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Perioperative opioids, the opioid crisis, and the anesthesiologist

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Introduction

From April 2020 through April 2021, 75,673 Americans died from opioid overdoses, nearly one-quarter of which directly involved prescription opioids.¹ This represents the first time mortality has exceeded 75,000 in a 12-month period. Moreover, many people who abuse heroin and fentanyl begin opioid use with a prescription pill.² Both the lay and academic presses have focused considerable attention on the misuse and abuse of opioid medications. However, many anesthesiologists may not understand the role perioperative anesthesia practice and pain medicine can play in addressing this issue. In this review, we summarize current evidence related to perioperative opioid administration. We also make suggestions for how anesthesiologists can reduce opioid-related harm and bring value to their healthcare systems. Finally, we provide some caveats to these suggestions given existing gaps in research and highlight areas for future research.

Post-discharge opioids and the opioid epidemic

New persistent postoperative opioid use and opioid use disorder

Substantial rates of persistent postoperative opioid prescribing in previously opioid-naïve patients have been identified in nearly every surgical cohort,³⁻⁶ albeit with highly variable definitions of this phenomenon.⁷ For example, 7.7% of patients >65 years undergoing minor surgery continue being prescribed opioids during the first postoperative year,⁴ while 3.1% of patients undergoing cardiac, thoracic, intraabdominal, and pelvic surgeries have an opioid prescription dispensed 90 days or more postoperatively.³ Other investigators have identified rates of 2.2% at 6 months in retrospective data encompassing 1.35 million patients undergoing any type of in-hospital surgery,^{8,9} 4.3-8.3% for prospectively collected, self-reported opioid use 6 months after total knee and hip arthroplasty,¹⁰ approximately

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Conflicts of Interest

Dr. Brummett is a consultant for Heron Therapeutics (San Diego, CA), Vertex Pharmaceuticals (Boston, MA), Alosa Health (Boston, MA), and Benter Foundation (Pittsburgh, PA), and he provides expert medical testimony. Dr. Hah is a consultant for Nalu Medical (Carlsbad, CA) and SPR Therapeutics (Cleveland, OH).

6% for an opioid prescription received 90-180 days after a variety of major and minor surgeries,⁶ and—perhaps most alarmingly—4.8% for an opioid prescription received during the 90-180 days following common pediatric surgeries.¹¹

Traditionally, opioids have been a mainstay of treatment for postoperative acute pain and have been prescribed with the assumption that patients will cease use once postoperative pain resolves. However, patients typically stop opioid use long before pain cessation occurs.^{12,13} Studies have shown that among those with persistent opioid use surgeons are rarely the prescribers more than 3 months after surgery.¹⁴ While some of the persistent opioid prescribing could be due to non-surgical issues,¹⁵ claims data studies using non-surgical control cohorts found much higher rates among those undergoing surgery, suggesting surgery and postoperative prescribing as the triggering event.^{5,6} Some of the persistent opioid prescribing would also be expected to be attributable to new chronic post-surgical pain, but studies have shown similar prescribing rates following both major and minor surgery⁶ and no association with change in self-reported pain after joint arthroplasty.¹⁰ Thus, the driving factors for postoperative opioid consumption may extend beyond postoperative pain intensity and the direct treatment of surgical pain to encompass misuse for preexisting pain conditions, sleep, anxiety, and other patient-level factors (see “Preoperative considerations” section below).

It is important to note that significant data heterogeneity exists regarding new persistent postoperative opioid use incidence. Much of this variance appears to depend on the stringency of the definition used and the cohort evaluated: Studies of new persistent postoperative opioid use have observed incidence of this condition ranging from 0.01 to 14.7%.^{7,16} While there are prospective studies showing rates of 4-8% after surgery,¹⁷ gaining a deeper understanding of the association between chronic postoperative opioid use and these negative opioid-related outcomes will likely require moving beyond examining administrative claims and electronic health record data through which prescribing and consumption cannot be distinguished into large longitudinal cohorts of individual patients. This approach would also permit more granular study of opioid consumption rather than prescribing or prescription fills.¹⁶ Some working groups have suggested definitions for persistent opioid use;¹⁸ however, the cutoffs suggested are subject to similar critique as the more commonly published definitions and potentially offer greater specificity at the cost of lower sensitivity. Consensus definitions need to account for the data source (prospective, administrative, or prescription fulfillment data) and preoperative opioid status. Planned sensitivity analyses testing multiple definitions would allow for comparisons between studies and avoid the challenges of a “consensus” definition by a given group.

It is important to recognize that persistent opioid use is not synonymous with opioid use disorder (the diagnostic term for addiction), and that further research is needed to characterize the prevalence of opioid use disorder directly resulting from persistent postoperative opioid use. Similar research is needed to characterize the prevalence of postoperative opioid misuse and its relation to persistent postoperative opioid use. One obstacle to such research is that opioid use disorder is generally underrecognized and frequently goes undocumented in the electronic health record, where this diagnosis is seen much less frequently compared with the true prevalence of the condition.^{7,19-22} The

undercounting of patients with opioid use disorder or misuse may be particularly salient to surgical patients, in whom opioid misuse rates more than 7 times greater than the general population have been reported (albeit in a cohort of joint reconstruction and spine patients in whom opioid use is more common).²³

Among opioid-naïve patients presenting for surgery, increasing numbers of refills and the duration of postoperative opioid use are strongly associated with the development of opioid misuse,²⁴ and prescribing smaller amounts of opioids after surgery and limiting refills in the context of optimized perioperative pain management is warranted. However, the causality of this relationship has not been established; it may be due to patient-level factors, such as preoperative pain, sleep, and mood, rather than opioid consumption itself. Additionally, care must be taken to avoid stigmatizing particular populations based on racial, ethnic and sociodemographic factors. To decrease the potential for this, patients can be assessed preoperatively for risk for substance use disorder in a standardized, high-throughput manner and referred for specialized addiction medicine evaluation, if indicated.

Persistent postoperative opioid use is more common in preoperative opioid users

Not surprisingly, preoperative opioid use is associated with longer durations of postoperative opioid prescribing, more refills after surgery, and increased postoperative daily oral morphine equivalent consumption.^{25,26} It is also a clear risk factor for chronic postoperative opioid use.^{10,27-31} Between 64-77% of chronic opioid users prior to surgery continue to fill opioids postoperatively.^{28,29} This is particularly concerning in the context of surgery performed to address chronic pain, as there may be an expectation that opioid consumption will cease after surgery. In a prospectively collected cohort of patients undergoing arthroplasty who reported opioids use preoperatively, those reporting preoperative opioid use for another pain complaint beyond their knee or hip pain had an adjusted 2.4x increased odds of self-reported opioid use 3 months after arthroplasty.³² Additionally, higher preoperative opioid doses and longer duration of preoperative use lead to increased risk of chronic use and continued opioid prescription fulfillment postoperatively.^{10,33} Most concerning is the association of preoperative opioid prescription fulfillment with increased mortality,³⁴ morbidity, and postoperative healthcare utilization.^{35,36} These mortality and morbidity findings may be related to increased infectious risk secondary to opioid-induced immunosuppression.³⁷ Given that more than 20% of patients presenting for elective surgery are already prescribed opioids,³⁸ evidence-based interventions, prescribing guidelines, and policies should be developed for these patients that are distinct from those for opioid-naïve patients as their expected trajectories of postoperative opioid use likely differ.

Excess opioid prescribing

Excessive post-surgical opioid prescribing can result in a surplus of medications, increasing the possibility of diversion and misuse.^{39,40} Surgeons' share of first-start opioid prescriptions to opioid-naïve patients increased more than 18% from 2010-2016, likely as a result of the increasing attention paid to opioid prescribing by primary care physicians.⁴¹ A 2017 study of opioid prescribing after 5 outpatient surgeries revealed wide variation in the number of pills prescribed for the same surgery;³⁹ overall, surgical patients included in a 2017 systematic review took only 29-58% of prescribed opioid pills.⁴⁰

The issue of perioperative opioid overprescribing has substantial societal consequences. Among U.S. adults reporting opioid misuse or opioid use disorder in 2015, 36% obtained the opioids for their most recent misuse from their own prescription, and 47% from a friend or relative's prescription.²⁰ This brings into focus the need for strategies such as storage education⁴² and home disposal kits⁴³ to decrease opioid diversion.

While excess prescribing of opioids is a societal concern, untreated post-surgical pain and the acute-to-subacute-to-chronic pain transition represent major unmet needs for further research.^{44,45} A recent systematic review and meta-analysis in this journal emphasized the lack of high-quality evidence available regarding pharmacotherapy for the prevention of these conditions.⁴⁶ Advancements in personalized perioperative pain care may enable identification of suboptimal pain trajectories and preemptive treatment of patients at risk for development of chronic post-surgical pain; the large-scale NIH Common Fund-supported Acute to Chronic Pain Signatures network (<http://a2cps.org/>) aims to address this research need.⁴⁷⁻⁵⁰ Simpler acute pain descriptors may also prove helpful: Pain intensity predicts remote pain resolution, opioid cessation, and patient-reported surgical recovery when assessed 10 days after both major and minor operations conducted under either general or local anesthesia.^{49,51} However, it is noteworthy that decades of excess post-discharge opioid prescribing demonstrate that liberal opioid administration is unlikely to address the issue of persistent post-surgical pain. Furthermore, multiple studies have shown little or no association between pain scores and the amount of opioid prescribed after surgery. This suggests that for the majority of patients who undergo surgery, conservative opioid prescribing can reduce the overall excess of unused prescription opioids without worsening postoperative pain-related outcomes.⁵²⁻⁵⁶ While there are likely some surgeries for which opioids do not need to be prescribed routinely, they remain a cornerstone of acute postoperative pain management. Anecdotal reports of surgeons refusing to prescribe opioids based on institutional pressures or misapplication of state and federal policies and guidelines are concerning. It is critical that anesthesiologists and surgeons continue to attend to the pain needs of patients with opioids as appropriate.

While many anesthesiologists in the United States may feel disconnected from post-surgical opioid prescribing and pain management, it is important to recognize that anesthesiologists in other countries, including Australia and many European countries, are responsible for post-discharge prescribing.^{57,58} Moreover, given the increased interest in transitional pain services and the perioperative surgical home in the U.S. and Canada,⁵⁹⁻⁶² the role of anesthesiologists in prescribing opioids, identifying risk, and counseling patients on safe use, storage and disposal is likely to grow in the coming years.

Preoperative considerations

Identify patients at risk for persistent postoperative opioid use or misuse

The first practical step anesthesiologists can take is to identify patients at risk for postoperative persistent opioid use or misuse. Investigators have identified several risk factors for prolonged opioid use or opioid misuse (Figure 1). Those of potential relevance to anesthesiologists conducting perioperative evaluations include current opioid use,^{11,63-65} prior history of opioid use,^{66,67} current or prior substance use

disorder,^{11,56,66,68-75} smoking,^{56,71,76,77} coexisting psychiatric disease (particularly anxiety and depression),^{30,33,56,65-68,70,73,74,77-81} more medical comorbidities (higher Elixhauser comorbidity index),⁷⁷ history of chronic pain,^{11,69,71,82,83} and younger age.^{64,66,67,69,70,77} Conflicting evidence exists for sex,^{11,64-68,75,77} although studies focused on perioperative prescribing have identified female sex as a risk factor for persistent postoperative opioid use consistent with studies of chronic pain conditions.

What to do once you've identified patients at risk

Set expectations—Anesthesiologists can play a key role in setting patient expectations for pain management during the perioperative period. Doing so may help mitigate risk for postoperative opioid use and subsequent persistent use and misuse. For example, a systematic review incorporating 3,523 surgical patients found that lower expectations of postoperative pain correlated with lower actual postoperative pain in 8 of 13 identified studies.⁸⁴ However, patients with erroneous expectations that they should have no or minimal pain in the postoperative period may request or consume more opioids if their pain is greater than anticipated. Between 10-36% of postoperative patients expect complete analgesia from pain medication,⁸⁵⁻⁸⁷ which is inconsistent with normal postoperative recovery and represents an unreasonable expectation of the efficacy of opioids. A brief conversation in the preoperative holding area to set appropriate expectations for postoperative acute pain (e.g., “You will have pain after surgery. You will receive medication for your pain, but it is not likely to take away all of your pain.”) may be feasible for anesthesiologists in every practice setting. Further research is warranted into whether this is particularly beneficial for patients having surgeries with high incidences of postoperative acute pain such as spine or thoracic surgery.

Coordinate transitions of care—Most preoperative chronic opioid users have a “usual prescriber,” and a return visit within 30 days of surgery with the usual prescriber is associated with decreased odds of high-risk opioid prescribing (multiple prescribers, co-prescribing of benzodiazepines, high-dose opioid prescriptions, and new long-acting prescriptions). Those without a usual prescriber also show more high-risk prescribing postoperatively. While these data are derived from an administrative claims database rather than a longitudinal cohort,⁸⁸ the concept of engaging the usual prescriber in the perioperative course is consistent with the spirit of a transitional pain service.⁵⁹⁻⁶² Consequently, elective surgical patients with preexisting pain or substance use disorders but without pain or addiction medicine specialists can be referred to establish care that can continue through the phases of perioperative care. Anesthesiology groups with dedicated preoperative evaluation and acute pain services are well positioned to coordinate this care; otherwise, OR anesthesiologists can communicate these concerns to the surgical service.

Patients with chronic pain and those at risk for the development of chronic pain postoperatively may also benefit from care at a specialized transitional pain clinic prior to surgery.⁵⁹⁻⁶² Pain physicians at these centers evaluate such patients preoperatively, help manage expectations regarding postoperative pain control, and make recommendations to anesthesiologists and surgeons about intraoperative and immediate postoperative pain management, including post-discharge tapering plans.^{89,90} After discharge, patients continue

to be followed in the clinic in order to ensure that acute and subacute pain is managed appropriately, and to minimize the risk of transitioning to new chronic pain or exacerbating extant chronic pain. Managing these at-risk patients properly with non-opioid medications, interventional techniques, and psychological counseling has been hypothesized to lessen their chances of developing harmful postoperative opioid use patterns.⁹¹ While there are some early descriptions of pre-post data suggesting decreased postoperative opioid consumption for both opioid-naïve and -tolerant patients following implementation of transitional pain services,^{59,92} we lack high-quality data on the efficacy and cost-effectiveness of transitional pain clinics. One thoughtful viewpoint examines the business case for such clinics.⁹³ In their absence, anesthesiologists can encourage referrals to a pain medicine specialist or engaged primary care provider for potentially challenging patients.

Optimization of preoperative opioid use

Opioid tapering and cessation—About 20% of patients presenting for surgery use opioids preoperatively, with frequency and dose varying with the type of surgery.³⁸ Given concerns that preoperative opioid use may increase postoperative morbidity and healthcare utilization, there has been increased attention paid to preoperative opioid weaning and cessation programs. There is particular interest in weaning patients using high doses preoperatively, generally defined as >90 oral morphine equivalents daily.⁹⁴

A proposed template for such a high-dose opioid taper program involves regular clinic visits over a 10-to-12-week period to assist with both opioid dose reduction and palliation of withdrawal symptoms. Participating patients have their opioid doses weaned by approximately 10% weekly if tolerated.⁹⁵ While clinical discretion is needed and care should be tailored to the individual, we have provided a sample weaning protocol for a hypothetical patient (Table 1). Preliminary studies suggest these programs may improve postoperative outcomes. A retrospective matched cohort study comparing 123 total knee or hip arthroplasty patients divided into three equal groups (opioid-dependent patients who weaned their dose by 50% preoperatively, opioid-dependent patients who did not wean their dose, and opioid-naïve controls) found that the weaned group and the opioid-naïve group had improvements in pain and functional outcomes (Western Ontario and McMaster Universities Osteoarthritis Index, University of California, Los Angeles activity score, and Short Form 12 version 2 Physical Component Score) that were significantly larger than those of the non-weaned group. Of note, the weaned group improved to a similar degree as the opioid-naïve group but did not reach the same absolute level of function because patients on opioids preoperatively had lower baseline scores. Furthermore, preoperative opioid use was self-reported by patients.⁹⁶ Given the resources and time required, further study is needed to ensure preoperative weaning will improve outcomes before such care becomes a standard of care. Moreover, lengthy opioid weaning programs require close coordination with surgeons, who may hesitate to delay surgery for a 2-3 month wean. An additional potential consideration is that large-scale observational data has identified an association between cessation of opioid therapy and overdose or suicide, although these data are not limited to preoperative weans.^{97,98} Patients and caregivers can be engaged in the decision to wean after explanation of the potential benefits.⁹⁹ Continued monitoring and support of

patients may be warranted in the context of opioid cessation whether it occurs before or after the operation.

Intraoperative considerations

Opioid administration during anesthesia care

Can anesthesia care modify susceptibility to opioid-related harm, including new chronic opioid use and opioid misuse? Some groups have suggested that “opioid-free anesthesia” should be standard of care, but the definition of this concept and the rationale for avoidance of intraoperative opioids remain unclear. Furthermore, opioid-free anesthesia practice may not be feasible for all case types, and the hemodynamic consequences of such an approach have not been evaluated (for example, some anesthesiologists utilize opioids to blunt the sympathetic response to direct laryngoscopy). Currently, there is no evidence that total avoidance of opioids during anesthesia improves outcomes other than postoperative nausea and vomiting. A meta-analysis comparing opioid-inclusive with opioid-free intraoperative anesthesia found no differences in pain scores or opioid consumption at 2, 12, or 24 hours postoperatively.¹⁰⁰ This meta-analysis did show, however, that opioids increase rates of nausea and vomiting. More recently, a multicenter randomized blinded trial of a standard balanced anesthesia technique plus remifentanyl and morphine compared with the same balanced technique plus dexmedetomidine (opioid-free) was halted prematurely due to increased incidence of severe bradycardia in the opioid-free group. The primary outcome of postoperative hypoxemia, ileus, or cognitive dysfunction occurred more frequently in patients in the opioid-free group compared with the opioid-receiving group.¹⁰¹ In terms of post-discharge opioid-related metrics, two large-scale administrative claims studies found no relationship between nerve blockade and chronic postoperative opioid use following total knee arthroplasty¹⁰² and shoulder arthroplasty,¹⁰³ thereby suggesting that simple regional anesthesia techniques alone cannot prevent poor outcomes.

There is evidence that regional anesthesia and multimodal analgesic techniques improve acute pain and reduce in-hospital opioid consumption.¹⁰⁴ However, there are no available studies to suggest that perioperative anesthesia practices can affect long-term opioid outcomes, and there is evidence that opioid-free anesthetic strategies may increase risk for perioperative adverse events without influencing the likelihood of persistent postoperative opioid use or preventing postoperative opioid overprescription.¹⁰⁵⁻¹⁰⁷ While anesthesiologists should be judicious, opioids remain an important tool for anesthetic care. We do note that the overall level of evidence related to opioid-free anesthesia is low, and that further research regarding the impact of intraoperative opioid use on intermediate- and long-term outcomes is needed.

Postoperative considerations

Postoperative order sets and “automatic” opioid administration

Evidence exists that in-hospital opioid use is highly associated with post-discharge opioid use.^{108,109} In addition, elimination of standing orders for opioids from post-cesarean-section order sets has been shown to decrease postoperative opioid consumption and discharge

opioid prescribing.¹¹⁰ Further research is warranted into whether changes in PACU opioid order sets can have a similar influence on postoperative opioid consumption and persistent use in other cohorts. It has been posited that limiting intraoperative opioids may lead to increased postoperative opioid use, which would be counterproductive.¹⁰⁵ However, changes in PACU opioid administration in concert with changes in hospital ward and discharge opioid prescribing by surgical services represent a more attractive opportunity for anesthesiologists to improve short- and long-term opioid outcomes when compared to intraoperative opioid elimination.

Educational and behavioral interventions

Educational and behavioral interventions initiated or coordinated by anesthesiologists or other members of the perioperative care team provide an avenue to curb postoperative opioid use.¹¹¹ For example, carpal tunnel surgery patients who reviewed a 1-page sheet that (1) recommended trialing non-opioid therapy before using prescribed opioids, (2) assessed opioid abuse risk factors and current opioid prescriptions, (3) provided education on the anticipated duration of opioid consumption after surgery, and (4) set expectations that the lowest opioid dose would be prescribed exhibited significantly decreased opioid consumption (mean 1.4 pills vs. 4.2 pills) over the first three postoperative days compared with a group that did not receive the educational intervention, without a significant difference in pain scores.¹¹² In another trial, arthroscopic rotator cuff repair patients randomized to an intervention group watched a 2-minute narrated video and read a handout detailing the risks of opioid overuse and abuse. Overall, a statistically significant 42% reduction in opioid consumption was reported in the three months after surgery with no differences in pain.¹¹³ However, a third randomized trial in which total hip or knee arthroplasty patients at risk for opioid-related harms were provided brochures detailing expectations for opioid use and pain control after surgery, rationale for opioid use following surgery, postoperative opioid tapering expectations, and opioid-related adverse effects found no significant reduction in the amount of opioids dispensed in the 90 days following surgery.¹¹⁴ While these data are not conclusive, anesthesiologists may consider formal or informal discussions related to postoperative opioid use in the preoperative holding area.

Behavioral interventions can be delivered to guide postoperative opioid tapering. In a randomized trial of motivational interviewing and guided opioid tapering support compared to usual care alone administered to patients who had undergone total hip or knee arthroplasty, patients randomized to the intervention were instructed to decrease their total daily opioid dose by 25% every seven days while monitoring for pain and adverse effects.¹¹⁵ Patients randomized to a taper experienced a 62% increase in the incidence of return to baseline opioid use after surgery (HR 1.62; 95% CI 1.06–2.46; $p = 0.03$), and a 53% increase in the incidence of complete postoperative opioid cessation (HR 1.57; 95% CI 1.01–2.44; $p = 0.05$) with no adverse effects on the duration of pain or patient-reported recovery. The intervention was delivered via phone calls weekly from two to seven weeks post-op and then monthly up to one year until patient-reported opioid cessation. However, patients receiving the motivational interviewing and guided tapering support intervention only required an average of 3 calls, demonstrating the feasibility of future scale-up of this intervention. Future research on interventions to promote postoperative opioid cessation

and opioid tapering among high-risk patients is warranted as these patients are less likely to fit into the framework of conservative opioid prescribing. The increase in use and reimbursement of telehealth amid the COVID-19 pandemic further facilitates such access for transitional pain services.^{116,117}

Behavioral interventions provide a promising avenue to limit postoperative opioid use and encourage postoperative opioid cessation. In a small randomized controlled clinical trial, patients assigned to a digital behavioral health intervention stopped opioids five days sooner without differences in self-reported pain when compared to a digital health information control group.⁹³ However, further research is needed to develop interventions specific to those at highest risk, including those with anxiety, chronic pain, or opioid tolerance. Web- and smartphone-based interventions are attractive, as they address some of the cost and access barriers to in-person behavioral treatments.

Perioperative management of patients with opioid use disorder

The anesthesiologist's intersection with the opioid crisis is most apparent when encountering a patient with a history of opioid use disorder. Opioid use disorder results in substantial morbidity and mortality, including opioid-related overdoses.¹¹⁸ It is associated with multiple comorbidities including psychiatric diagnoses, human immunodeficiency virus, and hepatitis C.¹¹⁹ The prevalence of this condition is estimated to be anywhere from 0.8% to 4.6% nationwide.^{20,21} Given the rapidly changing landscape of treatment to address the opioid crisis, anesthesiologists should be aware of the various Food and Drug Administration-approved opioid use disorder treatment formulations and considerations for perioperative opioid management. Currently, three medications (buprenorphine, methadone, and naltrexone) are Food and Drug Administration-approved to treat opioid use disorder in various formulations. All these treatments have demonstrated reductions in illicit opioid use and mortality, yet most patients with opioid use disorder do not receive any of them.¹²⁰⁻¹²⁷

Acute pain management in patients receiving opioid use disorder treatment can be particularly challenging given the heightened postoperative opioid requirements for pain control. However, rigorous research to inform evidence-based management is lacking with most recommendations derived from expert opinion and case reports.¹²⁸⁻¹³⁰ Based on observational studies, continuation of buprenorphine and methadone opioid use disorder treatment after surgery may reduce supplemental opioid needs.¹²⁸ Further, suboptimal pain management in patients receiving methadone may trigger disengagement from care and serious downstream effects of possible relapse, overdose, or suicide.^{128,129}

Buprenorphine is a partial mu opioid receptor agonist and antagonist at the kappa and delta opioid receptors. Given its high affinity for the mu receptor, buprenorphine competitively displaces other mu-receptor agonists and can reduce opioid binding by 80-95% at clinical dose ranges.¹³¹ Given these considerations, older algorithms recommended the discontinuation of buprenorphine before major surgery to allow for adequate analgesia from traditional mu agonists. However, preoperative discontinuation of buprenorphine may result in increased pain and higher opioid requirements.¹²⁹ Adequate pain control has been described with concomitant use of full opioid agonists with continuation of buprenorphine treatment. Rather than complete discontinuation, buprenorphine doses may be tapered to a

lower dose so that analgesia can be achieved with a full opioid agonist while maintaining treatment to minimize the risks of relapse. A potential target for buprenorphine dose reductions has been suggested as 8-12 mg daily of the sublingual tablet.¹³¹ Although patients receiving methadone for opioid use disorder treatment have not demonstrated an increased risk of relapse with concomitant use of other opioid analgesics, the same has not been demonstrated among patients receiving buprenorphine and continued surveillance after surgery is warranted.¹³¹ In general, buprenorphine can be restarted 12 to 24 hours after the last dose of a short-acting opioid or 24 to 48 hours after the last dose of a long-acting opioid if it had been discontinued.

Methadone, a full mu opioid receptor agonist with N-methyl-D-aspartate antagonist and serotonin and norepinephrine reuptake inhibition properties, is administered as a daily oral medication by certified specialty clinics.¹³²⁻¹³⁴ When prescribed for opioid use disorder treatment, patients receiving methadone are less likely to experience euphoria from heroin abuse.¹²⁹ Surgical patients can be instructed to take their usual methadone dose on the day of their scheduled procedure. Additional immediate-release opioids may be prescribed for the acute pain. Given the heightened risk of relapse, discontinuation of methadone is not generally recommended.¹²⁹

Naltrexone is Food and Drug Administration-approved for both the treatment of opioid use disorder and alcohol use disorder and acts as a competitive opioid antagonist at the mu opioid receptor.¹²⁹ The oral formulation was found to be no more effective than placebo but continues to be prescribed more frequently than the injectable formulation. This medication blocks the euphoria, analgesia, and sedation from opioid agonists. Some authors have suggested discontinuing naltrexone preoperatively with the last dose 2-3 days prior to surgery for the oral formulation, and 30 days prior to surgery for the injectable extended release formulation.¹²⁹ Prior to re-starting naltrexone after surgery, patients should not be taking opioid agonists for at least 7-10 days, as it will precipitate acute opioid withdrawal if administered to a patient actively using opioids. In the event that preoperative naltrexone discontinuation is not feasible (e.g. emergency surgery), nonopioid analgesics, nonpharmacologic treatment, and regional anesthetic techniques can be considered.¹²⁹ For surgeries in which opioids will not be required or can be avoided for perioperative care, there is no need to alter the naltrexone management. Of note, new longer-acting formulations of naltrexone are being trialed that would make such care coordination nearly impossible. Close communication with the patient's addiction specialist and surgeon will be required in such a situation.

Regardless of the perioperative management strategy chosen for opioid use disorder treatment, all patients receiving such therapy can be considered for perioperative multimodal analgesia, regional anesthesia techniques, and specialist referrals when needed (addiction medicine, psychiatry, pain medicine). The patient's addiction provider should be engaged in all decision making, and patients and their families must understand the plan and be engaged in decision making. Discharge planning should include a clear transition plan back to the maintenance treatment.

Influencing surgeon prescribing practices

Opioids—Anesthesiologists can serve as a resource for surgical colleagues regarding post-discharge prescribing. Multiple studies have demonstrated that the amount of opioid prescribed can be greatly reduced from traditional norms without adversely impacting patient-reported pain, satisfaction, or refill requests.^{54,56,108} While early analyses show that policy interventions have not led to meaningful decreases in opioid prescriptions,^{135,136} the implementation of surgery-specific prescribing recommendations offers more promise.^{55,137,138} To facilitate this, opioid prescribing guidelines for many common surgeries are available at www.opioidprescribing.info, along with specific counseling recommendations such as setting expectations, encouraging non-opioid pain medication use, and describing adverse effects, appropriate vs. inappropriate use, and safe disposal.¹³⁹ These evidence-based prescribing recommendations from the Michigan Opioid Prescribing Engagement Network were created from patient-reported outcomes from health systems throughout the state of Michigan. Implementation of these recommendations in a cohort of >11,000 patients across 43 centers led to a significant decrease in post-discharge opioid prescribing without increases in pain or reduction in satisfaction.⁵⁵ These recommendations are updated approximately three times per year based on new data; post-surgical prescribing recommendations are also available from other large academic centers (e.g., Johns Hopkins and the Mayo Clinic).^{140,141} Ensuring that our surgical colleagues are aware of prescribing recommendations should be considered part of anesthesiologists' roles as complete perioperative physicians. As noted above, post-surgical prescribing *by anesthesiologists* is the norm in several other countries.

Naloxone—Naloxone, an opioid receptor antagonist, has been shown to be effective in treating opioid overdose when administered in intravenous, intramuscular, and intranasal forms.¹⁴² Naloxone prescribing increased nationally between 2014-2017, but only approximately 2% of patients with risk factors for opioid-related overdose received a naloxone prescription.¹⁴³ While these data were not specific to perioperative care, one can assume the rates of postoperative prescribing of naloxone were the same or lower. Costs between the different formulations and delivery systems vary widely.¹⁴⁴ Most recommend intranasal formulations of naloxone given higher patient acceptance compared to injectable formulations. Anesthesiologists should assist in identifying patients with risk factors for opioid overdose such as obesity and co-prescribed benzodiazepines.^{145,146} Given that evaluation for these risk factors is a routine part of the preoperative evaluation, anesthesiologists are well placed to identify patients who would benefit from naloxone prescription and communicate this to surgeons.

Conclusion

Anesthesiologists have a unique opportunity to show value in the healthcare system by positively impacting the devastating opioid epidemic. A wide variety of surgeries have been linked with excess opioid prescribing and the development of new persistent postoperative opioid use. Although continued research is required to clarify the relationship between perioperative opioid use and concrete opioid-related harms, there are several practical steps anesthesiologists can take to improved acute and chronic postoperative outcomes.

Furthermore, there is a pressing need to develop a personalized approach to perioperative opioid-related risk stratification, management, and the prevention of persistent post-surgical pain.

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Summary Statement

We summarize current evidence related to perioperative opioid prescription fulfillment and use and discuss the role of personalized anesthesia care in mitigating opioid-related harms without compromising analgesia.

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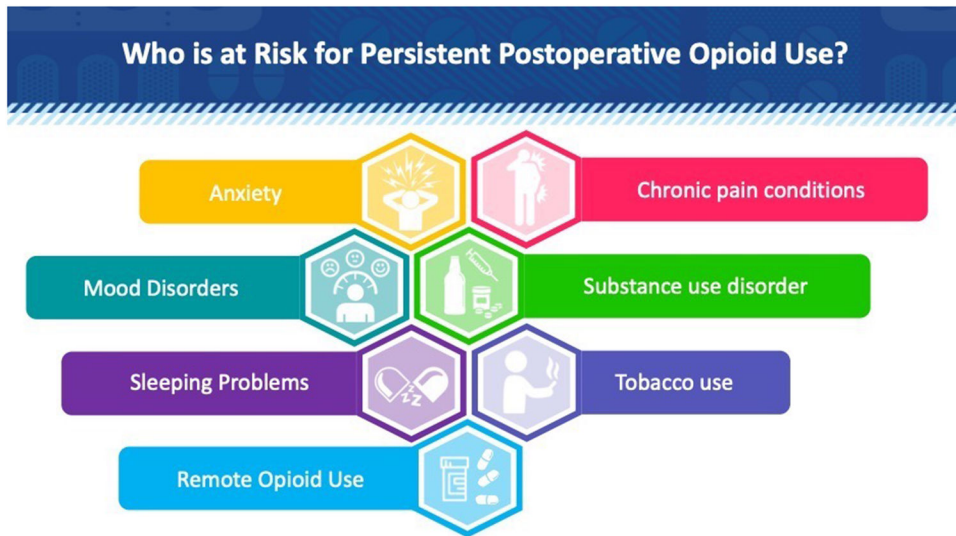


Figure 1.
Risk factors for persistent postoperative opioid use.

Table 1:

Sample preoperative opioid tapering protocol for a patient taking 150 mg daily oral morphine equivalents of oxycodone (conversion to oral morphine 1:1.5). We recommend a taper every week by 10% of original dose until 30% remains. Then, taper by roughly 10% weekly (as feasible with available pill sizes). Clonidine 0.1-0.2 mg PO TID PRN or 0.1-0.2 mg/24 hr TD q7d PRN can be considered for withdrawal symptoms, with close attention paid to potential hypotension or anticholinergic effects. A pause in the weaning protocol may be appropriate based on patient response.¹

Week	Oxycodone dose (daily mg)	Oral morphine equivalents (daily mg)
1	100	150
2	90	135
3	80	120
4	70	105
5	60	90
6	50	75
7	40	60
8	30	45
9	25	37.5
10	20	30
11	15	22.5
12	10	15
13	5	7.5
14	0	0

¹Berna C, Kulich RJ, Rathmell JP: Tapering Long-term Opioid Therapy in Chronic Noncancer Pain: Evidence and Recommendations for Everyday Practice. Mayo Clinic Proceedings 2015; 90: 828-842