a myocardial infarction, in patients with arrhythmias or congestive heart failure; concomitant use with MAOI within 14 days is contraindicated. All three agents meet the Beers Criteria.

MONITORING: Watch for CNS-depressive effects, particularly if combined with other sedating medications.

NMDA Receptor Antagonists

DEXTROMETHORPHAN

EVIDENCE: A meta-analysis of 14 trials and 848 patients suggests that perioperative dextromethorphan use reduced postoperative opioid consumption at 24 to 48 hours and pain scores at one, four to six and 24 hours.[248] It may also attenuate the sensation of acute pain at doses of 30-90 mg, without major side effects, and reduce the amount of analgesics required in 73% of postoperative patients.[250] A study in abdominal hysterectomy patients found both a preoperative 40 mg oral dose and postoperative 40 mg PO three times daily for two days to be analgesic-sparing and attenuate pain.[531] Similar results were found with a three-day regimen of 90 mg PO daily (starting preop) in patients undergoing surgery for bone malignancy.[532] Patients who receive dextromethorphan 40 mg IM plus a lidocaine infusion (3 mg/kg/hr) appear to have better pain relief and a faster recovery of bowel function than those who take either drug alone or other active analgesic agents.[293] Of note, the injectable formulation is not available in the United States, and dextromethorphan can only be administered enterally.
MECHANISM OF ACTION: N-methyl-D-aspartate (NMDA) receptor antagonist that binds to receptor sites in the spinal cord and CNS, thereby blocking the generation of central acute and chronic pain sensations that arise from peripheral nociceptive stimuli and reducing the amount of analgesics required for pain control.
COMPARED TO KETAMINE: Although ketamine is widely used as a multimodal adjunct worldwide, dextromethorphan does not appear to share the same level of popularity and is rarely used as an adjunct for postoperative analgesia. The use of dextromethorphan perioperatively may provide similar benefits to preemptive ketamine therapy in a simple oral, intramuscular or IV formulation. Further investigation, particularly a head-to-head randomized trial alongside placebo, may help clarify whether the different NMDA antagonists provide similar levels of relief with a similar incidence of dysphoric or other side effects. Additional research may also explore whether the simultaneous use of more than one NMDA receptor antagonist offers any benefits, as it is unclear whether this approach can result in additive, synergistic or antagonistic effects.[248] In those patients thought to particularly benefit from the use of IV ketamine in the perioperative period, it may be reasonable to transition to an oral NMDA agent, such as dextromethorphan, for continued pain relief. The dosing recommendation made in these guidelines is dextromethorphan 40 mg PO three times daily, which may be reasonable to continue for up to seven days in some patients.[531]
DOSING: 30-90 mg PO administered 30-90 minutes prior to surgery. Doses of 40 mg PO three times daily have also been studied for two days following surgery.
CONTRAINDICATIONS AND CAUTIONS: Avoid in patients taking MAOIs and within 14 days of MAOI use.
MONITORING: May cause dizziness or somnolence. Additional monitoring is not required.
DISCHARGE: Dextromethorphan has not been studied at discharge, but oral formulations may be considered for the continued postoperative treatment of patients who have experienced significant relief from other IV NMDA antagonists (e.g., ketamine).

KETAMINE

EVIDENCE: A large meta-analysis concluded that ketamine reduces pain intensity and analgesic use across multiple different settings and surgeries and likely decreases PONV without increasing side effects.[533] Ketamine IV is associated with lower postoperative opioid requirements and, in most studies, less postoperative pain in opioid-tolerant patients.[278-280,534-536] IV ketamine has also been associated with a lower risk of CPSP.[535,537] While current literature does not support the routine use of IV ketamine for every surgical case, it is reasonable to use the agent to treat patients with preexisting pain, those on COT and those who are predicted to have difficult-to-control postoperative pain (assuming no contraindications exist). Outside the perioperative setting, most studies on ketamine for the treatment of acute or chronic pain are small, uncontrolled and either unblinded or ineffectively blinded; in addition, patient selection, dosing and the route of administration differ across studies. The use of intranasal ketamine in the emergency department for the management of acute traumatic pain and renal colic has been validated, as has use of the drug in the surgical setting following molar extractions and pediatric tonsillectomies.[538-541] Oral ketamine also appears to be moderately effective for certain pain conditions, none of which routinely occur in the acute postoperative period.[542] Intranasal and oral dosing may be considered when clinical

judgment deems the continued use of ketamine be of benefit and the risks or restrictions of IV ketamine pose a barrier.

MECHANISM OF ACTION: Ketamine antagonizes N-methyl-D-aspart (NMDA) receptors in the CNS.

DOSING: Typically, the effective IV bolus dose is 0.1-0.5 mg/kg in the surgical setting, followed by an infusion of 0.1-0.5 mg/kg/hr throughout surgery. Dosing is highly related to concomitant anesthetic and analgesic agents, and much higher ketamine doses may be used for sedation while lower doses (typically less than or equal to 0.3 mg/kg) may avoid psychomimetic side effects. Following surgery, a continuous infusion of 0.1-0.3 mg/kg/hr may be continued based on the provider's discretion and hospital policy. Due to the lack of readily available oral ketamine products, it is reasonable to start considering the discontinuation of an IV ketamine infusion following surgery within 24-48 hours. Intranasal ketamine is typically dosed at 0.5 mg/kg (max 50 mg) IN once. Of note, the half-life of IN ketamine is short, and IN dosing will only provide temporary relief. Repeated IN doses are an unreasonable form of continued pain control. Oral dosing can be initiated at 0.25-0.5 mg/kg/dose and administered every four to eight hours; the half-life of orally administered ketamine is six to 10 hours.

CONTRAINDICATIONS AND CAUTIONS: Avoid in patients with seizure disorders, psychosis, poorly controlled hypertension, heart failure, arrhythmia, increased intracranial pressure (e.g., brain lesions, intracranial bleeding), a recent stroke, severe respiratory insufficiency or post-traumatic stress syndrome. Ketamine can cause dose-dependent sedation.

ADVERSE EFFECTS: Hypertension, tachycardia, myocardial depression, increased intracranial pressure, vivid dreams, anxiety, hallucinations, tremors, tonic-clonic movements, nausea and sedation.

MONITORING: If used in the postoperative period, it is recommended to check vital signs 15, 30 and 60 minutes following the start of infusion (or the administration of a bolus dose), then every four hours for remainder of the infusion. In the case of acute changes in vital signs or intolerable psychomimetic effects, stop ketamine and consider the administration of benzodiazepines to manage psychomimetic effects.

DISCHARGE: Due to the unavailability of ketamine products in the outpatient setting, it is recommended that ketamine be tapered and discontinued prior to discharge. If ketamine is used for more than 48-72 hours, consider a taper prior to discontinuation. Ketamine is a Schedule III drug with potential for abuse.

MAGNESIUM SULFATE

EVIDENCE: A meta-analysis of use of perioperative IV magnesium sulfate in 20 RCTs demonstrated improved postoperative pain both at rest and with movement as well as reduced opioid requirements. The greatest benefit was seen in patients who received magnesium both intraoperatively and postoperatively. None of the included studies reported toxicity.[274] Another meta-analysis found lower postoperative pain scores four to six hours after surgery and reduced opioid use in surgical patients receiving magnesium sulfate.[275] Magnesium sulfate can be a useful analgesic adjunct in patients receiving TIVA. It appears to reduce propofol, atracurium and postoperative morphine consumption in gynecologic surgical patients.[543] In a study of gynecologic patients undergoing laparotomy under TIVA, pain scores, analgesic consumption and shivering incidents were lower in the magnesium group than in the control group, and it was concluded that magnesium sulfate improved the quality of postoperative analgesia during TIVA.[544] Magnesium may also reduce the requirements for propofol, rocuronium and fentanyl in spinal surgical patients.[276] In addition, magnesium infusions during spinal anesthesia have been shown to improve postoperative analgesia and reduce the cumulative consumption of analgesics after total hip replacement arthroplasty.[545] Postoperative IV magnesium sulfate infusions may also increase the time to analgesic need and reduce the total consumption of analgesics required after spinal anesthesia.[546] In major non-laparoscopic GI surgeries, magnesium has been shown to decrease postoperative ileus and pain.[547] Due to the high therapeutic index and relative cost effectiveness of magnesium, the agent may be a reasonable addition to many pain management regimens and can be routinely recommended in major abdominal surgeries.[277]

MECHANISM OF ACTION: Magnesium is thought to blunt somatic, autonomic and endocrine reflexes provoked by noxious stimuli during surgery.

DOSING: Usual regimens of magnesium sulfate IV include a loading dose of 30-50 mg/kg followed by a maintenance dose of 6-20 mg/kg/hr (continuous IV infusion) until the

end of surgery. However, a single bolus of magnesium without a maintenance infusion may also be effective for postoperative analgesia. Magnesium has a relatively large therapeutic index, with concerns of accumulation mostly in the renally impaired population.

CONTRAINDICATIONS: Avoid in patients with heart block and use caution when using prolonged infusions in patients with renal impairment.

MONITORING: Cardiovascular monitoring is recommended to prevent hypotension. Slow administration (>10 minutes) of the loading dose of magnesium sulfate may minimize cardiovascular side effects, such as hypotension and bradycardia. It is recommended that blood pressure be monitored at least every three to five minutes during rapid administration.

DISCHARGE: Magnesium is available in multiple oral formulation, but caution is advised regarding the risk of diarrhea. Oral magnesium supplementation may be appropriate for some patients after discharge.

NSAIDS

EVIDENCE: NSAIDs (e.g., ibuprofen, ketorolac, celecoxib, meloxicam) have been shown to decrease opioid consumption and occurrence of opioid-related side effects.[202] A review of multimodal anesthesia concluded that 600 mg of ibuprofen is as effective as 15 mg of oxycodone hydrochloride.[183] In a meta-analysis of 52 randomized trials of multimodal analgesia with nonopioid analgesics, use of NSAIDs reduced opioid consumption, pain intensity, nausea and vomiting and sedation compared with morphine alone.[548] A 2005 meta-analysis reported that NSAIDs in conjunction with opioid treatment significantly decreased pain scores and morphine requirements 24 hours postoperatively, with a decrease in morphine consumption at 24 h of 50% with the COX-2 inhibitor rofecoxib and by 40% with other NSAIDs. The authors found that the addition of NSAIDs or COX-2 inhibitor to a multimodal analgesic regimen also decreased the incidence of PONV, and sedation in both small and large surgeries.[548]

NONSELECTIVE NSAIDS: Administration of ketorolac reduces opioid consumption by 25% to 45%, thereby reducing opioid-related side effects, including ileus, nausea and vomiting.

MECHANISM OF ACTION: NSAIDs inhibit proinflammatory prostaglandin production via the inhibition of COX-1 and COX-2 enzymes.

OPTIONS: Ibuprofen, naproxen, ketorolac, diclofenac, indomethacin and selective COX-2 inhibitors (e.g., meloxicam, celecoxib). Topical options include diclofenac 1% gel or 1.3% patch.[549]

DIFFERENT SIDE EFFECT PROFILES: In general, COX-2 selective NSAIDs (celecoxib, meloxicam) have a lower risk of GI and bleeding side effects but a higher risk of cardiac side effects (e.g., myocardial infarction (MI) and stroke).[550,551] Nonselective NSAIDs (naproxen, ibuprofen) have a lower risk of cardiac complications but a higher risk of GI and bleeding side effects. While it is reasonable to recommend the use of a nonselective NSAID (e.g., ketorolac) preoperatively or at induction in most surgical cases where NSAID use is desired, it is advised that the risk of GI side effects and bleeding be considered. It is suggested that COX-2 selective NSAIDs (e.g., celecoxib) be used for high-risk patients without cardiovascular contraindications. In some patients and for some high-risk surgeries in which blood loss is of concern, it may be reasonable to withhold NSAIDs altogether.

SURGERY-SPECIFIC COMPLICATIONS AND CONCERNS:

Anastomotic leak after colorectal surgery: Postoperative NSAID use may increase the risk of anastomotic leaks.[552,553] Potential mechanisms include a reduction in prostaglandin-mediated collagen deposition, diminished collagen cross-linking and increased anastomotic microthrombosis. One study found that patients who received NSAIDs perioperatively during primary colorectal anastomosis had higher rates of anastomotic leakage than those not taking NSAIDs (13.2 vs 7.6%, p = 0.010); this effect was primarily associated with nonselective NSAIDs (14.5%), not selective COX-2 inhibitors (9%). There was no effect on mortality.[554] Another study of patients undergoing colorectal surgery, however, failed to find an association between ketorolac use and anastomotic leakage.[555] A meta-analysis of six randomized controlled trials showed similar dehiscence rates between no-NSAID and NSAID-treated patients undergoing colorectal surgery (P=0.17).[556] NSAIDs may be useful for reducing perioperative opioid requirements in colorectal surgery patients; however, current studies are examining whether these medications have an adverse effect on anastomotic healing.

Postoperative kidney function: Literature on the effect of perioperative NSAID use on postoperative kidney function in patients with normal kidney function is somewhat mixed. NSAIDs appear to have uncertain effects on the

risk of postoperative acute kidney injury, but they may slightly increase postoperative serum creatinine levels. It is uncertain whether NSAIDs elevate the need for renal replacement therapy, increase the risk of death or increase lengths of hospital stay.[557] In general, clinical judgment must be used when considering perioperative NSAIDs. Most clinicians agree that NSAIDs be avoided in those with renal dysfunction.

Postoperative bleeding: Literature is somewhat mixed on the association of NSAIDs and the risk of clinical postoperative bleeding, but most experts support the use of NSAIDs for many surgical patients in whom the concern for bleeding is relatively low.[551] The antiplatelet effects of NSAIDs are caused by the reversible inhibition of COX-1. The relationship between the time of NSAID discontinuation and perioperative clinical bleeding is not well-defined, as the elimination half-life of each medication correlates poorly with COX inhibition and platelet aggregation. A long-held belief has been that NSAIDs, particularly ketorolac, increase the risk of surgical bleeding. However, more recently ketorolac was not shown to increase incisional or GI bleeding in patients under 75 years old.[558] Recent meta-analyses in pediatric neurosurgery patients and plastic surgery patients both found no increased risk of postoperative bleeding.[559,560] The risk of operative site bleeding with ketorolac versus parenteral opioids in the perioperative setting appears to be comparable.[561] The risk of GI bleeding and bleeding at the operative site with ketorolac may be dose-related and higher in patients older than 75 years. The risk of GI bleeding (but not postoperative surgical site bleeding) is associated with the duration of administration; it is recommended that ketorolac be given for no more than five days. In contrast, highly selective inhibitors of COX-2 have little or no effect on platelets, making these agents the first-line treatment for patients at high risk of perioperative bleeding; however, such decisions must be balanced with the increased cardiovascular risk associated with COX-2 selective agents.

CONTRAINDICATIONS AND CAUTIONS: NSAIDs can increase the risk of myocardial infarction and stroke. They are contraindicated in those who have suffered a myocardial infarction or underwent recent coronary artery bypass graft surgery. These medications can also increase the risk of GI-related complications, including bleeding, ulceration and perforation of the stomach or intestines. This risk is especially pronounced in the elderly (Beers Criteria) and in patients with prior peptic ulcer disease or GI bleeding. Caution is advised for patients on concomitant anticoagulants or antiplatelet agents. Avoiding use in patients with chronic kidney disease, cirrhosis or heart failure is recommended. The risk of renal injury is higher in patients who are elderly, dehydrated or suffer from other comorbidities, including heart failure, diabetes and cirrhosis.

SPECIAL CONSIDERATIONS: It is suggested that use of ketorolac be limited to five days, given its GI risks, and limited to 15 mg every six hours in patients who are older than 65 years or weigh less than 50 kg as well as and in those with moderately elevated serum creatinine.

MONITORING: Check serum creatinine levels and discuss any history of GI ulceration prior to initiation.

RECOMMENDED DURATION OF USE: The American Society of Anesthesiologists' *Practice Guidelines for Acute Pain Management in the Perioperative Setting* recommends an around-the-clock NSAID regimen (either COX-2 selective or nonselective) for postoperative pain management unless contraindicated. Use the lowest effective dose for the shortest possible duration.

(TABLE 10)

Risk of Gastric Ulcer Bleeding with NSAIDs[562]

INDIVIDUAL NSAID	ADJUSTED CONDITIONAL RR (95% CI)
LOW	
Celecoxib	1.0 (0.4-2.1)
Ibuprofen	4.1 (3.1-5.3)
Naproxen	7.3 (4.7-11.4)
Indomethacin	9.0 (3.9-20.7)
HIGH	
Ketorolac	14.4 (5.2-39.9)

SOURCE: Lanas A, García-Rodríguez LA, Arroyo MT, et al. Risk of upper gastrointestinal ulcer bleeding associated with selective cyclo-oxygenase-2 inhibitors, traditional non-aspirin non-steroidal anti-inflammatory drugs, aspirin and combinations. Gut. 2006;55(12):1731-1738. doi:10.1136/gut.2005.080754

(TABLE 11)

GI Risk Factor Assessment and NSAID Therapy[563]

GI RISK FACTOR ASSESSMENT	TREATMENT
HIGH RISK History of previously complicated ulcer, especially recent ***OR*** more than two risk factors: • Age >65 years • High-dose NSAID therapy • Previous history of uncomplicated ulcers or • Concurrent use of aspirin, corticosteroids or anticoagulants	Alternative therapy or COX-2 inhibitor + PPI
MODERATE RISK • 1 - 2 risk factors	NSAID + PPI
LOW RISK • No risk factors	NSAID alone

SOURCE: American College of Gastroenterology Guidelines, 2009

Pharmaceutical Agents with Analgesic Potential

While all of the pharmacologic agents listed are backed by supporting (albeit occasionally limited) literature, there are several interesting agents that currently lack sufficient evidence but may be useful for certain patients. They include:

ANTIPSYCHOTICS

See above.

ASCORBIC ACID (VITAMIN C)

EVIDENCE: Moderate-level evidence suggests that a preoperative dose of vitamin C can be used as an adjunct for its opioid-sparing abilities; surgical types included a 50-mg/kg dose in laparoscopic colectomy and a 2 g dose in laparoscopic cholecystectomy.[564-566] Evidence also supports a 50-day course of vitamin C supplementation for the prevention of complex regional pain syndrome after extremity surgery.[567]
MECHANISM OF ACTION: Vitamin C is thought to exert its antinociceptive effects primarily based on antioxidant properties by scavenging a wide range of reactive oxygen species, thereby protecting cells, tissues and nerves from oxidative damage.
SPECIAL CONSIDERATIONS: Additional studies are needed to determine the overall effectiveness and optimum dosage of vitamin C. Ascorbic acid is generally safe, and its potential benefits likely outweigh any potential risks.

CAFFEINE

EVIDENCE: A meta-analysis of available RCTs concluded that, when added to other analgesics, caffeine (doses >/= 100 mg) can increase the likelihood that a patient will experience good pain relief.[568,569] Animal studies and preclinical human research suggests that caffeine may attenuate the increase in postoperative pain associated with poor sleep prior to surgery.[570]
MECHANISM OF ACTION: Methylxanthine that stimulates CNS. Caffeine also antagonizes the A(1) and A(2) subtypes of adenosine receptors, which appear to be relevant for pain-signal processing and transmission.

CAPSAICIN

EVIDENCE: Topical capsaicin (specifically an 8% transdermal patch) is effective for the treatment of neuropathic peripheral pain.[571,572] The topical cream and patch are also effective for the management of postsurgical neuropathic pain.
MECHANISM OF ACTION: Selectively stimulates nociceptive neurons via multiple mechanisms.
SPECIAL CONSIDERATIONS: Capsaicin is available as a 0.025, 0.075, and 0.1% topical cream, which can be applied three to four times daily at the site of pain.

MEMANTINE

EVIDENCE: There is limited evidence regarding the effectiveness of memantine for the treatment of acute pain in the surgical setting. One small study found an analgesic benefit in patients undergoing dacryocystorhinostomy, who received a single oral dose of 20 mg preoperatively.[573] A meta-analysis found questionable benefit when the agent was used for chronic pain and raised concerns regarding adverse effects, including dizziness.[574] The interest in memantine is due to its mechanism at the NMDA receptor.
MECHANISM OF ACTION: Low- to moderate-affinity, noncompetitive NMDA receptor antagonist.
SPECIAL CONSIDERATIONS: Memantine is only available in oral formulations. With additional studies, it may be reasonable to consider for patients who have responded well to other NMDA antagonists, such as ketamine.

NICOTINE

EVIDENCE: Antinociception from neuronal nicotinic receptor activation has been demonstrated in several animal models.[575-577] In women undergoing uterine surgery, intranasal nicotine (3 mg) administered postoperatively may improve analgesia and reduce morphine requirements.[362] A 2014 meta-analysis of nine studies (nicotine administered as a transdermal patch in six and as a nasal spray in three) found that cumulative opioid consumption at 24 hours was significantly reduced; however, this effect was limited to nonsmokers and nicotine administration was associated with a much higher rate or PONV and need for rescue antiemetics.
MECHANISM OF ACTION: Nicotine's analgesic effects are thought to stem from the activation of native, descending inhibitory pain pathways via neuronal nicotinic-receptor activation.
SPECIAL CONSIDERATIONS: Current nicotine products do not lend themselves to the easy administration of an exact intranasal dose.

OXYTOCIN

EVIDENCE: A meta-analysis of seven studies found a reliable association between exogenous oxytocin and decreased pain sensitivity.[578] However, the administration and dose of oxytocin, along with the target patient populations, varied widely among studies. In a small study of patients undergoing laparoscopic surgery, a local infiltration of subcutaneous oxytocin at the surgical site was found to reduce postoperative pain in a comparable manner to the infiltration of lidocaine.[579] While role of oxytocin in pain modulation has been well-defined in animal research, human studies are limited but encouraging.[580] Before a formal recommendation can be made on the routine use of oxytocin in the perioperative period, rigorous investigations are required. However, it may be reasonable to consider oxytocin for patients whose pain is inadequately controlled by other multimodal analgesic approaches.

MECHANISM OF ACTION: Produced in the hypothalamus, oxytocin is released into the peripheral circulation and CNS via the posterior pituitary during times of stress or pain.[578] In addition to activating its own receptors and decreasing pain signals, oxytocin binds to opioid receptors and stimulates endogenous opioid release in the brain.[578] Oxytocin also stimulates cannabinoid receptors and is known to relieve pain, induce a feeling of calm and reduce serum cortisol, stress and anxiety.[581]

DOSING: Although human studies vary widely in the dose and route of administration examined, it may be reasonable to administer oxytocin 20-80 international units (IU) SL or oxytocin 40 IU nasal postoperatively when managing patients whose pain is poorly controlled by other multimodal analgesic approaches.[579,582]

CONTRAINDICATIONS AND CAUTIONS: Overall, oxytocin is a safe medication with few adverse effects and no contraindications outside the peripartum population.

SPECIAL CONSIDERATIONS: Do not use in pregnant patients.

Nonpharmacological Interventions

Nonpharmacological interventions include a wide range of therapies that seek to modify behavior, emotion, cognition and/or sensory inputs.[583,584] Studies of cognitive behavioral interventions, mindfulness, guided imagery, relaxation, hypnosis and intraoperative suggestion have generally been shown to modestly reduce postoperative pain, analgesic use, depression, anxiety and catastrophizing attitudes.[584-586] Such psychological interventions may be delivered in surgical settings by psychologists, nurses or social workers. Delivery of some interventions may be conducted with online, video or audio materials. Studies of online cognitive behavioral interventions have shown small positive effects on pain relief; however, more research is needed in the perioperative patient population.[587] Meta-analyses of music therapy demonstrate decreased anxiety and better sleep in patients with chronic medical illness.[588] Aromatherapy has also demonstrated positive effects on anxiety, pain relief and opioid dose reduction in some nonsurgical populations.[589] Psychosocial interventions studied include educational information access, peer support and online social networking. No rigorous studies have compared different cognitive-behavioral programs, and there is insufficient evidence to recommend one intervention over another. In addition, some degree of patient interest and engagement may be required for certain cognitive-behavioral methods. That said, it is recommended that nonpharmacologic cognitive-behavioral modalities be offered to receptive patients, as such modalities are relatively inexpensive, unlikely to cause harm and may be beneficial.

Physical modalities for the management of postoperative pain include transcutaneous nerve stimulation (TENS), acupuncture and acupressure, massage, cold and heat therapy, continuous passive motion and immobilization or bracing.[590] A review of TENS use in surgical patients found an overall reduction in postoperative analgesic use of 25%, though the authors note wide heterogeneity in the TENS methods used.[591] Other studies of TENS therapy have been inconclusive. Evidence supporting the analgesic efficacy of acupuncture and massage is inconclusive, with no high-quality study supporting the use of either modality.[590] Similarly, compelling evidence supporting the efficacy of cold or heat therapy, continuous passive motion and bracing and immobilization is lacking. While

these interventions generally carry very little risk, there is limited evidence to endorse their effectiveness as part of a multimodal approach to perioperative pain management. Patient preference and the cost and availability of these physical interventions on surgical units must guide their selection and use.

Regional Anesthesia

For appropriate patients and procedures, regional anesthesia can be an important element in a comprehensive opioid-sparing multimodal analgesic plan. Though innovative surgeons and anesthesiologists have attempted to produce regional anesthesia since the 1890s, only in recent decades have advances in pharmacology, electronics and imaging technology improved the safety and efficacy of regional anesthesia, allowing wider, safer use of neuraxial and peripheral anesthesia and analgesia.[592,593]

Decades of effective use of neuraxial anesthesia and analgesia support the use of epidural, spinal and combined spinal-epidural (CSEA) techniques for anesthesia and analgesia in major surgical procedures.[594-600] While any neuraxial approach carries risks of hypotension, bleeding, infection and incomplete block, placement and careful management by anesthesia generally minimizes these risks, which must be carefully weighed against the considerable benefits for patients undergoing major procedures.[593] Delay in ambulation and time of discharge is a clear drawback to use of epidural analgesia, and with the wider use of nerve and plane blocks for abdominal procedures, neuraxial techniques may be increasingly reserved for major open procedures.

The availability of ultrasound guidance in the late 1970s paved the way for advances in the development of peripheral nerve and planar blocks.[601-603] Wider use of regional anesthetic techniques for both anesthesia and analgesia has the potential to improve surgical outcomes, reduce the need for opioid analgesia and avoid many of the risks associated with general and neuraxial anesthesia. Because peripheral nerve and plane blocks have far fewer cardiovascular and pulmonary effects, their safety profile is generally better than those of spinal and epidural techniques. Some of the interventions described below can serve as the sole mode of anesthesia, obviating the risks of general or neuraxial anesthesia altogether. Of course, no intervention is without potential for harm, and surgeons and anesthesiologists must make every effort to minimize the risks of nerve and vascular injury, bleeding, infection, intravascular injection, local anesthetic systemic toxicity, injury to surrounding anatomic structures and inadequate block. This is a rapidly evolving area of perioperative care, and surgical teams serve their patients best by staying abreast of research and developments in the field.

While full description of the peripheral nerve blocks and plane blocks is outside the scope of these guidelines, **TABLE 14** provides a short summary of many of the useful blocks referenced in this guideline. The majority of regional anesthetic blocks may be performed pre-, intra- or postoperatively. In most cases, blocks are most safely and effectively placed under ultrasound guidance. Close collaboration between surgeons and anesthesiologists is needed to determine which regional anesthetic procedures can be of use for a given patient and procedure. It is recommended that surgical teams be aware which neuraxial, peripheral and plane blocks may benefit their patients and whether the blocks should be single-shot or accompanied by placement of a catheter for wound infusion. For some of the techniques described below, placement of a catheter for continuous wound infusion can extend analgesia and reduce or eliminate pain in the immediate postoperative period.[604] Surgical teams are encouraged to adapt local workflows and staffing to efficiently incorporate regional anesthesia into routine perioperative patient care.

Single-shot blocks are limited in their analgesic effect by the limited duration of even “long-acting” anesthetics. While further research is needed to establish the efficacy and cost effectiveness of liposomal bupivacaine, preclinical evidence and the expert opinion behind many opioid-sparing surgical pathways suggest that it may be an important agent for extending the duration of single-shot blocks. Another strategy to extend the duration of blocks is the placement of catheters for the delivery of anesthetics by elastomeric, electric or spring-loaded pumps either by continuous infusion or under patient control. Continuous-infusion peripheral nerve blocks (CPNB) have been shown to provide good analgesia, to decrease opioid consumption and to decrease rates of opioid-related side effects.[605,606] Use of continuous wound infusion methods may be limited by time, cost, logistics related to maintaining infusion and

(TABLE 12)

Contraindications, risks and benefits of peripheral nerve and plane blocks

BENEFITS OF PERIPHERAL NERVE BLOCKS (PNBS)	CONTRAINDICATIONS AND RISKS
• Reduce requirements for systemic analgesics • Provides optimal anesthesia for: - Patients at risk of respiratory depression related to systemic or neuraxial opioids (e.g., obstructive sleep apnea, severe obesity, underlying pulmonary disease, advanced age) - Patients with another indication to minimize opioid use (e.g., in recovery with history of (h/o) OUD, h/o ORADEs) - Ambulatory surgical patients who may benefit from prolonged profound analgesia (using long-acting local anesthetics [LAs] or continuous PNB) - Patients with h/o acute, severe pain, poorly managed with systemic medication • As alternative to neuraxial, fascial plane blocks have less risk of neurovascular injury. Optimal analgesia for: - Patients with coagulopathies or those anticoagulants or antiplatelet agents (note: these patients are candidates for blocks in compressible locations only) - Patients for whom sympathetic blockade may cause hemodynamic problems (e.g., aortic stenosis) - Patients at elevated risk of urinary retention (e.g., age >65, male, BPH, diabetes, hypertension, history of urinary tract disease or surgery)	• Absolute contraindications include: - Patient refusal - Allergy to local anesthetics - Active infection at the site of injection • Relative contraindications include: - Patients with coagulopathy or receiving antithrombotic medication, especially if blocks are in a non-compressible location (e.g., paravertebral, lumbar plexus, proximal sciatic nerve block) - Pre-existing neurologic pathology or deficits in the distribution of the block - Caution with local anesthetic doses in patients with hepatic dysfunction - Doses listed are for adults, and it is recommended that they be reduced in patients with low ideal body weight or in children. It is advised that risks be discussed with the patient and consent obtained. Risks include: - Nerve injury - Vascular injury, bleeding and hematoma - Local anesthetic systemic toxicity (LAST) including seizure and cardiac arrest - Injury to adjacent structures such as bowel, lung, solid organs - Infection

risks of infection and catheter dislodgement.[177] Finally, the availability and feasibility of peripheral nerve blocks, liposomal bupivacaine and CWI pump systems depends to a large extent on institutional formularies.

In some cases, wider use of regional anesthesia and analgesia will require changes to operative workflow, formularies and equipment supply networks. Effective nonpharmacologic approaches to postoperative pain may play an important role in reducing perioperative reliance on opioid analgesia, and clinical experience has demonstrated that addition of certain agents may aid in prolonging the duration of block. Dexamethasone, dexmedetomidine and clonidine are agents commonly used for prolongation of local anesthetic peripheral nerve blocks. Caution is recommended with use of any perineural adjuvant, as none have FDA approval, and concerns for potential toxicity and adverse effect do exist. Continued research into the safety and efficacy of adjuvant agents is needed.

(TABLE 13)

Primary and Adjunctive Pharmacologic Agents for Regional Anesthesia

PRIMARY PHARMACOLOGIC AGENTS FOR REGIONAL ANESTHESIA

- It is recommended that amide anesthetic be a long-acting agent such as ropivacaine 0.5% or bupivacaine 0.5%. (Ropivacaine 0.2% and bupivacaine 0.25% are satisfactory alternatives in low body weight individuals.)
- Consider use of liposomal bupivacaine for thoracotomy, inguinal hernia, breast and colorectal surgeries.[265,399,610]
  - The manufacturer's site recommends injecting slowly, above and below fascial planes and into subcutaneous tissues using a 25-gauge or larger needle to maintain structural integrity of the liposomes. It is suggested that injections be 1-1.5 cm apart with 1-2 cc per injection site and can be mixed with 0.25% or 0.5% bupivacaine but NOT lidocaine.
  - There is also a volume expansion method involving dilution with normal saline up to 100 cc with 133 mg/10 cc vial.
  - See descriptions of amide anesthetics in "Multimodal Pharmacological Agents" for more information.
- Note: It is advised that clinicians exercise caution with use of amide anesthetics to avoid risk of local anesthetic systemic toxicity (LAST).
  - Total safe, cumulative dose of anesthetics will depend on patient-specific factors such as age, weight and liver function.
  - Generally, the limit on anesthetic administration is 4.5 mg/kg for lidocaine and 3 mg/kg for bupivacaine or ropivacaine.
  - Absorption of amide anesthetic varies greatly depending on route of administration. In order of greatest to least systemic absorption: IV, intercostal, caudal epidural, lumbar epidural, brachial plexus, IPLA, wound infiltration, subcutaneous.
- Surgical site infiltration of amide anesthetics (including liposomal bupivacaine) is not an absolute contraindication to the use of IV lidocaine, but surgical teams must be knowledgeable about safe concurrent use. Surgical teams are encouraged to consult a pharmacist as needed.
- NOTE: Mixing of liposomal bupivacaine directly with lidocaine renders liposomal bupivacaine ineffective.
- It is recommended that a lipid rescue kit (i.e. lipid emulsion 20% infusion and appropriate dosing recommendations) be made readily available in any area of practice that utilizes amide anesthetic agents.

ADJUNCTIVE PHARMACOLOGIC AGENTS FOR REGIONAL ANESTHESIA[607-609]

- Clonidine 0.5 mcg/kg; maximum dose of 150 mcg
- Epinephrine 5-10 mcg/ml
  - May extend duration of blocks via vasoconstrictive activity when used with lidocaine and mepivacaine (but not ropivacaine).
  - CAUTIONS: Vasoconstriction may cause neuronal damage. Hypertension and tachycardia may signal the possibility of vascular injection.
- Dexamethasone PF – 5 mg per side[611-613]
- Dexmedetomidine – 20 mcg per side[614]

(TABLE 14)

Peripheral Nerve and Plane Blocks for Common Surgeries[615-620]

FOR ALL BLOCKS:

- Most blocks do not provide coverage for visceral pain and, thus, are more useful for managing postoperative pain than as a sole anesthetic technique.
- Strongly consider the use of ultrasound guidance or direct visualization for all blocks.
- Most require large volumes of local anesthetic, with a typical injection volume of 15-30 mL per side.
- Amide anesthetic, preferably ropivacaine 0.5% or bupivacaine 0.5%. (Ropivacaine 0.2% and bupivacaine 0.25% are satisfactory alternatives in low body weight individuals.)
- Counsel patients on the risks associated with blocks, including vascular and neural injuries, abdominal visceral injury, solid organ injury, pneumothorax/hemothorax, transient sensory or motor blockade, infection and incomplete block.
- It is recommended that a discussion of risks and benefits of regional anesthesia be tailored to the specific needs of the patient and procedure.

Name	Descriptions and Applications	Details and Considerations
Transversus abdominis plane (TAP) block[351,621-632]	**Description:** Provides anesthesia to midline and lateral abdominal incisions **Applicable Surgeries:** - Colorectal procedures - Laparotomy - Herniorrhaphy - Appendectomy - Abdominoplasty	Injection of local anesthetic into the plane between the internal oblique and transversus abdominis muscles in the anterior or lateral abdominal wall. Although landmark-based approaches exist, this block is typically performed with ultrasound using a linear, high-frequency transducer. For the classic approach, coverage is most consistently reported from cutaneous dermatomes T10-L1 (umbilicus and below), and will provide unilateral analgesia to the skin, muscles and parietal peritoneum of the anterior abdominal wall. May be performed bilaterally but caution with total dose of local anesthetic. If more cephalad coverage is desired, consider rectus sheath and subcostal TAP blocks.
Subcostal TAP block[316,633]	**Description:** Provides anesthesia to upper abdomen and intercostal nerve distribution T6-9 **Applicable Surgeries:** - Open cholecystectomy - Hepatic surgery - Upper abdominal incisions	Local anesthetic is injected into the fascial plane between the posterior rectus sheath and the transversus abdominis muscle in the upper anterior abdominal wall.

(TABLE 14)

Peripheral Nerve and Plane Blocks for Common Surgeries[615-620] *continued*

Name	Descriptions and Applications	Details and Considerations
Quadratus Lumborum (QL) Blocks[634-637]	**Descriptions:** **QL1:** Anesthetizes the cutaneous branches of the iliohypogastric and ilioinguinal nerves as well as subcostal nerves T12-L1; for abdominal surgery below the umbilicus **QL2:** T4-T12/L1 dermatomes; for any abdominal surgery **Transmuscular QL block (TQL):** T4-T12/L1 dermatomes, so may be used for any abdominal surgery Use bilateral QL blocks for midline incisions **Applicable Surgeries:** - Colectomy, cholecystectomy, appendectomy (open or laparoscopic) - Ileostomy placement - Exploratory laparotomy - Nephrectomy, kidney transplant - Open prostatectomy - Gastrectomy - Anterior abdominal wall hernia repair - Abdominoplasty - Iliac crest bone graft	Local anesthetic is deposited in the plane between the aponeurosis of the transversus abdominis muscle and the thoracolumbar fascia at a point just lateral to the quadratus lumborum muscle. Thus, needle entry is in the lateral or posterior abdominal wall. Local anesthetic injection occurs between the latissimus dorsi and quadratus lumborum muscles in the posterolateral abdominal wall. Approach is in the patient's flank, just above the iliac crest. Anesthetic is deposited in the fascial plane between the QL and the psoas major. Due to its location, this is considered an advanced block. When using QL block as the sole anesthetic for herniorrhaphy, instill the sac containing the peritoneum with local anesthetic to anesthetize the abdominal visceral nerves. QL block risks spread of local anesthetic to the paravertebral space. TQL blocks may result in lower extremity weakness.
Rectus Sheath (RS) Block[263,304,351]	**Description:** Anesthetizes the terminal branches of intercostal nerves 9-11, providing anesthesia over the midline anterior abdomen **Applicable Surgeries:** - Vertical midline or paramedian incisions - Midline laparotomy - Open ventral or umbilical herniorrhaphy	Injection of local anesthetic deep to the rectus abdominis muscle and above the posterior rectus sheath. This sheath only extends along the upper 2/3 of the rectus abdominis muscle, stopping between the umbilicus and pubis. Thus, the block is performed at or above the level of the umbilicus on either side of midline and medial to the midclavicular line. Typically inject 10mL per side. Up to one third of patients may exhibit variations in anatomy, wherein the anterior cutaneous branch of the nerve courses superficial to the anterior wall of the rectus sheath. Because these nerves do not penetrate the posterior wall of the rectus sheath, these patients are at risk for incomplete block. RS block carries risk of puncture to inferior epigastric vessels.

(TABLE 14)

Peripheral Nerve and Plane Blocks for Common Surgeries[615-620] *continued*

Name	Descriptions and Applications	Details and Considerations
Ilioinguinal (IL) and Iliohypogastric (IH) Nerve Block[638-642]	**Description:** Anesthetizes the lower abdomen **Applicable Surgeries:** - Open inguinal hernia repair - Pfannenstiel incision	The IL and IH nerves lie within the fascial plane between the internal oblique and transverse abdominis muscles at or above the level of the anterior superior iliac spine (TAP plane, but be aware that at this level, there are usually only two muscular layers clearly visible). These nerves may pierce the internal oblique muscle at or below the anterior superior iliac spine (ASIS) to travel within the plane between the external oblique aponeurosis and internal oblique muscle as they course inferomedially. There are often small vessels that course within the TAP plane with the II/IH nerves and may be useful for identification of the appropriate plane. Typically 10-20 mL of local anesthetic is injected into the plane with the nerves. When using II/IH block as the sole anesthetic for herniorrhaphy, instill the sac containing the peritoneum with local anesthetic to anesthetize the abdominal visceral nerves. II/IH nerve blocks risk blockade of the femoral nerve with incorrect needle placement and puncture of the inferior epigastric vessels.

(TABLE 14)

Peripheral Nerve and Plane Blocks for Common Surgeries[615-620] *continued*

Name	Descriptions and Applications	Details and Considerations
Thoracic Interfascial Plane Blocks (PECs I, PECs II, Serratus Plane Blocks, Transversus Thoracic Muscle Plane Block)[643-645]	**Applicable Surgeries:** For thoracic or breast surgery as well as rib fractures **Descriptions:** **PECs I:** Will block the lateral and medial pectoral nerves (innervate the pectoralis major and minor muscles). May be used for breast surgery, cardiac device or portacath placement. **PECs II:** Blocks the anterior and lateral divisions of the intercostal nerves from T2-T6 as well as the long thoracic nerve (innervates the serratus anterior muscle) and thoracodorsal nerve (innervates the latissimus dorsi muscle). Used for more extensive breast surgery, possibly upper arm fistula surgery; typically includes injection in the PECS I plane as well. **Serratus Plane:** Dermatomes T2-T9 in the anterolateral thorax via blockade of the intercostal nerves T2-T9, as well as the long thoracic and thoracodorsal nerves. For thoracotomy or VATS, rib fractures, may be used for breast surgery that includes axillary dissection or reconstruction surgery. Also has been used for esophagectomy and anastomosis. **Transversus Thoracic Plane Block (TTPB, formerly parasternal bock):** Provides cutaneous analgesia via blockade of the anterior cutaneous branches of intercostal nerves 2-6. Indicated for midline chest wall pain including sternotomy, implantation of cardiac devices, fractures of the sternum or medial ribs or medial breast surgery	**PECs I:** Injection of local anesthetic between the pectoralis major and minor lateral to the mid-clavicular line at the level of the third to fourth ribs. **PECs II:** PECs I plus injection of local anesthetic between the pectoralis minor and serratus anterior muscles in the mid-clavicular line (10mL and 20mL in each plane, respectively). **Serratus Plane Block:** Local anesthetic is injected in the fascial plane between the latissimus dorsi and serratus anterior muscles at the level of the fifth rib along the mid-axillary line; alternatively, the anesthetic may be injected deep to the serratus muscle above the rib for a deep serratus plane block. **TTPB:** Local anesthetic (10-20mL per side) is deposited between the internal intercostal muscle and transversus thoracis muscle, medial to the midclavicular line between the third and fourth ribs. This may be considered an advanced block and requires precise needle tip visualization.

(TABLE 14)

Peripheral Nerve and Plane Blocks for Common Surgeries[615-620] *continued*

Name	Descriptions and Applications	Details and Considerations
Erector Spinae Plane Block[262,396-398,646]	**Description:** Local anesthetic spreads cranio-caudally anterior to the erector spinae muscle and diffuses into the paravertebral spaces where it anesthetizes the dorsal and likely ventral ramus of the spinal nerve roots, and may spread laterally to anesthetize the intercostal nerves. **Applicable Surgeries:** Used initially for thoracic surgery, however more recently used for abdominal surgery as well as surgery on the proximal lower extremities. May provide both visceral and somatic analgesia.	The injection is performed in the posterior thorax, where local anesthetic is deposited between the erector spinae muscle and the tip of the transverse process of the vertebrae (classically T5-T7; however, case reports of use up to T2 and down to L4). Consider use of saline solution for hydro-dissection, injecting LA only after confirmation of proper placement of needle tip. While a linear ultrasound probe is adequate in most cases, consider using a curvilinear probe in obese patients and those with dense musculature. In theory dural puncture may be possible if the block is performed too medially and deeply.

(TABLE 14)

Peripheral Nerve and Plane Blocks for Common Surgeries[615-620] *continued*

Name	Descriptions and Applications	Details and Considerations
Brachial Plexus Block[647]	**Description:** The plexus may be blocked at multiple locations along its course. **Applications:** Interscalene block: For surgery on the shoulder and upper arm, also clavicular surgery when combined with cervical plexus block. The inferior trunk (C8-T1) is usually spared. Supraclavicular Block: Surgery on the arm, elbow, forearm and hand as well as shoulder surgery Infraclavicular Block: arm, forearm, elbow and hand surgery	The expected distribution of anesthesia and the complications vary based upon block location. Brachial plexus block has been found to improve arteriovenous fistula patency at three months. 7-15mL of local anesthetic is deposited around the superior and middle trunks of the brachial plexus between the anterior and middle scalene muscles, approximately at the level of the cricoid cartilage (C6). 20-25mL of local anesthetic is injected around the trunks and divisions of the brachial plexus, superficial and posterior to the subclavian artery. For surgery on the distal forearm, inject most of the anesthetic beside the artery just above the first rib. The cords of the brachial plexus are blocked cephalad, posterior and caudal to the axillary artery, which lies posterior to the pectoralis muscles and medial to the coracoid process. This block typically requires 20-30mL of local anesthetic to target all three cords. Blocks the terminal branches of the plexus (median, ulnar, radial and musculocutaneous nerves) around the axillary artery in the axilla, between the biceps, triceps and coracobrachialis muscles. Five to 10mL of anesthetic are injected around each nerve. For surgery of the upper arm, supplemental anesthesia of the intercostal brachial nerve may be required. Caution in patients with contralateral recurrent laryngeal nerve dysfunction. It is recommended that patients for whom hemidiaphragmatic paralysis would be detrimental not undergo interscalene block as the phrenic nerve is typically blocked as well. The risk is lower but still possible (quoted at 50%, possibly lower with ultrasound guidance) with supraclavicular block. The musculocutaneous nerve typically lies away from the artery in the plane between the biceps and coracobrachialis muscles. For brachial plexus blocks there is risk of injury to the vertebral artery, carotid artery or thyrocervical trunk.

(TABLE 14)

Peripheral Nerve and Plane Blocks for Common Surgeries[615-620] *continued*

Name	Descriptions and Applications	Details and Considerations
Intercostal Nerve Blocks (ICNB)	**Description:** Adequate analgesia requires blockade of two dermatomes above and below the level of the surgical incision. Does not provide visceral analgesia. **Applications:** Thoracic and upper abdominal surgery, rib fracture	Beginning about three cm lateral to the intervertebral foramen, the intercostal nerve is found between the innermost and internal intercostal muscles, typically (but not always) within the subcostal groove. The nerve lies inferior to the intercostal artery. ICNB is approached along the rib proximal to the midaxillary line, most commonly at the angle of the rib. Although ICNB may be performed with a landmark-based technique by walking underneath the rib, it is preferable to perform the block with direct visualization from the surgical field or percutaneously with ultrasound. Once the needle is in the plane of the nerve, 3-5mL of local anesthetic is injected at each level. Consider the addition of epinephrine given the vascularity of the intercostal space in order to delay systemic absorption. Intercostal nerve blocks risk proximal spread and unintentional spinal anesthesia.

(TABLE 14)

Peripheral Nerve and Plane Blocks for Common Surgeries[615-620] *continued*

Name	Descriptions and Applications	Details and Considerations
Paravertebral Nerve Blocks (PVB) [648]	**Description:** PVB is in effect a unilateral block of the spinal nerve, including the dorsal and ventral rami and sympathetic chain ganglion. While PVBs can be performed at any level, they are most frequently performed at the thoracic level due to anatomic considerations. **Applications:** Breast surgery, herniorrhaphy, thoracotomy, open cholecystectomy, open nephrectomy, minimally-invasive cardiac surgery, bilateral blocks for midline abdominal surgery or conventional cardiac surgery	The thoracic paravertebral space is a wedge-shaped region adjacent to the spinal column, bound anteriorly by the parietal pleura, medially by the vertebral body, disc and intervertebral foramen, and by the costotransverse ligament (a continuation of the innermost intercostal muscle) and transverse process posteriorly. For a single-level PVB, a total of 20-25mL of long-acting local anesthetic is injected, whereas 4-5mL is injected at each site for multi-level PVB. Consider the addition of epinephrine given the vascularity of the paravertebral space in order to delay systemic absorption. PVBs are unlikely to cause bleeding that results in an epidural hematoma, however they are subject to the same coagulation precautions as other neuraxial procedures. Contraindicated in Empyema, malignant mass within the paravertebral space, patients in whom pneumothorax would not be tolerated Unilateral PVBs may be considered as an alternative to TEA for patients in whom sympathectomy and subsequent hypotension is unlikely to be tolerated; however, PVB does risk bilateral spread and thus bilateral sympathectomy. PVBs are contraindicated in patients with hypovolemia.

Technique:

Description of each technique is beyond the scope of these guidelines. Many online resources can be found for education on regional anesthetic blocks. The following are reputable sites that may serve as a reference for anesthesiologists and surgeons:

Resources:

1. https://www.nysora.com
2. http://www.usra.ca/regional-anesthesia/specific-blocks/home.php
3. https://members.asra.com/pain-resource/regional-anesthesia/ (requires ASRA membership)
4. https://academic.oup.com/bjaed/article/10/6/182/299472
5. https://www.youtube.com/channel/UCV8d6B_W6KmPoL_bWXeYiqQ

Harm Reduction

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Harm Reduction

Harm reduction is a set of practical strategies and ideas aimed at reducing negative consequences associated with illicit drug use. The approach is predicated on respecting patients and their choices, removing stigma and meeting people where they are without judgment. In an ideal world, patients would be compelled to stop using drugs by logical physician counseling, but the simplistic directive to "stop using because you may die" is ineffective and often deleterious to the physician-patient relationship. In reality, patients must possess the internal resolve to pursue recovery; that process is best aided by building patient trust, which can be accomplished with a harm reduction approach.

Initially developed in response to the U.S. AIDS epidemic, the harm reduction philosophy has been used in recent years for the treatment of people who inject drugs (PWIDs); however, its principles broadly apply to most patients with SUDs. Injection drug use is intertwined with the opioid epidemic. The use of illicit and IV drugs has increased commensurate with the rise in opioid prescriptions, and roughly 75% of injection heroin addictions originate with prescription opioids.[649]

IV drug use (IVDU) presents a tremendous challenge to public health and is a principal mechanism by which many communicable diseases are spread:

- **HIV/AIDS:** In 2016, injection drug use accounted for 9% of new HIV diagnoses, 13% of new AIDS diagnoses and approximately 20% of new HIV/AIDs diagnoses.[650]
- **Hepatitis B and C:** Injection drug use accounts for the majority of new hepatitis C (HCV) infections.[651] Acute HCV infections have increased about 3.5-fold since 2010.[652] Of the 1,371 cases of hepatitis B reported in 2016, more than 34.4% of cases indicated the use of injection drugs.[653] In Colorado, the age-adjusted HCV rate has increased by 129% since 2012, primarily due to IVDU; 894 new cases were reported in 2016 alone.[654]
- **Endocarditis:** The overall incidence of acute bacterial endocarditis is hundreds to thousands of times higher among those who inject drugs than in those who do not (150-2,000 cases /100,000 person-years versus 1.7-6.2 cases/100,000 person years).[655] According to the CDC, the incidence of hospitalizations for endocarditis among drug-dependent patients has increased twelvefold since 2010 and is associated with an 18-fold increase in health care costs.[656]
- **Soft-tissue and invasive bacterial infections:** Significant infections, such as wound botulism, osteomyelitis, epidural abscess, necrotizing fasciitis and invasive methicillin-resistant Staphylococcus aureus (MRSA), have all been linked to IVDU. A 2018 report found that PWID were 16.3 times more likely to develop invasive MRSA infections.[657]

Harm reduction aims to prevent infections and other negative sequelae of IVDU. Of the thousands of patients who present with opioid-related health concerns, ranging from withdrawal to constipation to overdose to injection-related infections, few are ready to quit on the day they visit the hospital. Harm reduction helps sustain health and life until the time patients who inject drugs are ready to pursue treatment and recovery. Given the unprecedented scope and destruction of this epidemic, clinicians can and must do better in counseling and treating addicted patients who are not ready to stop using.

Stigma and Bias As Obstacles to Health Care:

OUD is a medical disease defined by genetic predisposition and long-term changes in brain structure and function. Clinically, patients often suffer from uncontrollable, compulsive drug cravings that render them powerless, even in the face of catastrophic social and health-related consequences.[658] Health care clinicians often view patients with SUDs negatively and approach them in a manner that erodes both clinician empathy and patient care.[659] As a result, patients who misuse opioids and injection drugs often go to great lengths to avoid medical care, including signing out against medical advice before treatment is complete. It is imperative that clinicians make the hospital setting a welcoming and safe place for those who seek help.

Evidence-based harm reduction strategies, rather than fear- and stigma-driven ultimatums, improve patient and community outcomes.[660] Harm reduction and therapeutic relationship-building is especially critical in communities where buprenorphine and methadone treatment programs are scarce and plagued by long waiting lists. This inaccessibility means that most opioid users will continue to misuse drugs, many within hours of discharge. Certain barriers remain to be addressed: many surgeons are unfamiliar with harm reduction principles, unaware of how to perform effective interventions and lack the education and resources needed to integrate harm reduction into their practices.

Harm Reduction continued

Practice Recommendations

1. **It is recommended that patients with OUD be managed without judgment; addiction is a medical condition and not a moral failing. Caregivers are encouraged to meet patients where they are, infusing empathy and understanding into the patient/medical provider relationship.**
   a. Clinicians are encouraged to seek out educational opportunities to better understand addiction and end the stigma associated with OUD.
   b. It is suggested that a harm reduction mentality incorporate the following:
      i. Humanism – Seek to accept and understand patients without moral judgment.
      ii. Pragmatism – Abstinence is merely an ideal; it is recommended that messaging be targeted toward harms and concerns over health rather than moral and societal standards.
      iii. Individualism – See the patient as an individual.
      iv. Autonomy – Respect patients' decisions.
      v. Incrementalism – Small step-by-step improvements often open the door to further treatment and recovery.
      vi. Accountability without termination – Patients are responsible for their own choices and behaviors. While their decisions may go against medical advice, terminating the relationship may cause the patient harm.
   c. Counsel patients and allow them to seek treatment—or not—at their own pace (Table 15). Pressuring or forcing patients into treatment for SUDs is ineffective, violates their autonomy and creates an adversarial rather than therapeutic relationship.

(TABLE 15)

Counseling Patients with Opioid Use Disorders

DO	DON'T
• Use respectful language when discussing patients' drug use. • Assess patients' readiness to change. • Respect patients' decisions regarding treatment. • Encourage patients to be honest with providers about any drug use. • Make information available that is specific to the needs of patients.	• Don't use negative terminology such as "addict" or "junkie." • Don't tell patients they are ruining their lives or are "going to die." • Don't attempt to pressure patients to begin substance abuse treatment. • Don't make assumptions about the mental or physical health of patients with OUD. • Don't let the stigma associated with injection drug use affect how patients are treated.

Harm Reduction continued

2. It is recommended that surgical teams be knowledgeable about the prevention of soft tissue infections, serious invasive bacterial pathologies and viral infections associated with injection drug use. By counseling patients on safer injection practices, surgical teams may prevent complications of IVDU. Preventing the acquisition and transmission of infectious diseases reduces health care costs, improves patient health and decreases risk for surgical teams. Prior to discharge, it is advised that patients be counseled to:

a. Practice good hygiene.
   i. Always encourage hand washing and cleansing of the injection site.
   ii. Recommend the use of alcohol pads to sterilize skin prior to injection.
   iii. Warn patients not to lick their needles prior to injection.

b. Use sterile equipment.
   i. Reusing equipment increases the risk of bacterial contamination.
   ii. Patients can obtain new equipment for free through local syringe access programs (formerly referred to as needle exchange programs).
   iii. If such resources are unavailable, advise patients to purchase needles, syringes and alcohol pads at a pharmacy.
   iv. The average heroin injection drug user injects three to five times per day.

c. Use sterile water to prepare the product.
   i. Many infections stem from unsafe water supplies; some users report using river water, toilet water or saliva to dissolve product into an injectable form.
   ii. Bottled water is NOT sterile. Used water bottles are contaminated and pose a high risk of infection.
   iii. Optimally, patients should use single-use containers of sterile water.
   iv. If single-use containers of sterile water are unavailable, it is recommended that water be sterilized by heating it at rolling boil for 10 minutes and allowing it to cool.

d. Avoid "skin popping" or "muscling," colloquial terms for injection into subcutaneous or muscle tissue rather than into a vein. These practices predispose patients to abscesses and soft-tissue infections.

e. Viral infections can be prevented by never sharing injection materials, including needles, syringes, cookers and cottons.

f. *The Guide to Getting Off Right* is a resource for people who inject illicit drugs written collaboratively by medical professionals and people who inject drugs.

3. It is recommended that any patient who injects drugs be offered testing, vaccination and treatment as appropriate for HCV, hepatitis B virus (HBV) and HIV. Clinicians are also encouraged to refer patients who inject drugs to local syringe access programs upon discharge where they can obtain sterile injection materials and support services, including counseling, HIV/hepatitis testing and treatment referrals.

a. Patients who inject illicit drugs are among the most vulnerable patients surgical teams will encounter. They frequently avoid contact with medical professionals and thus hospitalization may pose a rare opportunity for testing, prevention and/or treatment of blood-borne pathogens in this patient population.

b. HCV is the most common blood-borne pathogen in the United States, with an estimated 44,700 new cases in the last year. Injection drug use is the most important risk factor of HCV infection.
   i. HCV is a curable disease when treated with medications such as sofosbuvir or combination medications such as ledipasvir/sofosbuvir.
   ii. The U.S. Preventive Services Task Force recommends screening all adults for HCV; surgical teams are encouraged to test any patient who inject drugs for HCV.

c. HBV is a preventable disease. Clinicians are encouraged to test patients who inject drugs for HBV and/or offer a first HBV vaccination to patients who inject drugs, with directions to complete their course at an outpatient clinic such as a harm reduction or syringe access program.

d. HIV testing should be offered to all patients who inject drugs.

e. Syringe access programs are cost effective for reducing HIV transmission and prevalence.[661]

f. The additional resources these centers often provide (e.g., sterile water, cooking units and cleaning solutions) also can help reduce such dangers.

g. The World Health Organization suggests a "compelling case that needle and syringe programs substantially and cost effectively reduce the spread of HIV among PWIDs and do so without evidence of exacerbating injecting drug use at either the individual or societal level."[662]
h. In 2000, the AMA adopted a position strongly supporting the efficacy of these programs when combined with addiction counseling.[663]
i. An online list of local syringe access and harm reduction programs can be found through the North American Syringe Exchange Network. **APPENDIX D** contains a list of syringe exchange programs across Colorado.

4. Surgeons are encouraged to work with hospitals and establish take-home naloxone programs to provide the antidote to high-risk patients at discharge. If naloxone cannot be given at time of discharge, it is recommended that patients receive a prescription and be informed about the over-the-counter availability of naloxone in most Colorado pharmacies.

a. In 2018, the U.S. Office of the Surgeon General issued an advisory urging health care systems to increase access to naloxone, joining the CDC, WHO and AMA in advocating for the wider availability of naloxone.
   i. The advisory states, "For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and friends of people who have OUD, and community members who come into contact with people at risk for opioid overdose, knowing how to use naloxone and keeping it within reach can save a life."[664]
b. Colorado law protects physicians who prescribe naloxone. The State-Specific Policy Summaries Third-Party Naloxone Bill (Colorado SB 13-014) removes the following:
   i. Civil liability for prescribers
   ii. Criminal liability for prescribers
   iii. Civil liability for layperson administration
   iv. Criminal liability for layperson administration
c. A 2018 national survey by the American Psychiatric Association found that nearly one in three people reports knowing someone who is or has been addicted to opioids.[665]
d. PWID have contact with other people at risk of overdose. While patients will rarely rescue themselves with naloxone, they can often use the drug to rescue others who may have inadvertently overdosed.
e. It is recommended that family members and friends be counseled on recognizing the signs of overdose and using naloxone.
f. The risk is widespread; the antidote is not. Despite their effectiveness, take-home naloxone programs are present in fewer than 10% of U.S. counties.[666]
g. A list of pharmacies that participate in Colorado's standing-order naloxone protocols can be found at www.stoptheclockcolorado.org.

(TABLE 16)

Naloxone for High-Risk Patients

It is recommended that naloxone be dispensed directly to high-risk patients at discharge who:

- Received care for opioid intoxication or overdose
- Have a suspected SUD or nonmedical opioid use
- Are prescribed more than 50 mg MME per day
- Are receiving an opioid prescription for pain AND
  - A prescription for methadone or buprenorphine
  - A history of acute or chronic pulmonary disease
  - A history of renal dysfunction, hepatic disease or cardiac comorbidities
  - Known or suspected excessive alcohol use or dependency
  - Concurrent use of benzodiazepines or other sedatives
  - Known or suspected poorly controlled depression
- Are taking opioids but have unreliable access to emergency medical services
- Were recently released from incarceration
- Have resumed opioid use after a period of abstinence

Harm Reduction continued

Policy Recommendations

1. Harm reduction agencies and community programs that provide resources for PWID should be made readily accessible to all Coloradans in need.

a. The passage of C.R.S. §25-1-520 in 2010 legalized the establishment of syringe access programs with local jurisdiction approval.
b. Community programs aimed at providing needle exchange and disposal services, sterile equipment, free counseling and HIV/hepatitis screening are cost effective for preventing the transmission of blood-borne pathogens.
c. These programs, many of which also provide basic medical and social services to this high-risk population, should be well funded and expanded beyond their current levels.

2. When local programs are unavailable for PWID, hospitals are encouraged to establish programs to provide services like safe syringe exchanges.

a. Colorado SB 19-227, Harm Reduction Substance Use Disorders, limits clinician liability by allowing out-of-hospital syringe access.
b. This recommendation is especially applicable to rural communities, which are particularly vulnerable to communicable disease outbreaks and are unlikely to have local syringe access programs.
c. Hospitals should consider partnering with their local health departments and state and federal authorities to establish programs that support harm reduction.
d. Ideally, such initiatives will be funded by national or state governments, nonprofit organizations or grants to make these services cost effective for participating hospitals.

Treatment of Opioid Use Disorder

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Treatment of Opioid Use Disorder

Of the estimated 2.1 million Americans with OUD, fewer than 20% receive evidence-based medication for addiction treatment (MAT).[152] The consequences of this treatment gap are substantial, including dramatically increased risks of overdose injury and death; the transmission of HIV, viral hepatitis and invasive bacterial infections; and a range of risky and criminal behaviors. OUD is a chronic, relapsing medical illness. Like patients with other chronic illnesses, those diagnosed with OUD require ongoing, comprehensive, evidence-based care. Abstinence-oriented treatments are ineffective for the treatment of OUD and have relapse rates greater than 80%.[667] The gold standard for the treatment of OUD employs one of the three FDA-approved medications: methadone, buprenorphine and naltrexone. It is important to recognize that opioid dependence and opioid addiction are different entities; patients may be physically dependent on buprenorphine or methadone, but when maintained on these medications, the risks and behaviors seen with addiction are avoided. People receiving MAT can lead fulfilling, productive lives while maintained on medication.

Overwhelming evidence demonstrates that patients receiving MAT have lower morbidity and mortality, higher treatment retention rates, lower rates of opioid-related hospital admissions and lower rates of readmission.[668] As many surgeons and anesthesiologists are aware, 25% or more of patients with OUD will leave the hospital against medical advice due to cravings, withdrawal symptoms, fear of stigma or mistreatment or social pressures.[669] Patients whose withdrawal is managed with buprenorphine or methadone are less likely to leave against medical advice and have shorter, less complicated admissions.[670,671] Finally, patients with OUD have an increased risk of overdose death following hospitalizations in which they did not receive opioid-agonist treatment.[672]

The stigma surrounding OUD leads some patients to conceal their disease, and past negative experiences with the health care system may make other patients wary of medical clinicians. Surgeons and anesthesiologists have an opportunity to radically change how they treat this patient population by screening patients consistently and offering help to those with OUD in a non-stigmatizing, compassionate manner. Finally, surgical care teams can engage with hospitalists and addiction medicine specialists to help ensure that patients with untreated OUD have the opportunity to begin MAT while hospitalized and to be referred to continuing outpatient care. Patients started on buprenorphine in the hospital are more than twice as likely to be in treatment one month later than those who only receive referrals.[673] By adopting these novel approaches, surgeons and anesthesiologists can make an enormous contribution to the lives of people with OUD, their families and their communities.

Practice Recommendations

1. **Surgical teams are encouraged to screen all patients for SUDs.**
    a. Surgical clinicians should be aware that many patients with SUDs conceal their disease.
        i. Between 8-29% of hospitalized patients have a non-alcohol SUD, but only 64% of those are identified as having an SUD by their hospital treatment teams.[674]
    b. A non-stigmatizing, medically accurate, empathic approach to the patient interview is most effective for eliciting an accurate substance use history.
        i. The principles and techniques of motivational interviewing can be powerful tools when engaging with patients with SUDs.
    c. Laboratory tests, medical records and PDMPs are unreliable predictors of SUDs.
    d. When OUD is suspected, an opioid-specific screening tool like the RODS can be administered and scored in two to three minutes **(SEE APPENDIX B FOR SCREENING INSTRUMENTS)**.
        i. OUD is defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) and replaces “opioid addiction” and “opioid dependence” as a diagnostic entity.

(TABLE 17)

Summarized DSM-5 Diagnostic Categories and Criteria for OUD

CATEGORY	CRITERIA
Impaired Control	• Opioids used in larger amounts or for longer than intended • Unsuccessful efforts or desire to cut back or control opioid use • Excessive amount of time spent obtaining, using or recovering from opioids • Craving to use opioids
Social Impairment	• Failure to fulfill major role obligations at work, school, or home as a result of recurrent opioid use • Persistent or recurrent social or interpersonal problems that are exacerbated by opioids or continued use of opioids despite these problems • Reduced or given up important social, occupational, or recreational activities because of opioid use
Risky Use	• Opioid use in physically hazardous situations • Continued opioid use despite knowledge of persistent physical or psychological problem that is likely caused by opioid use
Pharmacological Properties	• Tolerance as demonstrated by increased amounts of opioids needed to achieve desire effect; diminished effect with continued use of the same amount • Withdrawal as demonstrated by symptoms of opioid withdrawal syndrome; opioids taken to relive or avoid withdrawal

SOURCE: Psychiatric Times, DSM-5[675]

2. MAT is the gold standard for the management of OUD. Surgeons are encouraged to consult addiction medicine to aid in managing the complex medical needs of patients with OUD and in initiating treatment with MAT.

a. Methadone, buprenorphine and naltrexone are the three FDA-approved medications for the treatment of OUD. Methadone is a full opioid agonist and buprenorphine is a partial agonist. Methadone and buprenorphine are sometimes termed "opioid-agonist treatments" to distinguish them from naltrexone, which is a full opioid antagonist. **TABLE 18** describes the different characteristics of MAT agents.

b. The treatment of OUD is the most direct way to ensure a patient's long-term health.

c. It is recommended that any patient with an untreated OUD be offered buprenorphine or methadone while hospitalized and transitioned to outpatient MAT upon discharge. For the majority of hospitalized patients, initiation with buprenorphine is preferred.

d. It is suggested that surgical clinicians identify the services within their institutions that can initiate MAT and coordinate a transfer of care to outpatient MAT clinicians.

e. Hospitalized patients with OUD may be particularly receptive to treatment. When admitted for opioid-related illnesses, a fear of bad outcomes as well as forced abstinence can illuminate the benefits of treatment. Sixty-seven percent of hospitalized patients with SUDs report a desire to cut back or stop using, and 44% of those with OUD report a strong desire to receive MAT.[674]

f. It is important to be aware that abstinence-oriented or "detox" programs are ineffective for the treatment of OUD and dramatically increase the risk of relapse and overdose death.

g. It is recommended that patients with OUD be managed with empathy and respect. Even in brief encounters, surgical clinicians can convey care and compassion. It is important to remember that patients are more likely to seek and accept care—both for their surgical condition and for their OUD—from empathic clinicians.

(TABLE 18)

Characteristics of Medications for Treatment of OUD

CHARACTERISTIC	METHADONE	BUPRENORPHINE	NALTREXONE
Brand Names	Dolophine, Methadose	Subutex, Suboxone, Zubsolv	Depade, ReVia, Vivitrol
Class	Agonist (fully activates opioid receptors)	Partial agonist (activates opioid receptors but produces a diminished response even with full occupancy)	Antagonist (blocks the opioid receptors and interferes with the rewarding and analgesic effects of opioids)
Use and effects	Taken once per day orally to reduce opioid cravings and withdrawal symptoms	Taken orally or sublingually (usually once a day) to relieve opioid cravings and withdrawal symptoms	Taken orally or by injection to diminish the reinforcing effects of opioids (potentially extinguishing the association between conditioned stimuli and opioid use)
Advantages	High strength and efficacy as long as oral dosing (which slows brain uptake and reduces euphoria) is adhered to; excellent option for patients who have no response to other medications	Eligible to be prescribed by certified physicians, which eliminates the need to visit specialized treatment clinics and thus widens availability	Not addictive or sedating and does not result in physical dependence; a recently approved depot injection formulation, Vivitrol, eliminates need for daily dosing
Disadvantages	Mostly available through approved outpatient treatment programs, which patients must visit daily	Subutex has measurable abuse liability; Subozone diminishes this risk by including nalxone, an antagonist that induces withdrawal if the drug is injected	Poor patient compliance (but Vivitrol should improve compliance); initiation requires attaining prolonged (e.g. 7-day) abstinence, during which withdrawal, relapse, and early dropout may occur

SOURCE: NEJM[338]

3. **It is recommended that surgical patients receiving buprenorphine or methadone for the treatment of OUD be maintained on their medication regimen to prevent relapse and to ensure physiologic stability and optimal surgical outcomes. It is advised that the dose of buprenorphine or methadone not be reduced prior to surgery or in patients in pain. Involvement of addiction medicine clinicians or hospitalists familiar with MAT is encouraged.** **(SEE "MANAGING PERIOPERATIVE PAIN IN PATIENTS RECEIVING MEDICATION FOR ADDICTION TREATMENT).**
   a. It is suggested that all patients undergoing MAT be continued on their medication during the perioperative period to improve pain control and reduce the use of opioids and risk of relapse after discharge.[677,678]
   b. The discontinuation of buprenorphine or methadone complicates clinical assessments and treatment, increases the risk of withdrawal and leaving against medical advice and requires the patient to restart treatment after discharge.
   c. Surgical teams are encouraged to consult anesthesia or pain medicine to optimize nonopioid postsurgical pain management for patients on MAT. Because the undertreatment of pain can trigger relapse and medical exposure to opioids may trigger aberrant use, surgical teams are encouraged to maximize the use of nonopioid multimodal analgesia for this patient population.
   d. Surgical care teams should be aware that MAT does not provide adequate analgesia for acute pain.
   e. Surgical teams are encouraged to notify the outpatient buprenorphine or methadone provider of the patient's admission and anticipated length of stay. This communication prevents hospitalized patients from being mistaken for program dropouts and ensures continuity of care on discharge.
   f. Rare situations in which clinicians may consider modifying the dosage or holding medications include:
      i. Patients with severe sedation or respiratory depression. If not sedated but receiving additional sedating medications, monitor closely but do not withhold OUD medications.
      ii. Patients with a corrected QT interval (QTc) greater than 500 on methadone. In the perioperative period, acute illness and new medications can change the QTc and elevate risk. Consider decreasing the dose of medications that further prolong the QTc, including methadone.
      iii. Patients with newly decompensated liver disease.
      iv. Patients taking medications that have significant interactions with methadone. Methadone dose adjustments may be required. Consult a clinical pharmacist for a more complete list of interactions.
      v. Drugs that may INCREASE the concentration and effect of methadone include azole antifungals, some SSRIs, tricyclic antidepressants, erythromycin, ciprofloxacin and quetiapine. If using these medications, closely monitor for sedation and unintentional overdose and consider alternative medications if possible.
      vi. Drugs that may DECREASE the concentration of methadone include rifampin, many antiretrovirals, phenytoin and carbamazepine. If using these medications, closely monitor for opioid withdrawal and consider alternative medications if possible.

Treatment of Opioid Use Disorder continued

4. **Surgical teams are advised that naltrexone—a full opioid antagonist—may have a substantial impact on perioperative pain management. It is recommended that naltrexone be held prior to elective procedures.**
   a. Naltrexone is approved by the FDA for the management of alcohol use disorder and OUD.
   b. As an opioid antagonist, naltrexone blocks the analgesic effects of most opioids.
   c. Naltrexone comes in two forms, an oral tablet and a long-lasting monthly depo injection.
   d. When treating patients on naltrexone, surgeons are encouraged to coordinate care with anesthesiology and the patient's MAT provider, especially prior to elective surgeries.
   e. Hold naltrexone upon presentation for acute pain that may require opioids. The half-life of naltrexone is approximately 12 hours for the oral form and 5-10 days for the intramuscular depo form.
   f. Patients who have been taking naltrexone but have discontinued use and no longer have detectable levels may have lower opioid tolerances, so it is advised that caution be used when administering opioids.
   g. If naltrexone is still present, a multimodal approach to pain control may include NSAIDs, APAP, ketamine, local/regional anesthesia and procedural sedation with nonopioids as appropriate. **(SEE "MANAGEMENT OF PERIOPERATIVE PAIN IN PATIENTS RECEIVING MAT")**
   h. If naltrexone is still present and opioids are necessary, high-dose, high-potency opioids can be used to out-compete naltrexone at the opioid receptor. Patients must be closely monitored, at minimum with pulse oximetry and telemetry, to prevent over-sedation and unintentional overdose.

Policy Recommendations

1. **Increase local, state and federal funding for MAT services.**
   a. The treatment gap for OUD is unacceptably high. An adequate response to this public health crisis requires a substantial investment in a system capable of serving the needs of all patients impacted by the opioid epidemic.

2. **Repeal the X-waiver requirement for prescribing buprenorphine.**
   a. It is not in the public's best interest to require clinicians to have a waiver to treat patients with OUD, especially when no such waiver is required to prescribe opioids.
   a. While more than 900,000 U.S. physicians are licensed to write prescriptions for opioids, fewer than 32,000 are authorized to prescribe buprenorphine for the treatment of OUD.[679]
   b. The waiver requirement is a barrier to treatment and adds to the stigma surrounding OUD.
   c. Repeal of the X-waiver requirement is endorsed by the World Health Organization, the American College of Emergency Medicine, the American Academy of Clinical Toxicology and the American Society of Addiction Medicine.
   d. Similar deregulation has enabled the widespread use of buprenorphine in France, which has led to a 79% decline in the country's opioid overdose deaths since 1995.[680]
   e. Legislation designed to eliminate the requirement for clinicians to obtain a DEA waiver to treat OUD with buprenorphine, such as the Mainstreaming Addiction Treatment Act (H.R. 2482), should be supported. Elimination of the waiver requirement will greatly aid efforts to close the treatment gap for OUD.

Treatment of Opioid Use Disorder continued

3. **Ease regulations around 42 CFR Part 2 to facilitate the sharing of critical health data.**
   a. 42 CFR Part 2 requires any patient with an SUD to provide explicit permission for a treating provider to share information about their medical care, even with other clinicians involved in their treatment.
   b. 42 CFR provided an essential safeguard for privacy from 1975 until HIPAA was enacted in 1996. However, 42 CFR Part 2 has created two separate, poorly-aligned systems of care that often place patients in danger.
   c. Opioid treatment programs (OTPs) that treat patients with methadone cannot disclose this fact to other health care professionals; as a result, many primary care clinicians, specialists and hospital-based physicians are left unaware of a patient's maintenance on methadone.
   d. This proves dangerous when physicians prescribe QTc-prolonging drugs, benzodiazepines and other medications that interact with methadone.
   e. Separating SUDs from the rest of medicine further stigmatizes a disease process that might otherwise be normalized.
   f. CO's CURE supports efforts to align 42 CFR Part 2 with HIPAA, while ensuring that patients' personal health information is not inappropriately shared with law enforcement agencies, health insurers, data clearinghouses, employers and other entities outside the patient-physician relationship.
   g. CO's CURE joins the AMA, the American Hospital Association, the American Society of Addiction Medicine and others in its call to better align SUD treatment with the rest of medicine.

4. **It is recommended that telemedicine for addiction treatment be widely available and that telemedicine clinicians be permitted to prescribe buprenorphine without a face-to-face encounter.**
   a. The 2018 Special Registration for Telemedicine Clarification Act directs the DEA to amend its rules regarding the face-to-face encounters required by the 2008 Ryan Haight Act when prescribing controlled substances.
   b. The Ryan Haight Act effectively prevents clinicians from treating patients with OUD in remote areas and unnecessarily hinders care.
   c. The DEA is expected to release new rules soon that will allow the prescribing of buprenorphine via telemedicine without an initial face-to-face encounter.
   d. CO's CURE encourages a loosening of these restrictions to allow clinicians to better treat patients with OUD in rural and other hard-to-access areas.

5. **Decrease the regulations surrounding OTPs to reduce barriers for methadone maintenance treatment.**
   a. To be enrolled in an OTP and receive treatment with methadone, a patient must have been using opioids for at least 12 months. It is recommended that no patient be required to wait 12 months for treatment for a life-threatening disease.
   b. It is suggested that counseling requirements within OTPs be decreased. While most patients benefit from case management and counseling, patient autonomy is violated by the rigid requirements mandated by state and federal regulations.
   c. It is advised that a patient's ability to access proven medications like methadone and buprenorphine never be conditional upon other treatment modalities. There are many other disease states that would benefit from psychosocial therapy in addition to medication management, but clinicians would never accept making one a requirement of the other.
   d. Allow nurse practitioners to have a full scope practice within OTPs. Current regulations prohibit nurse practitioners from ordering methadone within an OTP. No such medical restrictions exist outside of OTPs.

6. **It is suggested that subsidies be provided for OTPs in rural areas.**
   a. OTPs are currently clustered around Colorado's Front Range. There are only two on the Western Slope and none on the Eastern Plains.
   b. Not all patients respond to buprenorphine, and methadone may be the only effective treatment for a significant number of patients with OUD.
   c. Select patients significantly benefit from the structure of an OTP.
   d. OTPs are not financially viable in rural areas because there are too few patients to cover operational expenses.
   e. Incentives that support the development of new OTPs in rural areas of the state would help those who live in these currently underserved communities.

The Future and Ending the Opioid Epidemic in Colorado

As clinicians, we stand with our patients and their families who are impacted by opioid use disorder. We have witnessed the devastation this epidemic has wrought across Colorado and are committed to ending the suffering of our patients and communities.

The CO's CURE guidelines offer a vision for how clinicians and health care leaders on the front lines of this epidemic can change how we deliver care to better serve our patients. If we take to heart the need to reduce our opioid usage, we can decrease the number of Coloradans who develop opioid use disorders in our care. If we embrace and continue to innovate alternatives to opioids for pain control, we will be able to manage pain more effectively and safely than ever before. If we integrate harm reduction into our practices and strive to better understand patients who struggle with injection drug use and OUD, we can end the stigma that surrounds this disease and decrease overdose deaths. If we consistently offer medication-assisted treatment to every patient with OUD for whom we care, we can close the treatment gap and ensure that all who yearn for recovery are provided the tools and the resources they need. The time to make these changes is now. In doing so, we can uphold our sacred oath to serve our patients and communities in their times of need and resolve to address this epidemic together.

CO's CURE aims to harness the power of health care professionals across Colorado working together with common purpose. CO's CURE resources are available to any Colorado physician. As you endeavor to change your practice and adopt these guidelines, you can rest assured that medical practices and specialties across our state are doing the same. CO's CURE represents a philosophy of care that is inclusive and collaborative, and recognizes that the only way we can end the epidemic in Colorado and across the nation is by acting together.

On behalf of our sponsoring organizations—Colorado Hospital Association, Colorado Medical Society and Colorado Consortium for Prescription Drug Abuse Prevention—as well as the 13 medical specialties that have stepped forward to participate, we offer our gratitude and appreciation for the care and consideration you give these guidelines. The health of our state and its people depends on clinicians and leaders like you who are willing to be agents of change. Together, we can make a profound difference in the lives of Coloradans as we implement new, better standards of care. Together we can bring this deadly epidemic to an end.

Debra Parsons, MD, FACP
PRESIDENT, COLORADO MEDICAL SOCIETY

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Robert Valuck, PhD, RPh, FNAP
EXECUTIVE DIRECTOR, COLORADO CONSORTIUM FOR PRESCRIPTION DRUG ABUSE PREVENTION

Appendices

Appendix A

Patient Educational Resources

PRESCRIPTION OPIOIDS: WHAT YOU NEED TO KNOW

Prescription opioids can be used to help relieve moderate-to-severe pain and are often prescribed following a surgery or injury, or for certain health conditions. These medications can be an important part of treatment but also come with serious risks. It is important to work with your health care provider to make sure you are getting the safest, most effective care.

WHAT ARE THE RISKS AND SIDE EFFECTS OF OPIOID USE?

Prescription opioids carry serious risks of addiction and overdose, especially with prolonged use. An opioid overdose, often marked by slowed breathing, can cause sudden death. The use of prescription opioids can have a number of side effects as well, even when taken as directed:

- Tolerance—meaning you might need to take more of a medication for the same pain relief
- Physical dependence—meaning you have symptoms of withdrawal when a medication is stopped
- Increased sensitivity to pain
- Constipation
- Nausea, vomiting, and dry mouth
- Sleepiness and dizziness
- Confusion
- Depression
- Low levels of testosterone that can result in lower sex drive, energy, and strength
- Itching and sweating

receiving prescription opioids long term in a primary care setting struggles with addiction.

* Findings from one study

RISKS ARE GREATER WITH:

- History of drug misuse, substance use disorder, or overdose
- Mental health conditions (such as depression or anxiety)
- Sleep apnea
- Older age (65 years or older)
- Pregnancy

Avoid alcohol while taking prescription opioids. Also, unless specifically advised by your health care provider, medications to avoid include:

- Benzodiazepines (such as Xanax or Valium)
- Muscle relaxants (such as Soma or Flexeril)
- Hypnotics (such as Ambien or Lunesta)
- Other prescription opioids

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

American Hospital Association®

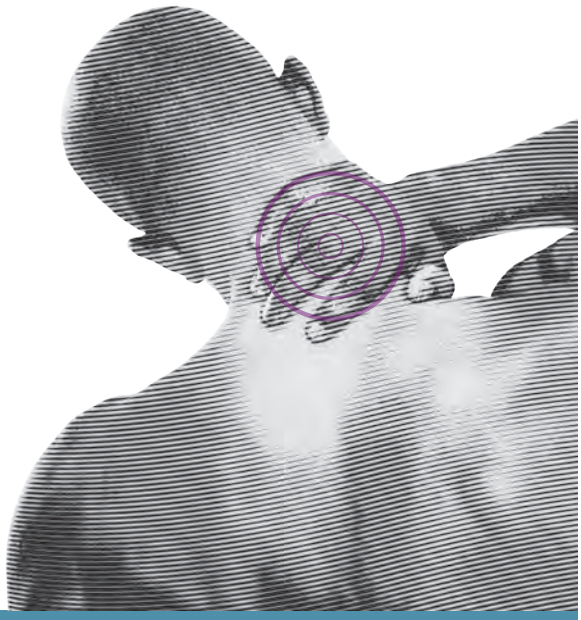
CS264107C May 9, 2016

SOURCE: CDC/AHA Opioid Factsheet for Patients

KNOW YOUR OPTIONS

Talk to your health care provider about ways to manage your pain that don't involve prescription opioids. Some of these options **may actually work better** and have fewer risks and side effects. Options may include:

- Pain relievers such as acetaminophen, ibuprofen, and naproxen
- Some medications that are also used for depression or seizures
- Physical therapy and exercise
- Cognitive behavioral therapy, a psychological, goal-directed approach, in which patients learn how to modify physical, behavioral, and emotional triggers of pain and stress.



Be Informed!

Make sure you know the name of your medication, how much and how often to take it, and its potential risks & side effects.

IF YOU ARE PRESCRIBED OPIOIDS FOR PAIN:

- Never take opioids in greater amounts or more often than prescribed.
- Follow up with your primary health care provider within ____ days.
  - Work together to create a plan on how to manage your pain.
  - Talk about ways to help manage your pain that don't involve prescription opioids.
  - Talk about any and all concerns and side effects.
- Help prevent misuse and abuse.
  - Never sell or share prescription opioids.
  - Never use another person's prescription opioids.
- Store prescription opioids in a secure place and out of reach of others (this may include visitors, children, friends, and family).
- Safely dispose of unused prescription opioids: Find your community drug take-back program or your pharmacy mail-back program, or flush them down the toilet, following guidance from the Food and Drug Administration (www.fda.gov/Drugs/ResourcesForYou).
- Visit www.cdc.gov/drugoverdose to learn about the risks of opioid abuse and overdose.
- If you believe you may be struggling with addiction, tell your health care provider and ask for guidance or call SAMHSA's National Helpline at 1-800-662-HELP.

LEARN MORE | www.cdc.gov/drugoverdose/prescribing/guideline.html

SOURCE: CDC/AHA Opioid Factsheet for Patients

Appendix A continued

SURGICAL

YOU are the most important member of your healthcare team. Ask questions and get the FACTS before taking opioids to manage your pain.

WHAT IS AN OPIOID?

An opioid is a strong prescription pain medication. Possible side effects include nausea, vomiting, sleepiness, dizziness and/or constipation.

Common opioids include:

Generic Name	Brand Name
Codeine	Tylenol® #3* or #4*
Fentanyl	Duragesic®
Hydrocodone	Vicodin®*, Norco®*
Hydromorphone	Dilaudid®
Methadone	Methadose®
Morphine	MS Contin®, Kadian
Oxycodone	Percocet®*, OxyContin®
Oxymorphone	Opana®
Tramadol	Ultram®, Ultracet®*

* Contains acetaminophen (Tylenol). Use caution if you're also taking acetaminophen separately.

SAFE STORAGE AND DISPOSAL

Store opioids out of sight and reach of children, teens, and pets

- Store opioids in private areas and lock up your pills if possible.
- Do not store your opioids in common rooms in the house (like bathrooms, kitchens) or in purses.
- Keep a count of how many pills you have left.

Dispose of all unused opioids

- Use a permanent medication drop box. To find one near you, visit: **Michigan-OPEN.org/takebackmap**.
- Drop off at a community Medication Take Back event.
- Use your household trash as a last resort.
  - Mix opioids (do not crush) with used coffee grounds or kitty litter in a plastic bag and throw away.
  - Scratch out personal information on the prescription label and dispose of the original container.

Do NOT flush opioids down the toilet.

Michigan-OPEN.org

Michigan OPEN is partially funded by the Michigan Department of Health and Human Services.

LEARN THE FACTS:

opioids & pain management

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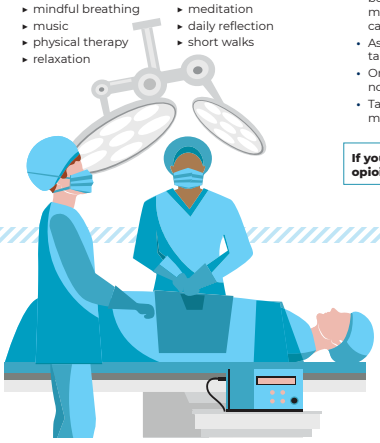
OPIOID PRESCRIBING ENGAGEMENT NETWORK

UNDERSTANDING PAIN AFTER SURGERY

The **GOAL OF PAIN MANAGEMENT** is to manage your pain enough to allow you to do the things you need to do in order to heal: walk, eat, breathe deeply and sleep.

Pain Expectations

- Feeling pain after surgery is normal.
- Pain is usually worst for the first 2-3 days after surgery.
- Your pain may be well controlled with a schedule of over-the-counter medications.
- Pain medication is only **one** part of your pain management plan.
- Other things you can do to help manage pain:
  - mindful breathing
  - music
  - physical therapy
  - relaxation
  - meditation
  - daily reflection
  - short walks



USING OPIOIDS SAFELY

BEFORE SURGERY:

- Ask your surgeon if you can use over-the-counter acetaminophen (Tylenol) or ibuprofen (Motrin or Advil) for your pain, before using an opioid.
- Tell your surgeon if you are currently taking any sedatives or benzodiazepines (like Valium or Xanax).

AFTER SURGERY:

- If you are still in a lot of pain after taking an over-the-counter pain medicine, use the opioid medicine your surgeon gave you.
- Do NOT mix opioids with alcohol, benzodiazepines (like Valium or Xanax), muscle relaxers, or other medications that can cause sleepiness.
- As your pain gets better, wait longer between taking opioids.
- Only use the opioids for your surgical pain. Do not use your opioids for other reasons.
- Talk to your surgeon if you are having trouble managing your pain.

If your pain is manageable, do not use your opioids.

Tell your doctor if you are pregnant or planning to become pregnant. Using opioid medications can cause harm to a fetus, including neonatal abstinence syndrome.

KNOW THE RISKS

You are at higher risk of developing a **DEPENDENCE OR ADDICTION** to opioids if you:

HAVE A HISTORY OF:

- Abusing alcohol, prescription, or recreational drugs
- Using tobacco
- Depression, anxiety, or other mood disorders
- Long-term (chronic) pain

TAKE OPIOIDS FOR LONGER THAN A FEW DAYS

TAKE OPIOIDS MORE OFTEN THAN YOUR SURGEON PRESCRIBED

You are at risk of an **OVERDOSE** if you:

HAVE A HISTORY OF:

- Sleep apnea
- Other breathing problems

MIX OPIOIDS WITH:

- Alcohol
- Benzodiazepines (like Valium® or Xanax®)
- Muscle relaxers
- Any medications that can cause drowsiness
- Recreational drugs

TAKE OPIOIDS MORE OFTEN THAN YOUR SURGEON PRESCRIBED

DO NOT SHARE YOUR OPIOIDS with others. Diversion (sharing or selling) of opioids is a felony.

SOURCE: Trifold patient guide for surgical pain management with opioids

Appendix A continued

SAFE **STORAGE** AND **DISPOSAL** OF OPIOIDS

Store opioids out of sight and reach of children, teens, and pets

- Store opioids in private areas and lock up your pills if possible.
- Do not store your opioids in common rooms in the house (like bathrooms, kitchens) or in purses.
- Keep a count of how many pills you have left.

Dispose of all unused opioids

- Use a permanent medication drop box. To find one near you, visit: **Michigan-OPEN.org/takebackmap**.
- Drop off at a community Medication Take Back event.
- Use your household trash as a last resort.

Mix opioids (do not crush) with used coffee grounds or kitty litter in a plastic bag and throw away.

Scratch out personal information on the prescription label and dispose of the original container.

Do NOT flush opioids down the toilet.

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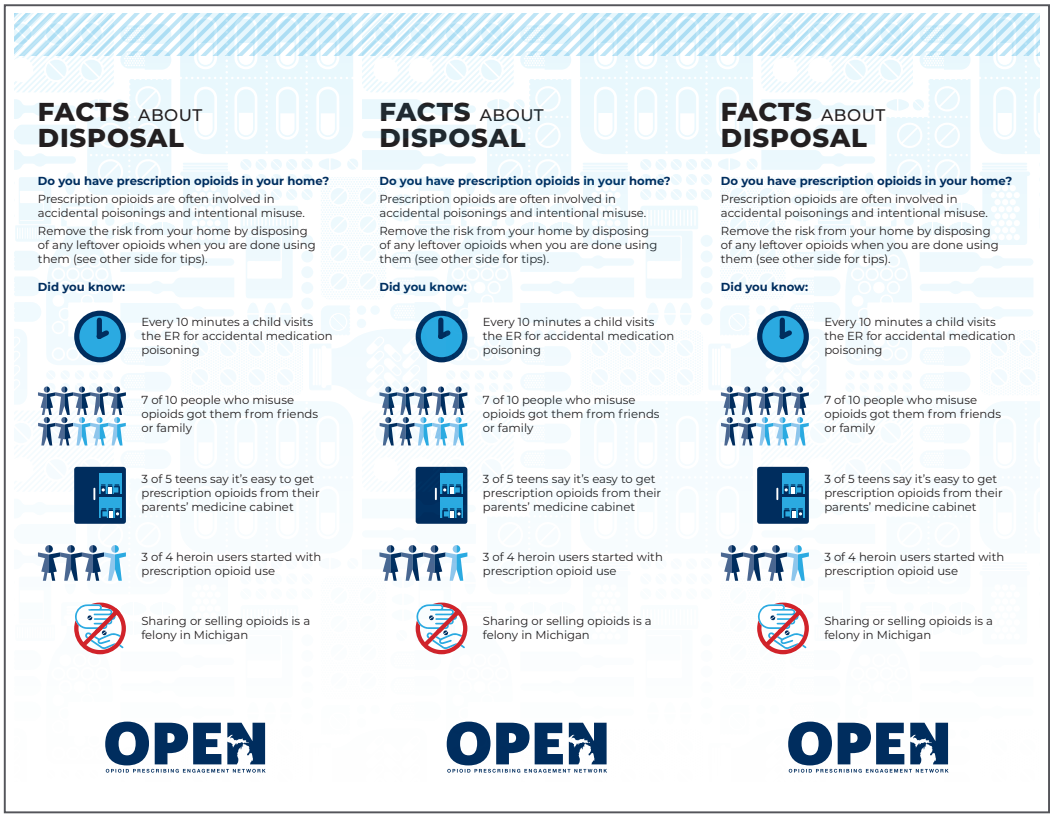

FACTS ABOUT **DISPOSAL**

Do you have prescription opioids in your home?

Prescription opioids are often involved in accidental poisonings and intentional misuse.

Remove the risk from your home by disposing of any leftover opioids when you are done using them (see other side for tips).

Did you know:

- Every 10 minutes a child visits the ER for accidental medication poisoning
- 7 of 10 people who misuse opioids got them from friends or family
- 3 of 5 teens say it's easy to get prescription opioids from their parents' medicine cabinet
- 3 of 4 heroin users started with prescription opioid use
- Sharing or selling opioids is a felony in Michigan

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OPIOID PRESCRIBING ENGAGEMENT NETWORK

SOURCE: Stock card for patients: safe storage and disposal of opioids

Appendix A continued

MANAGING PAIN
WITHOUT OPIOIDS

MINDFUL BREATHING can help manage pain and anxiety.

Aim to practice mindful breathing two times a day in 10-minute sessions.

Setting a timer can help when first starting.

Sit in a comfortable position.

It may be helpful to close your eyes or focus on an object.

Breathe in through your nose for five seconds — counting in your head "1, 2, 3, 4, 5."

Breathe out through your mouth for another five seconds — "1, 2, 3, 4, 5."

Keep this rhythm and focus on your breath for 10 minutes.

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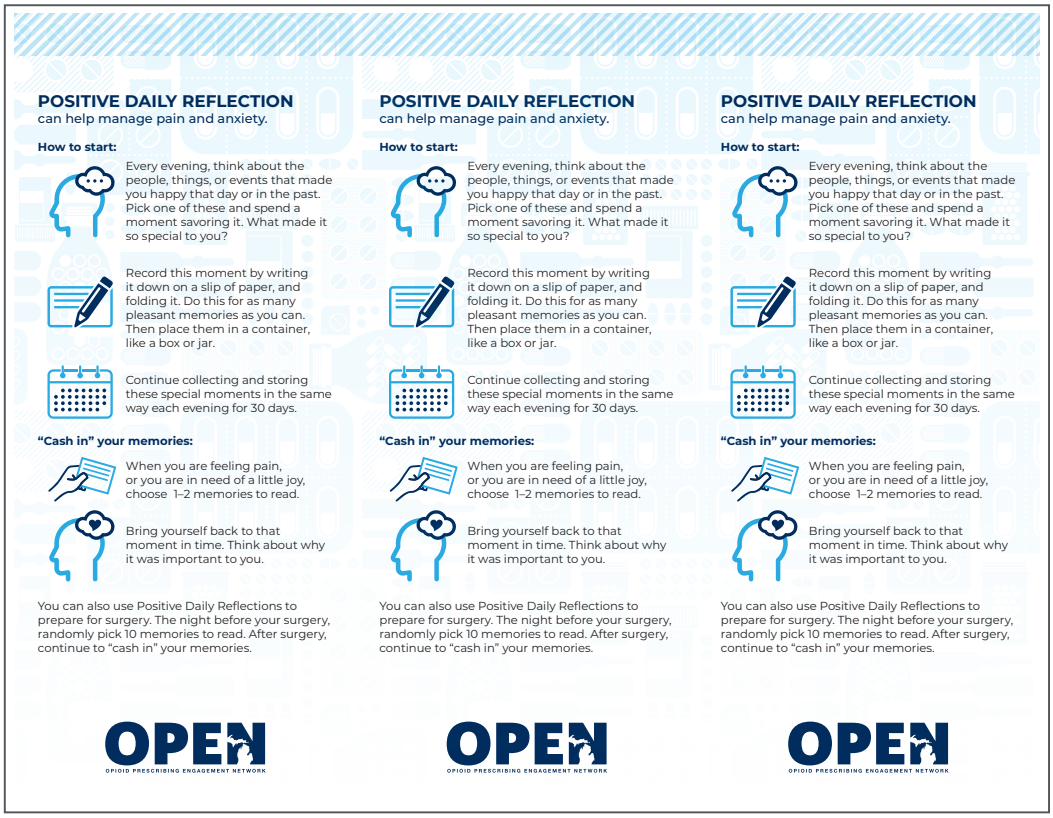

POSITIVE DAILY REFLECTION
can help manage pain and anxiety.

How to start:

Every evening, think about the people, things, or events that made you happy that day or in the past. Pick one of these and spend a moment savoring it. What made it so special to you?

Record this moment by writing it down on a slip of paper, and folding it. Do this for as many pleasant memories as you can. Then place them in a container, like a box or jar.

Continue collecting and storing these special moments in the same way each evening for 30 days.

"Cash in" your memories:

When you are feeling pain, or you are in need of a little joy, choose 1–2 memories to read.

Bring yourself back to that moment in time. Think about why it was important to you.

You can also use Positive Daily Reflections to prepare for surgery. The night before your surgery, randomly pick 10 memories to read. After surgery, continue to "cash in" your memories.

OPEN
OPIOID PRESCRIBING ENGAGEMENT NETWORK

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OPEN
OPIOID PRESCRIBING ENGAGEMENT NETWORK

SOURCE: Stock card for patients: managing pain without opioids (mindfulness/positive reflections)

MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

Managing Your Pain After Surgery Without Opioids

For patients participating in the Michigan Pain-Control Optimization Pathway (MPOP)

Thank you for participating in our program to help patients manage their pain after surgery without opioids. This is part of our effort to provide you with the best care possible, without exposing you or your family to the risk that opioids pose.

What pain can I expect after surgery?

You can expect to have some pain after surgery. This is normal. The pain is typically worse the day after surgery, and quickly begins to get better.
We recently conducted a study that found many patients are able to manage their pain after surgery with Over-the-Counter (OTC) medications such as Tylenol and Motrin. If you have a condition that does not allow you to take Tylenol or Motrin, notify your surgical team.

How will I manage my pain?

The best strategy for controlling your pain after surgery is **around the clock** pain control with Tylenol (acetaminophen) and Motrin (ibuprofen or Advil). **Alternating** these medications with each other allows you to maximize your pain control. In addition to Tylenol and Motrin, you can use heating pads or ice packs on your incisions to help reduce your pain.

How will I alternate your regular strength over-the-counter pain medication?

You will take a dose of pain medication every three hours.

- Start by taking 650 mg of Tylenol (2 pills of 325 mg)
- 3 hours later take 600 mg of Motrin (3 pills of 200 mg)
- 3 hours after taking the Motrin take 650 mg of Tylenol
- 3 hours after that take 600 mg of Motrin.

continued

See example - if your first dose of Tylenol is at 12:00 PM

12:00 PM	Tylenol 650 mg (2 pills of 325 mg)
3:00 PM	Motrin 600 mg (3 pills of 200 mg)
6:00 PM	Tylenol 650 mg (2 pills of 325 mg)
9:00 PM	Motrin 600 mg (3 pills of 200 mg)
Continue alternating every 3 hours	

We recommend that you follow this schedule around-the-clock for at least 3 days after surgery, or until you feel that it is no longer needed. Use the table on the last page of this handout to keep track of the medications you are taking.

Important:

Do not take more than 4000mg of Tylenol or 3200mg of Motrin in a 24-hour period.

What if I still have pain?

If you have pain that is not controlled with the over-the-counter pain medications (Tylenol and Motrin or Advil) you might have what we call "breakthrough" pain. You will receive a prescription for a small amount of an opioid pain medication such as Oxycodone, Tramadol, or Tylenol with Codeine. Use these opioid pills in the first 24 hours after surgery if you have breakthrough pain. **Do not take more than 1 pill every 4-6 hours.**

If you still have uncontrolled pain after using all opioid pills, don't hesitate to call our staff using the number provided. We will help make sure you are managing your pain in the best way possible, and if necessary, we can provide a prescription for additional pain medication.

continued

Appendix A continued

Day 1					
Time	Name of Medication	Number of pills taken	Amount of Acetaminophen	Pain Level	Comments
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
Total Daily amount of Acetaminophen **Do not take more than 3,000 mg per day**					

Day 2					
Time	Name of Medication	Number of pills taken	Amount of Acetaminophen	Pain Level	Comments
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
Total Daily amount of Acetaminophen **Do not take more than 3,000 mg per day**					

Day 3					
Time	Name of Medication	Number of pills taken	Amount of Acetaminophen	Pain Level	Comments
AM PM					
AM PM					
AM PM					
AM PM					

continued

AM PM					
AM PM					
AM PM					
AM PM					
Total Daily amount of Acetaminophen **Do not take more than 3,000 mg per day**					

Day 4

Time	Name of Medication	Number of pills taken	Amount of Acetaminophen	Pain Level	Comments
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
Total Daily amount of Acetaminophen **Do not take more than 3,000 mg per day**					

Day 5

Time	Name of Medication	Number of pills taken	Amount of Acetaminophen	Pain Level	Comments
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
Total Daily amount of Acetaminophen **Do not take more than 3,000 mg per day**					

continued

Appendix A continued

Day 6

Time	Name of Medication	Number of pills taken	Amount of Acetaminophen	Pain Level	Comments
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
Total Daily amount of Acetaminophen **Do not take more than 3,000 mg per day**					

Day 7

Time	Name of Medication	Number of pills taken	Amount of Acetaminophen	Pain Level	Comments
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
AM PM					
Total Daily amount of Acetaminophen **Do not take more than 3,000 mg per day**					

SOURCE: Patient instructions for managing surgical pain without opioids (MPOP)

Surgical clinicians can direct patients to takemedsseriously.org for education in safe use and disposal of prescription opioids.

Appendix B

Screening Instruments

A: Screening Tools for Risk of Developing Opioid Use Disorder[138]

Opioid Risk Tool — OUD (ORT-OUD)

This tool should be administered to patients upon an initial visit prior to beginning or continuing opioid therapy for pain management. A score of 2 or lower indicates low risk for future opioid use disorder; a score of >/=3 indicates high risk for opioid use disorder.

Mark each box that applies:	Yes	No
FAMILY HISTORY OF SUBSTANCE ABUSE		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
PERSONAL HISTORY OF SUBSTANCE ABUSE		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
AGE BETWEEN 16-45 YEARS	1	0
PSYCHOLOGICAL DISEASE		
ADD, OCD, bipolar, schizophrenia	1	0
Depression	1	0
SCORING TOTALS	____	____

Screener and Opioid Assessment for Patients with Pain-Revised

How often have you felt that things are just so overwhelming that you can't handle them?

How often is there tension at home?

How often have you been concerned that people will judge you for taking pain medication?

How often have you taken more pain medication than you were supposed to?

How often have others expressed concern over your use of medication?

How often have you run out of pain medication early?

How often have you attended an AA or NA meeting?

How often have you been sexually abused?

Although designed for use in the chronic pain population, the SOAPP-8 may help surgeons predict which patients are at elevated risk of developing aberrant opioid-related behaviors with an accuracy of nearly 80%.

Rapid Opioid Dependence Screen (RODS)

Instructions: [Interviewer reads] The following questions are about your prior use of drugs. For each question, please indicate "yes" or "no" as it applies to your drug use during the last 12 months.

1. Have you ever taken any of the following drugs?
   - a. Heroin ☐ Yes ☐ No
   - b. Methadone ☐ Yes ☐ No
   - c. Buprenorphine ☐ Yes ☐ No
   - d. Morphine ☐ Yes ☐ No
   - e. MS Contin ☐ Yes ☐ No
   - f. Oxycontin ☐ Yes ☐ No
   - g. Oxycodone ☐ Yes ☐ No
   - h. Other opioid analgesics *(e.g., Vicodin, Darvocet, etc.)* ☐ Yes ☐ No

If any drug in question 1 is coded "yes," proceed to quesitons 2 to 8.

If all drugs in question 1 are "no," skip to end and code "no" for opioid dependent.

2. Did you ever need to use more opioids to get the same high as when you first started using opioids? ☐ Yes ☐ No
3. Did the idea of missing a fix (or dose) ever make you anxious or worried? ☐ Yes ☐ No
4. In the morning, did you ever use opioids to keep from feeling "dope sick" or did you ever feel "dope sick?" ☐ Yes ☐ No
5. Did you worry about your use of opioids? ☐ Yes ☐ No
6. Did you find it difficult to stop or not use opioids? ☐ Yes ☐ No
7. Did you ever need to spend a lot of time/energy on finding opioids or recovering from feeling high? ☐ Yes ☐ No
8. Did you ever miss important things like doctor's appointments, family/friend activities, or other things because of opioids? ☐ Yes ☐ No

Scoring Instructions: Add number of "yes" responses for questions 2 to 8. If total is > 3, code "yes" for opioid dependent. If total is < 2, code "no" for opioid dependent.

Opioid Dependent: ☐ Yes ☐ No

B: Behavioral Health Screening Instruments

To access a wide range of behavioral health screening tools, including tools that can be administered and scored quickly, visit: https://www.integration.samhsa.gov/clinical-practice/screening-tools

Kessler-6

The Kessler-6 is one of many brief screening instruments for mental health disorders.[681] A score >13 suggests major mental health disorder, >5 suggests milder mental health disorder. Clinicians are encouraged to refer patients scoring >5 for behavioral health consultation and care.

K6+

Provider: _____

Provider ID: |___|___|___|___|___|___|___|___|

Date completed: ___ ___ / ___ ___ / ___ ___ ___ ___

Please use gummed lable if available

Patient or Client Identifier: |_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

Surname:

Other names:

Date of Birth: ___ ___ / ___ ___ / ___ ___ ___ ___

Sex: Male ☐ 1 Female ☐ 2

Address:

The following questions ask about how you have been feeling during the past 30 days. For each question, please circle the number that best describes how often you had this feeling.

Q1: During the past 30 days, about how often did you feel…	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. …nervous?	1	2	3	4	5
b. …hopeless?	1	2	3	4	5
c. …restless or fidgety?	1	2	3	4	5
d. …so depressed that nothing could cheer you up?	1	2	3	4	5
e. …that everything was an effort?	1	2	3	4	5
f. …worthless?	1	2	3	4	5

continued

Q2: The last six questions asked about feelings that might have occurred during the past 30 days. Taking them altogether, did these feelings occur more often in the past 30 days than usual for you, about the same as usual, or less often than usual? (If you never have any of the feelings, circle response option "4.")

More often than usual			About the same as usual	Less often than usual		
A lot	Some	A little		A little	Some	A lot
1	2	3	4	5	6	7

The next few questions are about how these feelings may have affected you in the past 30 days. You need not answer these questions if you answered "None of the time" to all of the six questions about your feelings.

Q3: During the past 30 days, how many days out of 30 were you totally unable to work or carry out your normal activities because of these feelings?
_____ (Number of days)

Q4: Not counting the days you reported in response to Q3, how many days in the past 30 were you able to do only half or less of what you would normally have been able to do, because of those feelings?
_____ (Number of days)

Q5: During the past 30 days, how many times did you see a doctor or other health professional about these feelings?
_____ (Number of days)

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
Q6 : During the past 30 days, have physical health problems been the main cause of these feelings?	1	2	3	4	5

Thank you for completing this questionnaire.

Appendix B continued

C: Screening Tools for Preoperative Anxiety

Instrument references	Framework/ psycho-physiological response	Sample subjects	Instrument descripton and scoring	Reliability	Validity	Feasibility	Level of evidence
State-Trait Anxiety Index (STAI)	No framework; reported BIS monitoring	Adult surgical patients under-going general or regional anes-thesia at Ankara Training and Research Hospital of Ministry of Health, Ankara, Turkey (n=52)	Consists of 2 20-item sections for state anxiety (STAI-S) and trait anxiety (STAI-T)	Reported as "supported by studies that demonstrated reductions in BIS and STAI correlated well with anxiolysis. Correlations between propo-fol dose for BIS of 65 and S-STAI was r^2=0.033 and T-STAI was r^2=0.067 from the original study.	Reported as "supported by studies"	20-30 minutes to complete on average, 40-item questionnaire potentially time consuming	2: prospective, randomized, single-blinded, controlled study
Standard visual analog scale (VAS) to measure anxiety	No framework; reported RR, HR, DBP, SBP	Adult surgical patients scheduled for abdominal surgery in Tehran, Iran (n=70)	Visual analog scale from 0-10 to measure anxiety; mean anxiety scores were compared before and after intervention	Reported as proved reliable from its use in several different research studies	Reported as proved valid from its use in several different research studies; correlation coefficient (r) of 0.55-0.84 between VAS and STAI	Simple too, data are limited based on 1 scale rating, easier to use in difficult clinical settings	2: randomized controlled clinical trial
20-item Spielberger State Anxiety Scale (SAI)	No framework; reported MAP, pain scores	Convenience sample of women with breast malignancy undergoing mastectomy at an urban hospital in western Tennessee (n-30)	20-item scale, anxiety level scores from T1 to T2 were compared	Internal consistency values for the SAI were reported as 0.958 at T1 and 0.973 at T2	Not reported	10 minutes to complete 20-item scale	3: quasi-experimental design
Visual Analog Scale (VAS)	No framework; reported HR variability	Adults waiting for surgery without pre-medication at a metropolitan teaching hospital in Taiwan (n=167)	VAS is a 10-cm horizontal line marked by vertical lines at 1-cm intervals; scores range from 0 indicat-ing "not anxious at all" to 10 indicating "extremely anxious"	Not reported	Report reference data for criterion validity of VAS for measur-ing anxiety, correlation with hospital anxiety (r=0.28) and STAI (r=0.5-0.6 or 0.78)	Simple tool, 5 seconds for patient to communicate anxiety level, patient can remain lying flat	2: randomized controlled clinical trial

SOURCE: Instruments to Measure Preoperative Acute Situational Anxiety[682]

Appendix B continued

A simple visual facial anxiety scale VFAS for assessing acute preoperative anxiety

Serial Number	A0	A1	A2	A3	A4	A5	A6	A7	A8	A9	A10
											

SOURCE: Cao, et al. PLOS ONE February 14, 2017 https://doi.org/10.1371/journal.pone.0171233

The Amsterdam Preoperative Anxiety and Information Scale (APAIS)

1. I am worried about the anesthetic
2. The anesthetic is on my mind continually
3. I would like to know as much as possible about the anesthetic
4. I am worried about the procedure
5. The procedure is on my mind continually
6. I would like to know as much as possible about the procedure

The measure of agreement with these statements should be graded on a 5-point Likert from 1 “not at all” to 5 “extremely.”

A score of ≥11 identify anxious patients in clinical practice.

Source: Moerman N, van Dam FSAM, Muller MJ, Oosting H. The Amsterdam Preoperative Anxiety and Information Scale (APAIS). Anesthesia and Analgesia. 1996;82:445-451

Appendix B continued

D: Risk Index for the Prediction of Chronic Postsurgical Pain[683]

Please ask the patient before surgery; no/yes

1. Have you suffered from preoperative pain in the part of the body operated on?
2. Have you suffered from preoperative pain elsewhere (chronic headache, back pain, etc.)?
3. Have you felt hopelessness, sadness or depression lasting longer than two weeks in the past 6 months?
4. Considering the last 6 months, have you felt extremely nervous and/or anxious?
5. Have you suffered from capacity overload/overstrain in the last 6 months?
6. Do you suffer form any of the following symptoms:
   Sleeping disorder, exhaustibility/exhaustion, frightening thoughts, dizziness, tachycardia, feeling of being misunderstood, trembling hands, or do you take any sleeping pills.
7. How do you see your convalescence? Do you think you will be fit for work again or to do your daily activities within the next 6 months?
   (belief that no recovery/resumption is possible after months)
8. Does the surgery imply an increased risk of nerve injury (thoracotomy, mastectomy, hernia repair, abdominal surgery, etc.)?
9. Does the patient undergo a removal/revision surgery or a primary surgery?
10. Will a non-laparoscopic or minimally invasive surgery be performed?
11. Will a mesh implantation be performed?
12. Is it inpatient (or ambulatory) surgery?

To score: 0 or 1 risk factors presented = low risk of developing CPSP, (2) 2 risk factors presented = moderate risk of developing CPSP, (3) 3 to 5 risk factors presented = high risk of developing CPSP.[683]

Appendix C

Understanding Pain: A Complex Biopsychosocial Phenomenon

The United States is not only besieged by OUD, it is also facing an epidemic of pain. Despite the fact that Americans consume a disproportionate number of the world's opioids, one-fifth continue to suffer from pain. Common sense and neuroscience agree that pain is not simply a process defined by receptors, neurological afferents and interactions between the spinal cord and brainstem. Rather, it is an experience that integrates these biological elements with psychological and social conditions.

To an extent not seen with other conditions, pain is a complex interplay of peripheral and CNS processes that are intertwined with each patient's biology, psychology and social circumstances. Although the experience of pain is literally "all in the head," it is significantly influenced by the context of the painful event or condition, mental health comorbidities and the patient's life experiences.

The Biology of Pain

Most physicians are aware of the distinctions between nociceptive pain (somatic or visceral), neuropathic pain, inflammatory pain and other less easily categorized types of pain (e.g., cancer pain, headache syndromes, fibromyalgia). Pain also differs in its duration, intensity, location and etiology. Sensorimotor pathways relay information about the nature of the pain stimulus. Cognitive and affective pathways evaluate and incorporate sensorimotor information, integrating it with information based on prior experiences and emotions.

Surgeons are encouraged to use opioid-sparing multimodal analgesia as outlined in these guidelines and to consult pain specialists for patients whose pain is not well managed. Regrettably, the indiscriminate prescription of opioids may have contributed to an epidemic of chronic pain. Opioid-induced hyperalgesia, a disorder that leads to the sensitization of pronociceptive mechanisms and a resultant decrease in the pain threshold, may contribute to persistent complaints.[353-355]

Advances in the neurobiology of pain shed light on the physiological explanations for individual differences in pain thresholds and analgesic responses. While it goes without saying that every patient is different, fresh insights into the genetic and molecular basis of pain perception from model organisms and human twin studies underscore the significant genetic contributors and polymorphisms in pain tolerance and analgesic responsiveness.[356-358] Gender-based research, another important area of ongoing study, consistently demonstrates differences in pain threshold, susceptibility to chronic pain and analgesia sensitivity between male and female patients.[359] Studies have also identified measurable electroencephalography signatures capable of predicting differences in pain tolerance between individuals.[360]

The Psychology of Pain

Neuroimaging studies demonstrate the significant extent to which cognitive and affective factors affect the experience of pain. The anticipation of pain and the patient's level of attention or distraction, mood, tendency to catastrophize and perceived level of control over their symptoms can modulate peripheral, spinal and central activity before, during and after a painful experience.

The context of a painful stimulus and a person's prior life events further influence the way in which they experience pain. For example, a woman who grew up loving dogs is at home with her new puppy. If she is suddenly nipped in the middle of the night with an intensity of "x," she will experience pain. However, her prior positive interactions with dogs, the safe surroundings (home) and her certainty that the nip came from the puppy will modulate her negativity of the experience. The same woman, who has always been wary of the ocean, is now at the beach. After finally mustering the courage to wade in, she hears a lifeguard shout, "Shark!" If she feels a nip at her ankles while in the water, she is likely to have a drastically different pain experience than she had with the puppy, even if the intensity of the two experiences is identical.

The anticipation of pain, expectations surrounding painful experiences and expectations of relief impact the experience of pain on neuroimaging and by patient report. Studies of normal subjects demonstrate the power of both the placebo effect and the nocebo effect; the same noxious stimulus can produce markedly different neuroimaging and patient experiences. Accordingly, a host of psychological interventions have demonstrated evidence for relieving the negative effects of the pain experience. These range from the use of supportive therapy, cognitive behavioral therapy, acceptance and commitment therapy, virtual reality therapy and mindfulness-oriented interventions that leverage insights into the cognitive and affective components of pain signaling.

The association between mental health, SUDs and the experience of pain is well established.[684] The vicious cycle of pain begetting depression and anxiety, which then impairs patients' ability to effectively manage their symptoms, is familiar to most physicians. Functional neuroimaging demonstrates shared neural mechanisms for both pain and depression and anxiety.[685-687]

Finally, it is important to acknowledge the critical role that physician empathy can play in promoting pain relief.688 Because the psychology of patient-physician interactions influences the way patients experience pain and analgesia, physician desensitization to pain complaints can undermine the quality of care and decrease the clinician's professional satisfaction.[689] Physicians who become frustrated when treating a patient with intractable pain are advised to consult with pain medicine and mental health specialists.

Social Determinants of Pain

While few physicians are equipped to address the deeply rooted social factors that contribute to their patients' pain, it is important to understand that poverty, racism, social stress and isolation affect these experiences.[690] Although pain is universally experienced, it is not universally understood. Patients, families and communities all value and understand pain differently. Furthermore, types of pain can be tempered by their social repercussions. Genital pain, for example, may be more isolating than back pain, as the former cannot be easily talked about with others. This ensuing isolation can intensify the pain experience. It is interesting to note that the brain activation sparked by social rejection or exclusion is very similar to that caused by physical pain. In an age of ever-widening income inequality and persistent racial disparities in health status, it is important to consider the measurable, complex impact that poverty and racism can have on pain perception.

The Biopsychosocial Model of Pain: Implications for Clinicians

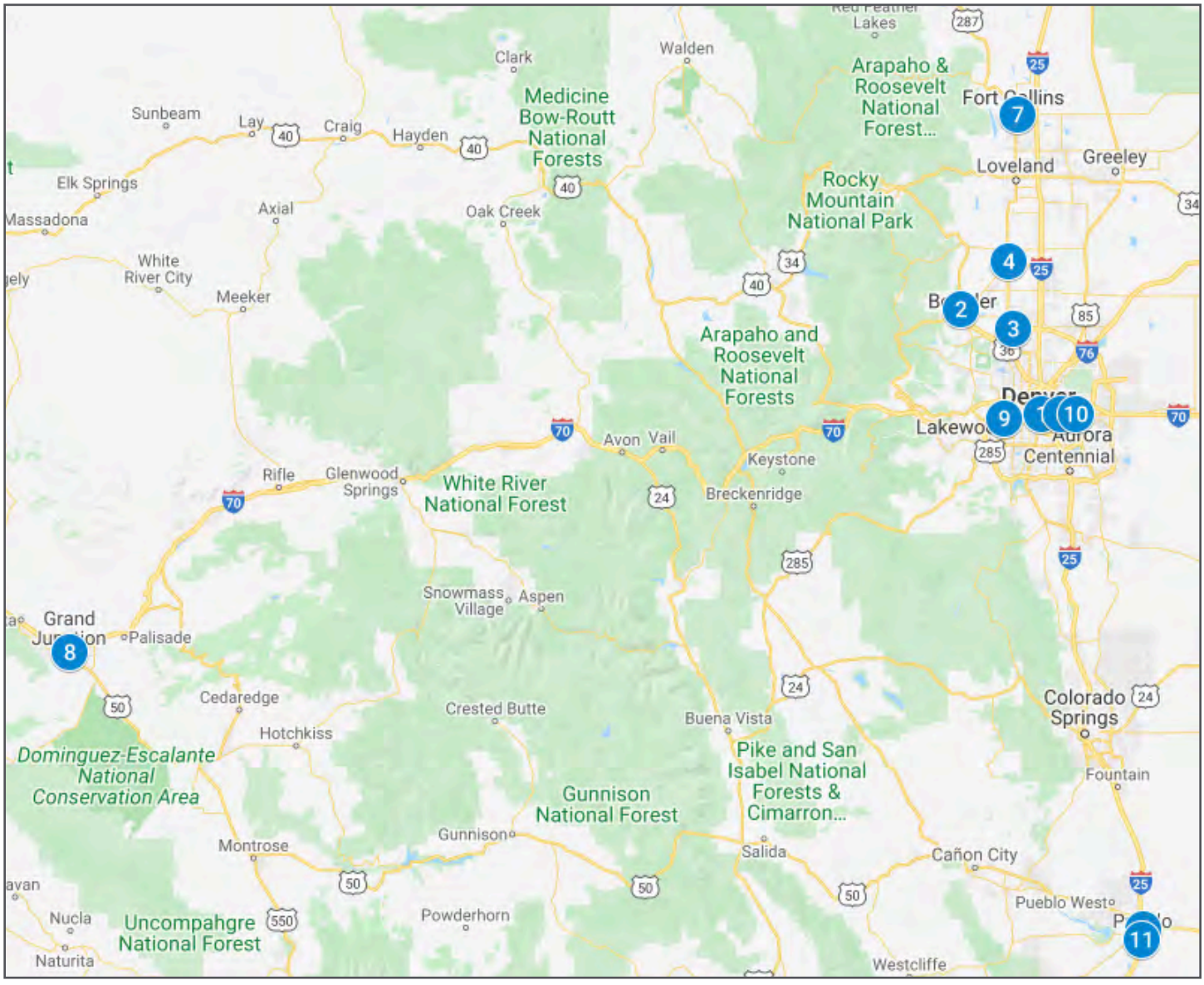
The biopsychosocial model of pain underscores the importance of valuing and addressing each of these components. While a review of the state of pain neuroscience is beyond the scope of these guidelines, functional neuroimaging suggests that there is far more interconnection between the sensory-discriminative and the cognitive-affective circuits than previously appreciated. The model in which "real" pain is biological and the psychological or affective components of pain are secondary (and, therefore, implicitly or explicitly less valid) is inaccurate and misleading. Researchers theorize that the neural networks involved in pain processing may integrate the sensory, cognitive and affective aspects of pain into a "common currency" that gives rise to one unified pain experience.[691]

To an extent not seen with other conditions, the biology of pain is the sociopsychology of pain. It is vital for physicians to recognize that the experience of pain is distinct for every individual; as such, the psychological and social determinants of pain are just as real—and worthy of treatment—as any observable injury. Physicians serve their patients best when they involve pain specialists, mental health clinicians, physical therapy and social workers in the management of patients with complex pain presentations.

Appendix D

Map and Listing of Syringe Access Programs in Colorado

(updated March 2020)



Appendix D continued

	Name	Address	Hours	Phone
1	Harm Reduction Action Center	112 E. 8th Avenue Denver, CO 80203	Mon–Fri 9 a.m.–12 p.m.	303.572.7800
2	The Works	3482 Broadway Boulder, CO 80304	Mon–Fri 10:30 a.m.–4:30 p.m.	303.413.7533 303.441.1100
3	Boulder County Public Health	1735 S. Public Road Lafayette, CO 80026	Tues & Thurs 10:30 a.m.–4:30 p.m.	720.564.2706
4	Boulder County Public Health	515 Coffman Street, #200 Longmont, CO 80501	Mon–Fri 10:30 a.m.–4:30 p.m.	303.678.6166
5	Southern Colorado AIDS Project	807 N. Greenwood Street Suite 200 Pueblo, CO 81003	Mon–Fri 10 a.m.–12 p.m. & 1:30–4 p.m.	719.621.1105
6	Denver Colorado AIDS Project	6260 E. Colfax Avenue Denver, CO 80220	Mon–Thurs, 1–6 p.m. Fri, 12–5 p.m.	303.837.0166
7	Northern Colorado AIDS Project	400 Remington Street, #100 Fort Collins, CO 80524	Mon, Thurs & Fri 1–5:45 pm Tues, 2–5:45 p.m. Wed, 1–6:45 p.m.	970.484.4469
8	Western Colorado AIDS Project	805 Main Street Grand Junction, CO 81501	Mon, Wed & Fri 12–4:45 p.m.	970.243.2437
9	Points West Syringe Service Program	645 Parfet Street Lakewood, CO 80215	Mon & Thurs 8 a.m.–6 p.m. Wed & Fri 8 a.m.–5 p.m.	303.239.7078
10	Aurora Syringe Access Services	1475 Lima Street Aurora, CO 80010	Mon–Thurs 1–4 p.m.	303.363.3077
11	Southern Colorado Harm Reduction Association	1249 E. Routt Avenue Pueblo, CO 81004	Sat 12:30–4:30 p.m.	719.289.7149
12	Rocky Mountain Cares LifePoint	Mobile SAP for DenverArea	Mon, Wed & Fri Mobile Outreach Exchange; hours vary	720.385.6898

Colorado Department of Public Health & Environment keeps an updated list of SEPs which may be accessed at https://www.colorado.gov/pacific/cdphe/reducing-infections-injection-drug-use

Appendix E

Initiating Medication for Addiction Treatment in the Hospital Setting

A: Quick Guide: Buprenorphine Starts in the Hospital

BRIDGE
TREATMENT STARTS HERE

Buprenorphine (Bup) Hospital Quick Start

- Any prescriber can order Bup in the hospital, even without an x-waiver.
- Bup is a high-affinity, partial agonist opioid that is safe and highly effective for treating opioid use disorder.
- If patient is stable on methadone or prefers methadone, recommend continuation of methadone as first-line treatment.

Uncomplicated* opioid withdrawal?**

NO → **Start Bup after withdrawal**
Supportive meds prn, stop other opioids

YES (stop other opioids)

Administer 8mg Bup SL

1 HOUR

Withdrawal symptoms improved?

NO → **No Improvement**

Differential Diagnosis:

- **Withdrawal mimic:** Influenza, DKA, sepsis, thyrotoxicosis, etc. Treat underlyling illness.
- **Incompletely treated withdrawal:** Occurs with lower starting doses; improves with more Bup.
- **Bup side-effect:** Nausea, headache, dysphoria. Continue Bup, treat symptoms with supportive medications.
- **Precipitated withdrawal:** Too large a dose started too soon after opioid agonist.

  Usually time limited, self resolving with supportive medications.

  In complex or severe cases of precipitated withdrawal, OK to stop Bup and give short acting full agonists.

YES

Administer 2nd dose

Inpatient: 8mg. Subsequent days, titrate from 16mg with additional 4-8mg prn cravings.
ED: 8-24mg. Consider discharge with higher loading dose.

Maintenance Treatment 16 mg Bup SL/day

Titrate to suppress cravings;
Usual total dose 16-32mg/day

Discharge

- Document Opioid Withdrawal and/or Opioid Use Disorder as a diagnosis.
- **If no X-waiver:** Use loading dose up to 32mg for long effect and give rapid follow up.
- **If X-waiver:** Check CURES (not required in Emergency Department if ≤7 day prescription), prescribe sufficient Bup/Nx until follow-up.

Overdose Education Naloxone Kit

Naloxone 4mg/0.1ml intranasal spray

Buprenorphine Dosing

- Either Bup or Bup/Nx (buprenorphine/naloxone) films or tab sublingual (SL) are OK.
- If unable to take oral/SL, try Bup 0.3mg IV/IM.
- OK to start with lower initial dose: Bup 2-4mg SL.
- Total initial daily dose above 16mg may increase duration of action beyond 24 hrs.
- Bup SL onset 15 min, peak 1 hr, steady state 7 days
- May dose qday or if co-exisiting chronic pain split dosing TID/QID.

*Complicating Factors

- Altered mental status, delirium, intoxication
- Severe acute pain, trauma or planned large surgeries
- Organ failure or other severe medical illness
- Recent methadone use

**Diagnosing Opioid Withdrawal

Subjective symptoms AND one objective sign

Subjective: Patient reports feeling "bad" due to withdrawal (nausea, stomach cramps, body aches, restlessness, hot and cold, stuffy nose)

Objective: ***[at least one]*** restlessness, sweating, rhinorrhea, dilated pupils, watery eyes, tachycardia, yawning, goose bumps, vomiting, diarrhea, tremor

Typical withdrawal onset:
≥ 12 hrs after short acting opioid
≥ 24 hrs after long acting opioid
≥ 48 hrs after methadone (can be >72 hrs)

If unsure, use COWS (clinical opioid withdrawal scale). Start if COWS ≥ 8 AND one objective sign.

If Completed Withdrawal:
Typically >72 hrs since last short-acting opioid, may be longer for methadone. Start Bup 4mg q4h prn cravings, usual dose 16-32mg/day. Subsequent days, OK to decrease frequency to qday

Opioid Analgesics

- Pause opioid pain relievers when starting Bup.
- OK to introduce opioid pain relievers after Bup is started for breakthrough pain. Do not use methadone with Bup.

Supportive Medications

- Can be used as needed while waiting for withdrawal or during induction process.

Pregnancy

- Bup monoproduct or Bup/Nx OK in pregnancy.
- Consider referencing buprenorphine in pregnancy guide.

The Bridge Program disseminates resources developed by an interdisciplinary team based on published evidence and medical expertise. These resources are not a substitute for clinical judgment or medical advice. Adherence to the guidance in these resources will not ensure successful patient treatments. Current best practices may change. Providers are responsible for assessing the care and needs of individual patients.

9.1.2019

PROVIDER RESOURCES

California Substance Use Line
CA Only (24/7)
1-844-326-2626

UCSF Substance Use Warmline
National (M-F 6am-5pm; Voicemail 24/7)
1-855-300-3595

SOURCE: Bridge To Treatment

Appendix E continued

B: Quick Guide: Methadone Starts in the Hospital

Quick Guide: Methadone Starts in the Hospital

Day 1: max daily dose 40 mg methadone

First dose
- Check COWS and Ramsay
- Administer 10-30mg methadone
- Recheck Ramsay in 1 hour

After 4 hours
- If endorsing withdrawal/cravings, check Ramsay
- If no sedation, order additional 5 - 10 mg dose
- Recheck Ramsay in 1 hour

After 4 hours
- If endorsing withdrawal/cravings, check Ramsay
- If no sedation and not at max daily dose, order additional 5-10 mg dose
- Recheck Ramsay in 1 hour

Day 2: max daily dose 50 mg methadone

First dose
- Check Ramsay, proceed if no sedation
- Give total daily dose from day 1 as single dose
- Recheck Ramsay in 1 hour

After 4 hours
- If endorsing withdrawal/cravings, check Ramsay
- If no sedation, order additional 5 - 10 mg dose
- Recheck Ramsay in 1 hour

After 4 hours
- If endorsing withdrawal/cravings, check Ramsay
- If no sedation and not at max daily dose, order additional 5-10 mg dose
- Recheck Ramsay in 1 hour

Ramsay sedation score:
1. Anxious/restless
2. Cooperative/oriented/tranquil
3. Response to commands
4. Brisk response to stimulus
5. Sluggish response to stimulus
6. No response to stimulus

Testing prior to first dose:
- ☐ Urine toxicology
- ☐ EKG for QTc interval
- ☐ Urine pregnancy test (PRN childbearing potential)
- ☐ DSM 5 criteria for opioid use disorder
- ☐ CURES report
- ☐ Consider HIV, HepB, HepC testing
- ☐ ***Pregnancy:***
  non-stress test or fetal heart tones as indicated

Contraindications/cautions:
Call experts as needed, may still start with support
- Allergy to methadone
- Respiratory depression
- Ramsay sedation scale ≥ 4
- QTC > 500
- Recent use of benzodiazepines, alcohol, or other sedatives
- Severe liver disease
- Comorbid alcohol withdrawal

Initial dose selection:
Anywhere from 10-30 mg may be selected. Patients should be dosed according to tolerance (expect lower tolerance with non-daily users, oral hydrocodone, smoked opium users, etc). May use morphine equivalent calculator as a guide. Withdrawal severity is not well correlated with tolerance.

Discharge prescriptions:
- Methadone may not be prescribed for opioid use disorder. Must be administered in methadone clinic.
- Naloxone 4 mg/0.1 ml intranasal PRN opioid overdose. Spray 0.1 ml into one nostril, call 911, if no response in 2-3 minutes repeat with second device in additional nostril. #1 pack of 2, 3 refills
- Consider pre-exposure HIV prophylaxis

Day 3: Follow instruction for day 2 above, but with first dose being total daily dose from day 2. Max dose on day 3 is 60 mg.
Subsequent days: Do not increase dose for 5 days. Can increase by 10 mg every 5 days subsequently.

Somnolence/respiratory depression: All patients should have order for naloxone 0.1 mg IV/IM q 1 to 2 minutes PRN RR < 8/min and difficult to arouse or Ramsay sedation scale ≥ 5, x 3 doses. Caution: the use of additional opioids or benzodiazepines during this time can increase risk of somnolence/respiratory depression, and should be avoided if possible. If RR < 8 or Ramsay > 2 at any time, do not give additional methadone. Consider dose decrease, and consult with experts.

Adjunctive meds: The following can be prescribed prn for symptoms of withdrawal (check for contraindications and drug-drug interactions).
- Acetaminophen 650 mg PO q 6 hours daily PRN pain
- Clonidine 0.1-0.3 mg PO q 6-8 hours PRN w/d symptoms (NTE 1.2 mg/day, hold if BP < 100/70)
- Diphenhydramine 25-50 mg, PO q 8 hours PRN insomnia/anxiety
- Loperamide 4 mg PO initially, then 2 mg PRN each additional loose stool (NTE 16 mg/24 hours)
- Ondansetron 4 mg PO q 6 hours PRN nausea
- Trazodone 50 mg PO qhs PRN insomnia
- Melatonin 3 mg PO qhs PRN insomnia

For clinical questions:
UCSF Substance Use Warm-line 855-300-3595 or https://tinyurl.com/yd4ymyx6 (M-F 9am-8pm ET)

SHOUT
SUPPORT FOR HOSPITAL OPIOID USE TREATMENT

SOURCE: Project SHOUT

Appendix F

Cannabinoids and Pain

Cannabinoids and Pain: Counseling Patients

- As of this writing, no definitive, high-quality studies support the safety and efficacy of dispensary or pharmaceutical cannabinoids for analgesia in chronic noncancer pain. Until better evidence is available, physicians are discouraged from endorsing the use of cannabinoids for pain management. No evidence supports the efficacy of cannabinoids for acute pain. Patients may be counseled that research suggests that chronic use of cannabis may in fact complicate pain management.[720,721]
- It is recommended that any patient with chronic pain be encouraged to seek care from a pain medicine specialist.
- It is suggested that patients be counseled that the use of any drug that lacks rigorous FDA drug development and safety profiles carries inherent risks.
  - The testing and regulation of dispensary cannabis is poor to nonexistent.
  - Products purchased at dispensaries may be mislabeled, of undetermined content and/or contaminated with harmful substances.
  - It is important to remind patients that cannabis dispensary workers are not trained or qualified to give medical advice.
- Adverse effects associated with cannabinoid use include:
  - The development of cannabis use disorder (CUD)
    - Historically, one in 10 cannabis users—and one in six users under the age of 18 years—will develop CUD.[692,693]
    - Dispensary cannabinoid products available now are far more potent than those sold even a few years ago. Rates of CUD associated with use of potent dispensary cannabinoids may be as high as 30%.[694]
    - CUD is associated with an increased likelihood of developing other SUDs.[695]
  - Cognitive and behavioral
    - Short-term adverse effects include deficits in attention, memory and learning. Chronic use of cannabinoids may cause permanent cognitive deficits.[696,697]
    - Daily use or high doses of Δ9-tetrahydrocannabinol (THC) can cause anxiety, paranoia and psychosis. Chronic cannabis use is associated with an increased risk of developing schizophrenia.[698-707]
    - Cannabis use is associated with higher rates of depression, anxiety and suicidality.[708-710]
  - Cardiovascular
    - Smoking or vaping cannabinoids increases the risk for stroke and heart disease.[711-714]
  - Pulmonary
    - Smoking or vaping cannabis in any form can harm lung tissues, scar small blood vessels and expose patients to many of the same toxins, irritants and carcinogens found in tobacco smoke.[715,716]
    - Second-hand cannabis smoke is harmful to the health of exposed contacts, particularly children and adolescents.[717]
  - Malignancy
    - Chronic cannabis use may increase the risks of testicular cancer and human papilloma virus (HPV)-related head and neck squamous cell carcinoma (HNSCC).[718,719]
- Pregnant or breastfeeding patients are strongly advised to avoid cannabis use due to known and unknown risks to the developing brain. The potential exists for birth defects, possible autism or spectrum disorders and other behavioral abnormalities in children of women who use cannabinoids in the perinatal period.[722]
- Despite the cautions above, medical clinicians may counsel their patients that many physicians, researchers, the AMA and the organizations represented in CO's CURE advocate for rigorous scientific research into the safety and efficacy of cannabinoids for pain management.

Introduction

The opioid epidemic has motivated physicians, researchers and patients to seek alternatives to opioids for the management of pain. Legalization and wider societal acceptance of cannabinoids, a broad term that describes the drugs derived from the plants of the genus Cannabis, has prompted some to ask whether cannabinoids might offer a safer, less-addictive alternative to opioid analgesia. While cannabinoids carry little risk of overdose death, their opioid-sparing potential and analgesic efficacy are unproven. Two ecological studies raised the possibility that medical cannabis legalization might reduce the use of opioids and rates of overdose death; however, subsequent individual-level research has challenged this hypothesis, and some states have seen rates of opioid-related harms increase after enactment of medical cannabis legislation.[723-725]

Research into the safety and efficacy of cannabinoids for analgesia has been largely limited to the study of chronic, neuropathic and cancer pain. Most of the existing studies of cannabinoids for medical use have been underpowered, unblinded or uncontrolled. A small number of observational studies of patients who use medical cannabis suggest that a subset of patients with chronic pain may successfully substitute cannabinoids for opioid analgesics.[726] Evidence regarding the efficacy of cannabinoids, including dispensary cannabis, for the management of acute pain is nonexistent.[721] Despite the lack of persuasive data—and the significant adverse effects associated with cannabinoids—in vitro research, animal studies, preclinical experience and case reports suggest that the analgesic and opioid-sparing potential of cannabinoids warrant human studies with rigorous design, larger sample sizes and more consistent measures of outcome.[730,731,740]

Though cannabinoids have been studied for decades, the barriers to cannabinoid research are many. In particular, plant-derived cannabinoids in the United States are classified as Schedule I substances for which research is tightly regulated. Furthermore, the pharmacokinetics of these substances are complex and depend on the composition of the synthetic or herbal product and the route of administration. The chemical content of unprocessed botanical cannabis varies significantly; there are more than 100 pharmacologically active cannabinoids, the most widely studied of which are THC and cannabidiol (CBD). The remaining cannabinoids and terpenes contribute to the smell, taste and possible pharmacologic effects of cannabis.[727] The three FDA-approved cannabinoids—CBD (Epidiolex), nabilone (Cesamet) and dronabinol (Marinol)—are isolated substances. The sale and possession of CBD products that contain no more than 0.3% THC (and thus lack psychoactive effects) are now legal under federal law.[728] While the AMA stands firmly against the legalization of recreational cannabis, it calls for "adequate and well-controlled studies of marijuana and related cannabinoids in patients who have serious conditions for which preclinical, anecdotal, or controlled evidence suggests possible efficacy and the application of such results to the understanding and treatment of disease."[729]

Evidence for Analgesic Properties of Cannabinoids

Well-described, shared neuropharmacological features and the substantial interactions of the mammalian endogenous cannabinoid system and endogenous opioid systems make an analgesic, opioid-sparing effect of cannabinoids physiologically plausible.[730-735] The human endocannabinoid system is composed of the cannabinoid receptors CB1 and CB2 and the endogenous human cannabinoids N-arachidonoylethanolamine (AEA), also known as anandamide and 2-arachidonoylglycerol. CB1 receptors are concentrated in presynaptic neurons in areas of the brain that regulate appetite, memory, fear and motor responses, as well as in the spinal cord, dorsal root ganglia, the gastrointestinal tract, liver, fat cells and skeletal muscle, while CB2 receptors are primarily found in macrophages and tissues that modulate inflammation.[708,736]

Both cannabinoid receptors and endocannabinoids are involved in the regulation of pain sensation, with modulatory actions at all stages of pain processing pathways.[737] The signal transduction systems of cannabinoid and opioid receptors are similar, and both are expressed in brain regions involved in antinociception, including the periaqueductal gray, raphe nuclei and central-medial thalamic nuclei.[731] Mu-opioid receptors and CB1 receptors are both found in the dorsal horn of

the spinal cord at the first synaptic contact for peripheral nociceptive afferent neurons.[738,739] In vitro and animal studies provide ample evidence to support the analgesic effects of cannabinoids; some studies also suggest that these substances may work synergistically to enhance opioid analgesia.[730,731,740]

Most meta-analyses of cannabinoids and pain in humans are limited by small sample sizes and the wide heterogeneity of cannabinoid products, patient populations, outcomes and study designs. A 2018 systematic review of 104 studies (47 RCTs and 57 observational studies, of which 46 were low or very low quality, 43 were moderate quality and 15 were high quality, per GRADE system) found moderate evidence of a 30% reduction in pain in patients using cannabinoids (29.0%) when compared with placebo groups (25.9%). The number needed to treat (NNT) to achieve a reduction in pain was 24. A 50% reduction in pain was reported by 18.2% of subjects in the cannabinoid groups compared to 14.4% in the placebo groups; however, these findings were statistically insignificant. The number needed to harm (NNH), notably, was 6. For comparison, the NNT for opioids is 4, and the NNH is 5. The authors note that the change in pain intensity seen with cannabinoids was equivalent to a 3-mm greater reduction on a 100-mm visual analogue scale when compared with placebo, well below the 30-mm threshold needed to represent a clinically significant difference. They acknowledge that their analysis is limited by the small sample sizes of the studies surveyed, with only 21 studies having more than 100 patients per treatment arm. They also note the short duration of most studies and observe that the efficacy of cannabinoids for pain appeared to wane over even a few days. The authors express concern that the short duration of most studies means that long-term adverse events, including the risk of iatrogenic dependence, cannabinoid tolerance and cannabinoid withdrawal syndrome, was not assessed by their review. They conclude that, while cannabinoids show modest benefit for the treatment of some pain conditions, they are unlikely to be effective for the management of chronic noncancer pain given their high NNT and low NNH.[741]

These findings of the Stockings review closely mirror those of a 2018 Cochrane review (Mücke) of cannabinoids for the treatment of chronic neuropathic pain, which similarly concludes that "there is a lack of good evidence that any cannabis-derived product works for any chronic neuropathic pain," while noting a high incidence of adverse effects.[742] A subsequent 2019 scoping review (Pratt) assessed data from 72 systematic reviews of medical cannabinoid use.[743] Notably, it judged only one review to be of high-quality and highlighted the occurrence of adverse effects in more than 80% of patients taking cannabinoids, including 36% reporting serious adverse effects.[743] The authors conclude that while a small number of reviews suggested analgesic benefit with cannabis use, most were unable to draw conclusions due to inconsistent findings, and finally, that the harms of cannabinoid use may outweigh potential benefits.[743] Until larger, more methodologically rigorous studies are conducted, the results of meta-analyses will be of limited value in guiding patients and clinicians.

Adverse Effects of Cannabinoids

Although the legalization of medical and recreational cannabis has likely led some patients to consider these compounds as generally safe, the studies discussed above note significant adverse effects with cannabinoid use, including dizziness, dry mouth, tachycardia, fatigue, somnolence, nausea, vomiting, disorientation, confusion, anxiety, cannabis hyperemesis syndrome, paranoia and hallucinations. A recent survey of Colorado emergency departments describes increased frequency of patient visits for significant cannabis-related adverse effects, including psychosis, suicidality, concomitant substance abuse, decrements in complex decision-making, motor vehicle collisions, cardiovascular and pulmonary complications, inadvertent pediatric exposures and hash-oil burn injuries (sustained when preparing drug concentrates). Contaminants found in cannabis can also expose users to infectious agents, heavy metals and pesticides.[744] A retrospective review of adolescent emergency department and urgent care visits found a significant increase in cannabis-associated visits.[745] Another retrospective review found significant increases in cannabis-related hospitalizations, emergency department visits and poison center calls in Colorado both after local medical marijuana policy liberalization and after local recreational legalization. Of note was the high prevalence

of mental illness presenting in patient visits cannabis-related codes, an association that warrants further investigation.[746]

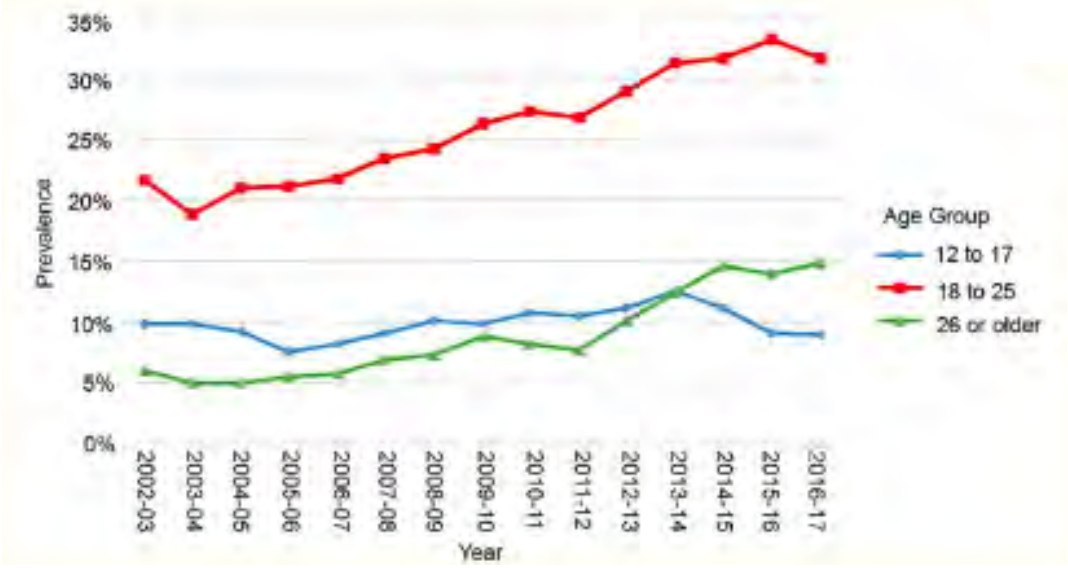
While the long-term adverse effects of cannabinoids require further research, a number of studies have associated THC exposure with the later development of schizophrenia,[698-707] depression,[709,711] anxiety[708] and suicidal ideation, attempts and completion.[710] A large prospective cohort study also linked cannabis use to a substantial risk for the later development of CUD,[747] estimating that 9% of adults and 17% of adolescent users will develop the disorder.[692] Both grey and white matter changes have been found in chronic cannabis users, as have volume reductions in the amygdala and hippocampus.[696,748-751]

National reporting systems and rigorous research into the short- and long-term adverse effects of cannabinoids are urgently needed.

Clinicians in Colorado are likely aware of the high incidence and prevalence of cannabis use in the state **(TABLE 1)**. An estimated 39% of patients who receive chronic opioid therapy for pain report also using cannabis.[752,753] When the opportunity arises, clinicians are encouraged to advise patients that current evidence does not support the use of cannabis as a safe, effective analgesic and that further research is warranted. It is recommended that patients with chronic pain who inquire about cannabis for analgesia be referred to a pain management specialist.

(FIGURE 11)

Cannabis Use In the Past Month In Colorado, by age group



SOURCE: Reproduced from Substance Abuse and Mental Health Services Administration National Survey on Drug Use and Health: State Estimates. Available at https://pdas.samhsa.gov/saes/state. Accessed November 2018

Appendix G

Cannabinoids: Anesthesia and Analgesic Considerations

Perioperative Considerations in Patients Who Use Cannabinoids

PREOPERATIVE CONSIDERATIONS

- Patient counseling is critical to mitigating the impact of cannabis use and withdrawal on perioperative pain management and on response to anesthesia.
  - Clinicians may advise patients that an accurate history of substance use can assist the surgical team in providing optimal perioperative care and pain management. Many patients are unaware that cannabis use can have a significant effect on perioperative pain and overall comfort.
  - Patients may be counseled that use of dispensary cannabinoids may complicate anesthesia, contribute to increased postoperative pain and increase risk of cerebrovascular events.
  - Many patients believe that cannabinoids are effective analgesics for chronic or acute pain.[754,755] Surgical care teams should educate patients that there is no evidence that cannabinoids can treat acute pain and that the evidence for safety and efficacy of cannabinoids for treatment of chronic pain is weak.
  - Patients who are chronic users of non-pharmaceutical cannabis are encouraged to abstain from cannabis for at least 72 hours prior to surgery. Patients who use FDA-approved cannabinoids at prescribed doses are not likely to experience perioperative adverse effects due to cannabis.[756]
  - Clinicians are encouraged to conduct an empathic, non-judgmental conversation about patient plans for continued cannabis administration during hospitalization and the possibility of cannabis withdrawal syndrome.
    - Because of the indeterminate content of dispensary cannabinoid products, it is recommended that surgical care teams discourage patients from inpatient use of these products.
    - It is recommended that clinicians and patients both be aware of the signs and symptoms of cannabinoid withdrawal syndrome (CWS) in order to accurately diagnose and manage CWS. **(SEE TABLE 20)**
- It is recommended that patients be asked about the type of cannabinoid used, frequency of use, route of use and time of most recent use.
- Because urine and plasma levels of cannabinoids do not correlate with degree of intoxication, a careful history is far more valuable than laboratory analysis in evaluating patients who use cannabinoids.[757]
- It is advised that patients with a history of recent and/or chronic cannabis use be flagged for provider review and history of cannabis use be incorporated into the preoperative medication reconciliation process.
- Patients who are acutely intoxicated with cannabinoids may exhibit marked anxiety, paranoia or psychosis, and may exhibit a more violent emergence from anesthesia.[720]
  - Patients using high-THC content cannabinoids may present with fever, tachycardia and hypertension, which can be mistaken for malignant hyperthermia, serotonin syndrome, MDMA overdose, neuroleptic malignant syndrome or thyrotoxicosis.
  - Delaying surgery for patients with angina or a history of coronary artery disease (CAD) for at least an hour after last use may reduce risk of myocardial infarction (MI) and other cerebrovascular events.[758]
- Prior to elective procedures, surgical teams are encouraged to consult behavioral health and/or pain medicine services as available and appropriate to aid in the management of surgical patients who are chronic cannabis users.
- It is recommended that surgical teams screen all patients for SUDs and that patients with CUD as defined by the DSM-V **(TABLE 20)** be referred for behavioral health or addiction medicine evaluation and care.

Perioperative Considerations in Patients Who Use Cannabinoids continued

INTRAOPERATIVE CONSIDERATIONS

- Chronic cannabinoid users have been shown to require higher induction doses of propofol.[759]
- Chronic cannabinoid use may render bispectral index (BIS) results an unreliable measure of anesthetic depth.[759]
- Some evidence suggests that chronic cannabis users have more pain, consume more opioid analgesia and have worse sleep in the immediate postoperative period.[760-762]
- It is recommended that multimodal analgesia, including the intraoperative use of regional anesthetic and analgesic interventions, be maximized in this patient population.

POSTOPERATIVE CONSIDERATIONS

- It is advised that surgeons, anesthesiologists and patients be aware that chronic cannabis users may exhibit signs of CWS in the postoperative period. Research suggests that 30-95% of regular users will experience CWS.[763]
  - It is suggested that clinicians and patients be aware of the signs and symptoms of cannabinoid withdrawal syndrome in order to accurately diagnose and manage it. Symptoms include irritability, insomnia, decreased appetite, depressed mood, restlessness and anxiety.[763] **(TABLE 20)**
  - Though some evidence in a non-surgical population suggests that cannabinoid agonist replacement (with nabiximol or dronabinol) may mitigate the symptoms of CWS, no drug is FDA-approved for this purpose. Careful consideration of the risks and benefits of off-label use of FDA-approved synthetic cannabinoids is needed before surgical teams use them to treat CWS.[763,764] Though anecdotally some surgical teams do prescribe dronabinol or nabiximol for patients who are chronic users of dispensary cannabinoids, no evidence supports or refutes the use or administration of cannabinoids to prevent CWS in the perioperative period.
  - Dispensary cannabinoids are of undetermined content, and it is recommended that surgical teams not endorse perioperative use of any agent that is not FDA-approved. It is advised that surgical care teams discourage patients from inpatient use of dispensary products.
- Surgical care teams are encouraged to consider drug-drug interactions (additive, synergistic or antagonistic) of cannabinoids and pharmaceutical agents including but not limited to warfarin, some antidepressants, proton-pump inhibitors, macrolides, HIV protease inhibitors, amiodarone and isoniazid, benzodiazepines and opioids.
- Cannabinoids may affect levels of cytochrome P450-metabolized drugs and alter function of membrane-transporters. It is likely that further pharmaceutical interactions with cannabinoids will be elucidated in the future.[765-768]
- It is suggested that particular caution be used in patients with impairment of renal and/or hepatic function.[769]
- It is encouraged that discharge counseling include information regarding interaction of cannabinoids with other pharmaceutical agents being prescribed.
  - It is recommended that patients with ongoing cannabis use be counseled after surgery on safe practices surrounding concomitant cannabis use with other medications that will be prescribed in the postoperative period. It is strongly encouraged that a pharmacist be included in this conversation.

Perioperative Care of Cannabis Users

With legalization and widespread use of cannabinoids, anesthesiologists in Colorado and across the United States more and more frequently encounter patients who are acutely intoxicated with cannabinoids and patients who are chronic cannabis users. Evolving evidence suggests that care of these patients requires a careful cannabis use history, an understanding of the effects of cannabinoids on anesthesia and perioperative pain, and awareness of the potential for CWS in this patient population. Ironically, the legalization of cannabis in Colorado has contributed to a widespread popular misperception that cannabinoids are effective analgesics; in fact, evidence increasingly suggests that cannabinoid use increases postoperative pain and analgesic consumption. There is a clear, urgent need to investigate the impact of cannabinoid use on anesthesia and surgical pain and to educate the public on the ways in which cannabinoid use complicates the perioperative course.

While the literature on this topic remains in its infancy, evidence from animal and preclinical models and clinical experience supports the hypothesis that cannabinoids have an effect on the nociceptive system.[721] In a retrospective review of over 3000 orthopedic surgery patients, patients with a history of cannabinoid use had higher pain scores in the early postoperative period and poorer quality of sleep.[762] Another report of 261 patients involved in motor vehicle crashes found that chronic cannabis users reported higher pain scores and consumed significantly more opioids following the trauma-related event.[760] Chronic cannabis users undergoing surgical procedures may have atypical anesthetic and analgesic needs including but not limited to:

- Difficult-to-control pain following surgery
- Possible cannabis withdrawal syndrome
- Unpredictable interaction of cannabinoids with other pharmaceutical agents

Cannabinoids and Expectations of Hospitalization: Patient Counseling Points

Perioperative counseling is critical in managing patient expectations of pain control, cannabinoid interactions with other analgesics and continued cannabis use after surgery. It is suggested that patients be approached in a non-judgmental manner in order to elicit a full, accurate cannabis use history and counseled that physiological effects of cannabinoids in the perioperative period are unpredictable. It is advised that patients be made aware that there may be significant adverse interactions of cannabinoids with anesthesia and that some chronic cannabis users have more postoperative pain than is typical. It is recommended that patients be counseled that there is no evidence that cannabinoids treat acute pain and limited evidence for their efficacy in treating chronic pain. In addition, it is recommended that patients be counseled on the significant adverse effects of cannabinoids use. **(SEE ABOVE, "COUNSELING PATIENTS: CANNABINOIDS AND PAIN.")** It is advised that any patient with chronic pain and/or CUD be referred to pain and/or addiction medicine specialists for further care.

Managing Perioperative Pain in Patients Who Use Cannabis

It is recommended that chronic cannabis users undergoing surgery be approached with the same multimodal analgesic treatments as other patients. Agents often reserved for difficult-to-manage pain (such as ketamine, lidocaine, dexmedetomidine) and regional anesthetic and analgesic interventions may be required as a part of an effective perioperative analgesic plan. Chronic cannabis patients may also have higher usage of adjuncts such as anxiolytics, antipsychotics and rescue opioids.

Effect of Cannabinoids on Anesthesia

It is recommended that a patient history of cannabis use prior to anesthesia assess dose, duration and frequency of use, whether recreational or medical use, type of product used (content of THC, CBD or synthetic cannabinoids) and time elapsed since last use. It is advised that if a patient is a chronic user, inquiries be made on past medical history of hyperreactive airway, hyperemesis syndrome or any other complications with previous surgeries and anesthesia exposure.[721] Due to the change in receptors and physiologic response that happens over time with chronic cannabis use, physiologic findings in the perioperative period may differ depending on if the patient is an acute or chronic user.[721] Acute use is more likely to produce tachycardia, hypertension, arrhythmias, coronary vasospasm or airway hyperreactivity. Chronic users are more likely to experience bradycardia (though they may also exhibit tachycardia), postural/orthostatic hypotension, sinus arrest, hyperreactive airway, intraoperative hypothermia, shivering, stroke and coronary vasospasm or myocardial infarction. Cannabinoids may inhibit platelet aggregation, which could theoretically lead to increased operative site bleeding, although this has not been described. In addition, cannabinoids are extensively metabolized by hepatic cytochromes, resulting in drug-drug interactions due to inhibition or induction of these and other enzymes or transporters.[770,771]

One of the major mechanisms of action shared by endocannabinoids and general anesthetics is modulation of GABA, therefore pharmacological interactions are to be expected. While the current clinical evidence available is mixed on the effect of cannabinoids on different anesthesia agents, the following conclusions can be tentatively made regarding the impact of cannabis use on anesthesia:

- Patients may require significantly higher doses of propofol during induction.[759,772,773]
- Patients may have higher tolerance to inhaled anesthetics such as isoflurane and sevoflurane.[774,775]
- For patients with recent (same day) cannabis use, BIS monitoring may not be reliable for the purpose of determining level of sedation.[776]
- There are currently no reports on the interaction between cannabinoids and non-depolarizing neuromuscular blockers.
- There is a theoretical synergistic action of cannabinoids and opioids, but clinical trials have been unable to demonstrate this effect and studies suggest increased postoperative opioid requirements.[731,777-779]
- There is no reported association between past medical history of cannabinoid hyperemesis syndrome (CHS) and risk of PONV in chronic cannabis users. Cannabinoids have not been found to prevent PONV.[780]
- If CHS is identified prior to surgery, it is recommended that cannabinoid cessation be encouraged; if CHS is experienced in the perioperative period, droperidol and haloperidol are suggested over other antiemetic agents (ondansetron, promethazine).[781,782]

As lipophilic compounds, cannabinoids are stored in adipose tissue and may be released over a prolonged period of time following frequent use, resulting in persistent effects or drug interactions.[783] Thus, it is widely recommended by experts that patients abstain from cannabis use for at least 72 hours prior to elective surgery. It is recommended that the FDA-approved anticonvulsant cannabinoid Epidiolex be continued through the perioperative period. There is little information to guide the management of other medicinal cannabinoids prior to surgery, but it is likely that continuation of FDA-approved cannabinoid drugs is safe during the perioperative period.

(TABLE 19)

Anesthetic Considerations in Patients Who Use Cannabis

Period	Considerations
Preoperative	Elevated risk of myocardial infarction within 1 hour after use Airway hyperreactivity Anxiety/paranoia Psychosis Need to assess for other drugs
Intraoperative	Tolerance to induction agents Elevated bispectral index Unknown cross-tolerance to other anesthetic agents Elevated risk of myocardial infarction within 1 hour after use Airway hyperreactivity
Postoperative	Unknown cross-tolerance to analgesics Possible heightened pain perception Withdrawal

Management of Cannabis Withdrawal Syndrome

Consideration should be given to the possibility of cannabis withdrawal syndrome in patients hospitalized for >48 hours who display irritability, anxiety, alterations of mood, tremor, fever and chills or abdominal cramping **(TABLE 17)**.[784] Research suggests that CWS is common in chronic cannabis users, and likeliness of CWS correlates with degree of cannabis use; for daily heavy users, up to 95% may experience CWS.[763] It is recommended that symptoms of CWS be managed empirically. At this point in time, there are no rigorous trials studying the use of FDA-approved cannabinoid products (such as nabiximol or dronabinol) as "replacement" cannabinoids, though there are anecdotal reports of such off-label use. Caution must be exercised with such off-label use, however, as studies of use perioperative synthetic FDA-approved cannabinoids for prevention of PONV have identified an unacceptable rate of psychotropic effects. Providers must be aware that there is no clinical evidence to support off-label use, and it is recommended that these products not be routinely prescribed. Finally, clinicians should be aware that CUD is a condition defined by the DSM-V **(FIGURE 12)** and that, as for patients with any SUD, it is recommended that patients with CUD be referred for behavioral health or addiction medicine evaluation and care.

(TABLE 20)

Cannabis Withdrawal Syndrome

Variable	Description
Signs and symptoms	Irritability/anger Anxiety/depressed mood Insomnia Altered dreams Anorexia Abdominal cramping Headaches Tremors Fever/chills
Onset	< 1 day for high-dose, chronic users
Duration	Up to several weeks
Treatment	Symptomatic therapy, synthetic THC

TCH indicates delta-9-tetrahydrocannabinol.

(FIGURE 12)

DSM-V Criteria for Cannabis Use Disorder

According to the DSM-5, (Diagnostic and Statistical Manual of Mental Disorders, fifth edition) the criteria for Cannabis Use Disorder is as follows:

1. Use of cannabis for at least a one-year period, with the presence of at least two of the following symptoms, accompanied by significant impairment of functioning and distress:
2. Difficulty containing use of cannabis—the drug is used in larger amounts and over a longer period than intended.
3. Repeated failed efforts to discontinue or reduce the amount of cannabis used.
4. An inordinate amount of time is occupied acquiring, using, or recovering from the effects of cannabis.
5. Cravings or desires to use cannabis. This can include intrusive thoughts and images, and dreams about cannabis, or olfactory perceptions of the smell of cannabis, due to preoccupation with cannabis.
6. Continued use of cannabis despite adverse consequences from its use, such as criminal charges, ultimatums of abandonment from spouse/partner/friends, and poor productivity.
7. Other important activities in life, such as work school, hygiene, and responsibility to family and friends are superseded by the desire to use cannabis.
8. Cannabis is used in contexts that are potentially dangerous, such as operating a motor vehicle.
9. Use of cannabis continues despite awareness of physical or psychological problems attributed to use, e.g., anergia, amotivation, chronic cough.
10. Tolerance to cannabis, as defined by progressively larger amounts of cannabis are needed to obtain the psychoactive effect experience when use first commenced, or noticeably reduced effect of use of the same amount of cannabis.
11. Withdrawal, defined as the typical withdrawal syndrome associated with cannabis, or cannabis or a similar substance is used to prevent withdrawal symptoms.

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