American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Perioperative Management of Patients on Preoperative Opioid Therapy

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Enhanced recovery pathways have quickly become part of the standard of care for patients undergoing elective surgery, especially in North America and Europe. One of the central tenets of this multidisciplinary approach is the use of multimodal analgesia with opioid-sparing and even opioid-free anesthesia and analgesia. However, the current state is a historically high use of opioids for both appropriate and inappropriate reasons, and patients with chronic opioid use before their surgery represent a common, often difficult-to-manage population for the enhanced recovery providers and health care team at large. Furthermore, limited evidence and few proven successful protocols exist to guide providers caring for these at-risk patients throughout their elective surgical experience. Therefore, the fourth Perioperative Quality Initiative brought together an international team of multidisciplinary experts, including anesthesiologists, nurse anesthetists, surgeons, pain specialists, neurologists, nurses, and other experts with the objective of providing consensus recommendations. Specifically, the goal of this consensus document is to minimize opioid-related complications by providing expert-based consensus recommendations that reflect the strength of the medical evidence regarding: (1) the definition, categorization, and risk stratification of patients receiving opioids before surgery; (2) optimal perioperative treatment strategies for patients receiving preoperative opioids; and (3) optimal discharge and continuity of care management practices for patients receiving opioids preoperatively. The overarching theme of this document is to provide health care providers with guidance to reduce potentially avoidable opioid-related complications including opioid dependence (both physical and behavioral), disability, and death. Enhanced recovery programs attempt to incorporate best practices into pathways of care. By presenting the available evidence for perioperative management of patients on opioids, this consensus panel hopes to encourage further development of pathways specific to this high-risk group to mitigate the often unintentional iatrogenic and untoward effects of opioids and to improve perioperative outcomes. (Anesth Analg 2019;129:553–66)

Patients receiving opioids who are scheduled for surgery are at risk of opioid-related morbidity, and thus require risk stratification and unique, multidisciplinary treatment.[1] Patients on preoperative opioids have a dose-dependent increased risk of poor surgical outcomes and adverse events related to opioid use in the perioperative period.[2,3] Opioid-induced respiratory depression occurs in 0.15%–1.1% of all surgical patients,[4–8] and is increased 3-fold in opioid-dependent patients.[3] Patients on opioids are at risk of poor pain control and suffering, at least in part

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due to anxiety regarding inadequate pain relief, in the perioperative period.[1,9,10]

Preoperative opioid use results in other untoward outcomes, such as delayed wound healing, increased surgical reintervention, prolonged hospital stay, higher readmission rates, greater health care costs, and increased mortality.[11–20] One of the greatest risk factors for prolonged postoperative opioid use and perioperative dose escalation is preoperative chronic opioid use.[17,21–28] In 66,950 patients undergoing total knee arthroplasty, 34.8% using opioids preoperatively became chronic users compared to only 5.0% of the opioid-naïve cohort.[17] Preoperative opioid use is a potentially modifiable risk factor that could be optimally managed to improve safety and long-term postoperative outcomes.[11,29]

While enhanced recovery programs improve perioperative outcomes for patients under a variety of surgeries, patients on chronic opioid therapy before surgery represent a subgroup that may still be at high risk for poor outcomes. Accordingly, a logical evolution of enhanced recovery pathway development is to incorporate evidence for improved outcomes for patients on chronic opioid therapy.

In this consensus document, we review the available literature and propose a novel classification scheme to define patient risk groups according to their preoperative opioid exposure. We discuss the evidence for preoperative, intraoperative, and postoperative management of patients in these risk strata. Finally, we suggest lines of inquiry for future research to increase the quality of available evidence for clinical practice. The goal of this document is to provide consensus statements that reflect the expert panel's evaluation of the evidence regarding: (1) the definitions, categorization, and risk stratification of patients on opioids; (2) optimal perioperative treatment strategies; and (3) optimal discharge and continuity of care management practices for patients on chronic opioids.

METHODS

The fourth Perioperative Quality Initiative was convened January 4–6, 2018 to consider the present opioid epidemic. This report is the result of a modified Delphi analysis performed by a fourth Perioperative Quality Initiative working subgroup charged with appraising the published evidence on perioperative management of patients on opioids before surgery. Details of the Perioperative Quality Initiative process have been published previously.[30]

Members of the American Society for Enhanced Recovery (Supplemental Digital Content 1, Appendix 1, http://links.lww.com/AA/C701) representing specialists in surgery, anesthesiology, neurology, pharmacology, nursing, and pain medicine met to review the literature and achieve consensus on recommendations for care of patients receiving preoperative opioids of any type. The panel created a condensed list of topics for which presentation of the evidence would be most helpful to clinicians. The topics chosen were: (1) the definitions of preoperative opioid use; (2) the effect of preoperative education and expectation management on perioperative outcomes; (3) the potential benefits of preoperative psychological optimization; (4) the potential impact of perioperative pain specialist consultation; (5) the role for multimodal pain management including regional anesthesia and adjunctive medications; (6) how perioperative opioids should be managed; and (7) the optimal perioperative management of patients being treated for opioid use disorder. The literature on each of these topics is vast, so only studies that evaluated the impact of an intervention aimed toward the care of patients on opioids preoperatively were evaluated. The strategy for topic 1, definitions of preoperative opioid use, was to sample the literature, and therefore does not represent a comprehensive or systematic review. For topics 2–7, a systematic review was performed to identify studies of interventions that could be incorporated into enhanced recovery pathways for optimal management of patients on opioids.

Systematic Search

Using MEDLINE and Embase search engines, a search was performed following the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines.[31] Search terms included surgery, surgical, operation, operative to first identify studies in the perioperative realm. Results were focused further through search of the following keywords: opioid, opiate, narcotic, morphine, methadone, hydromorphone, fentanyl, buprenorphine, tapentadol, hydrocodone, oxycodone, oxymorphone, tramadol, codeine, dependence, dependent, tolerance, tolerant, exposed, exposure, and use. We limited the search to humans, English language, adult patients, without date restrictions up through 2017 (Supplemental Digital Content 2, Table 1, http://links.lww.com/AA/C702). We excluded case reports, commentaries, letters, and editorials in the search. Review articles were used to identify relevant studies missed within the search results.

We included studies in which patients on opioids preoperatively were identified either as the primary study population or as a subgroup. We categorized these studies into groups that evaluated our topics of interest 2–7 as discussed. Studies evaluating risks and outcomes of preoperative opioids use, but not describing treatment/intervention effects were excluded. Also studies only demonstrating the surgery itself as the intervention improving postoperative opioid use were excluded. Results were reviewed at the title and abstract levels by 2 reviewers (D.A.E. and J.J.) for inclusion. The resulting list was independently reviewed by the same reviewers, and the strength of the evidence graded using Grading of Recommendations, Assessment, Development and Evaluations assessment guidelines.[32] When disagreement occurred, a third reviewer (M.D.E.) acted as tie-breaker. During the meeting, the literature search and the strength of the evidence were reviewed by the group. Based on the level of evidence, consensus statements were drafted and worded following National Institute for Health and Care Excellence guidelines (Table 1), to reflect the impression of the group of the overall strength of the evidence, using the modified Delphi process (Table 2).

RESULTS

The systematic search returned 1820 results. An additional 24 studies were identified by review of references and through review articles (Supplemental Digital Content 3, Figure 1, http://links.lww.com/AA/C703). Duplicates were removed, and title and abstract were reviewed, resulting in 338 articles. An additional 288 articles were excluded after full-text review, and the remaining 50 articles were categorized into 6 topic areas and their quality assessed. The results and discussion for each topic are now discussed beginning with the consensus statements in bold (also see Table 2).

Table 1. Format of Recommendations in Perioperative Quality Initiative Guidelines (From National Institute for Health and Care Excellence Guidelines)

Strength of Recommendations[a]	Definition
Strongly recommend	Committee believes the evidence is strong, supported by numerous high-quality prospective randomized trials.
Recommend	Evidence supporting the practice is not as strong, based on high-quality prospective and retrospective studies. Committee feels that benefits of the intervention outweigh the risk for the majority of patients.
Consider	There is a lack of quality research to make a recommendation. Committee feels the practice is safe and likely to be effective based on expert opinion.

[a]Based on National Institute for Health and Care Excellence guidelines.

DISCUSSION

Topic 1: Categorizing and Defining Preoperative Opioid Use

We recommend categorizing patients as opioid-naïve, opioid exposed, or opioid tolerant. We suggest that opioid-naïve be defined as a patient having no history of opioid use in the 90 days before surgery. We suggest defining opioid exposed as a patient having a history of any opioid exposure <60 mg morphine equivalent dose within 90 days preoperatively. We recommend defining opioid tolerant as a patient with a history of ≥60 mg morphine equivalent dose in the 7 days before surgery. We recommend use of the new opioid-naïve, exposed, and tolerant+ (O-NET+) classification scheme to categorize patients into low, moderate, and high-risk groups.

A taxonomy describing the degree of opioid use in the perioperative period has not been consistently defined. "Opioid-naïve" and "opioid tolerant" were the most common terms used to classify patients but there is no consistency in the definition of these terms. A survey of PubMed-listed studies showed that the term opioid-naïve is applied to patients without (or with low) previous opioid exposure; however, timeframes before surgery vary widely, ranging from 2 years to 7 days preoperatively, thus rendering this definition less useful.[21,33–39] We defined opioid-naïve as a patient having no history of opioid use in the 90 days before surgery, considering this a sufficient interval to be deemed without increased risk. Opioid tolerant was most often defined by using a cutoff value above which patients were considered tolerant (ie, the US Food and Drug Administration definition of opioid tolerance as a patient "who [is] taking at least 60 mg oral morphine equivalents/day … or an equianalgesic dose of another opioid for 1 week or longer").[40] Studies demonstrate that there is a dose inflection point between 40 and 60 mg morphine equivalent dose at which there is a significantly increased risk of opioid-related adverse events. To remain consistent with published literature and the Food and Drug Administration definition, and to reflect the increased risk of opioids above the inflection point, we defined opioid tolerant at a dose of 60 morphine equivalent dose or above.[2,12,41,42] On the other hand, even short-term and low-dose opioid exposure induces acquired pharmacokinetic and pharmacodynamic tolerance, and opioid receptor upregulation,[43] and thus may lead to an increase in the likelihood of prolonged use or abuse.[21,23,43] For these reasons, we defined any opioid use within 90 days of surgery as "opioid exposed." The actual preoperative risk for opioid-exposed patients, being somewhere between "opioid-naïve" and "opioid tolerant," is a gray zone to be defined by

Table 2. Consensus Statements and Recommendations

How do we categorize and define opioid use in the preoperative patient?
- We recommend categorizing patients as O-NET.
- We suggest defining opioid-naïve as no history of opioid use in 90 d before surgery.
- We suggest defining opioid exposed as history of >0 morphine equivalent dose and <60 mg morphine equivalent dose within the past 90 d.
- We recommend defining opioid tolerant as history of ≥60 mg morphine equivalent dose in the past 7 d.

How should patients be risk stratified preoperatively for opioid-related adverse events and poor outcomes?
- We recommend use of the new O-NET+ classification scheme to categorize patients into low-, moderate-, and high-risk groups (Figure 1).

How do we optimize moderate- to high-risk patients according to O-NET+ criteria before surgery?
- We suggest weaning opioids preoperatively to the lowest effective dose.
- We recommend optimizing management of psychosocial comorbidities before surgery.
- We recommend individualized preoperative education to promote shared pain management expectations.
- We recommend identification of and communication with the patient's outpatient opioid prescriber to anticipate discharge needs.
- We recommend referral to a perioperative pain specialist before surgery for highest-risk patients.

What are strategies for perioperative pain management in moderate- to high-risk patients according to O-NET+ criteria?
- We strongly recommend an individualized multimodal analgesia pain management strategy, including regional/neuraxial anesthesia, when appropriate, to minimize the use of opioids.

Is opioid-free intraoperative management feasible in moderate- to high-risk patients according to O-NET+ criteria?
- Opioid-free intraoperative management is feasible, and we suggest that it may be appropriate; however, there are insufficient data to recommend it.

What are strategies for managing postoperative pain in moderate- to high-risk patients according to O-NET+ criteria?
- We strongly recommend the routine use of nonopioid options as part of a comprehensive multimodal analgesia perioperative analgesia plan.
- We recommend the lowest effective opioid dose in the postoperative period.
- We recommend avoiding opioid dose escalation.
- We recommend the addition of opioids only in the setting of suboptimal analgesia after first-line administration of nonopioid options.
- We strongly recommend the use of nonpharmacological treatments of pain.

What are strategies for managing postoperative opioids at discharge in moderate- to high-risk patients according to O-NET+ criteria?
- We strongly recommend limiting discharge opioid prescription to the expected duration of pain that is severe enough to require opioids.
- We recommend postoperative coordination of opioid tapering with the patient's outpatient provider.

Abbreviations: O-NET, opioid-naïve, exposed, and tolerant; O-NET+, opioid-naïve, exposed, and tolerant plus modifiers.

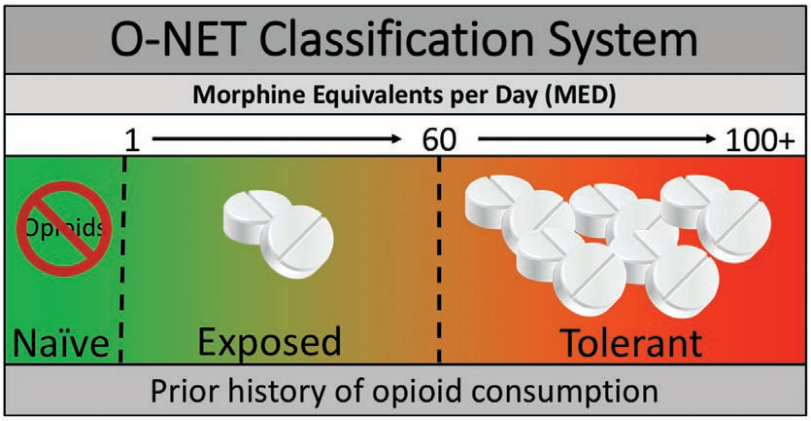

Figure 1. In the preoperative period, patients are divided into the classes opioid-naïve, opioid exposed, and opioid tolerant based on the milligram MED used. Opioid-naïve indicates no opioid use in the 90 d before surgery; opioid exposed, any amount <60 MED used in the 90 d before surgery; and opioid tolerant, ≥60 MED within 7 d of surgery. MED indicates morphine equivalent dose; O-NET, opioid-naïve, exposed, and tolerant. Figure reused with the permission of the Perioperative Quality Initiative (POQI). For permission requests, contact info@poqi.org.

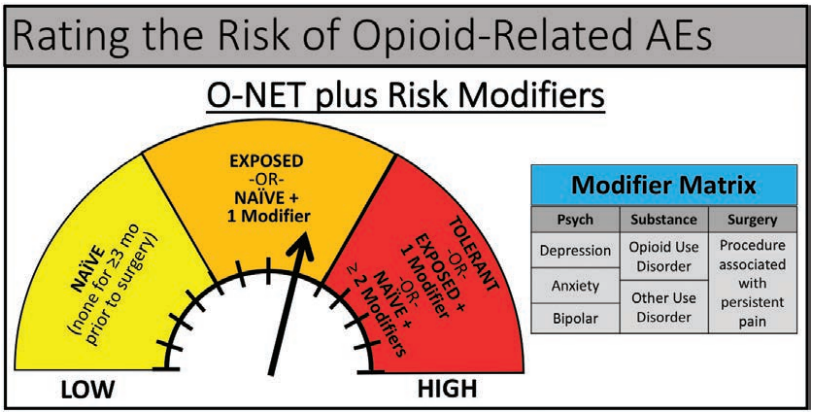

Figure 2. O-NET classes represent low-, moderate-, and high-risk groups for opioid-related adverse events and poor outcomes. Addition of comorbid risk factors known to influence the risk of opioid-related poor outcomes modify the risk group assignment. AE indicates adverse events; O-NET, opioid-naïve, exposed, and tolerant. Figure reused with the permission of the Perioperative Quality Initiative (POQI). For permission requests, contact info@poqi.org.

future research. For example, it is possible that a patient meeting the opioid tolerant definition a few weeks before surgery and who tapers down below 60 morphine equivalent dose before surgery would be at lower risk.

Taking the above into account, and on consensus of the fourth Perioperative Quality Initiative participants, we developed a conceptual framework termed the opioid-naïve, exposed, and tolerant (O-NET) classification scheme: opioid-naïve, exposed, and tolerant based on the patient's opioid use in the preoperative period (Figure 1). We then elected to develop this classification further to allow for its use in stratifying patients preoperatively into low-risk (opioid-naïve), moderate-risk (opioid exposed), and high-risk (opioid tolerant) categories (Figure 2). Many comorbid conditions, social situations, and surgical types can increase the risks of adverse outcomes related to opioids. To create a more realistic and patient-specific risk classification system, these factors were added as broad categories to the O-NET scheme as modifiers (addition of the + symbol: O-NET+). Uncontrolled psychiatric comorbidities (such as depression, anxiety, bipolar disease, and a history of dependency, addiction, or alcoholism) and behavioral tendencies (such as catastrophizing behavior, perceived self-efficacy) impact pain behaviors and opioid use. Certain types of surgery known to have a high incidence of postoperative acute or chronic pain (thoracotomy, spinal fusion) would be considered modifiers posing an increased risk for higher or prolonged use of opioids. The following 3 examples demonstrate how the opioid-naïve, opioid exposed, and opioid tolerant+ classification system can be used: (1) an opioid-naïve patient (initial O-NET classification is low risk) is identified to be severely depressed, unmedicated, and not seeing a caregiver for this comorbidity. This patient would be given a final opioid-naïve, exposed, and tolerant+ classification of moderate risk, and time allotting for elective surgery could be referred for treatment or provided concurrent consultation and management of depression in the perioperative period. (2) An opioid-exposed patient (initial O-NET classification of moderate risk) undergoing thoracotomy would be classified by O-NET+ as high risk, given the increased expected postoperative pain. (3) Finally, a patient presenting to the preoperative surgery clinic in preparation for shoulder replacement is found to be taking opioids at >60 morphine equivalent dose daily and is therefore classified as high risk by O-NET+. If reasonable and appropriate for this patient, a plan could be started to introduce multimodal analgesia facilitating an opioid taper to <60 morphine equivalent dose. If the timing allows this to occur at least 7 days before planned surgery, the patient would be considered moderate risk by O-NET+ on the day of surgery.

An advantage of using the classification scheme in the preoperative period is that modifiable factors can be identified and treated, or at a minimum, a plan instituted to manage the condition in the perioperative period (ie, treating anxiety or depression, ensuring regional anesthesia is used). By instituting a system to recognize and then manage modifiable risk factors, a patient's O-NET+ risk category could be

lowered, better optimizing them for surgery. The O-NET+ classification scheme can therefore be used both to identify risk factors and to direct preoperative optimization goals. Not all risk factors will be treatable in the lead time to surgery, and complete optimization may not be feasible, but by identifying the risks and establishing a plan to manage these there is the potential for improving the outcome and experience for the patient. The O-NET+ classification scheme was purposefully created with general categories, avoiding specifics (ie, the relative risks of the modifying variables were not included), to facilitate adoption and to allow for easy comparison across institutions to inform iterative improvement (Figure 3).

Topic 2: Education, Expectation Management

We recommend individualized preoperative education to promote shared pain management expectations.

There is a lack of evidence for specific educational interventions that may impact outcomes in patients on opioids. In our search, only a single study was found (Grading of Recommendations, Assessment, Development and Evaluations C).[44] In this study, 15% of patients presenting for orthopedic trauma were on opioids before the surgery. One group of patients was instructed before surgery that they would receive opioids for a maximum of 6 weeks. Seventy-three percent of those instructed stopped opioids by 6 weeks compared to 63% of those not instructed; however, at 12 weeks, there was no difference. Given the lack of quality data on this topic, we offer the following considerations based on literature supporting the general impact of education and expectation management for all patients.[45]

Optimization of care for the surgical patient begins in the clinic with identification and stratification of at-risk patients. An integral component of an enhanced recovery pathway is incorporation of the patient into the clinical care pathway as preoperative patient expectation management results in improved postoperative patient satisfaction and decreased need for opioids.[45–51] Patients with chronic pain or substance use disorders are likely to be apprehensive about their pain control or risk of relapse around surgery. These patients especially should be introduced to the multimodal pain management approach of the enhanced recovery pathway and how it might benefit someone in their risk class. They should also be informed of the relatively increased risks of being on opioids before surgery and educated on the adverse effects of opioids both in the perioperative setting

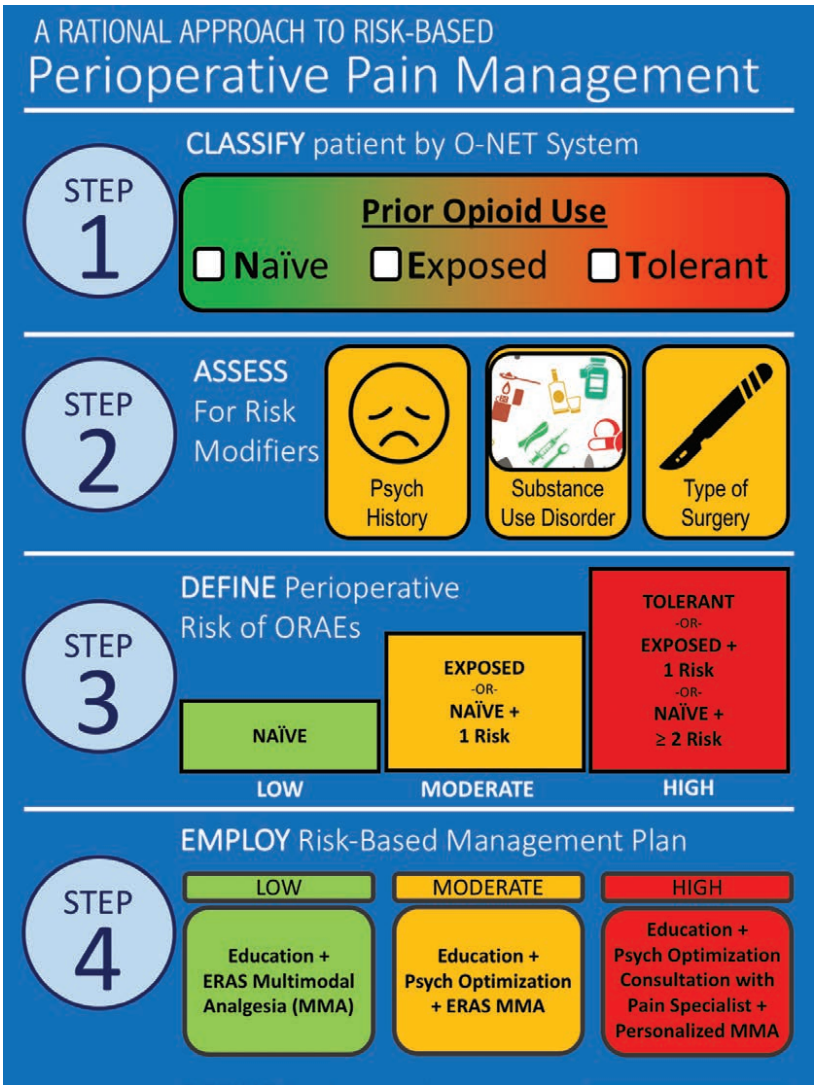

Figure 3. An approach for the use of O-NET+ classification in perioperative management of patients on preoperative opioids. First, classify patients using O-NET into naïve, exposed, or tolerant (step 1). Consider comorbid conditions that may increase risk, such as psychiatric diagnoses, a history of substance dependence, or invasive and painful surgery plan (step 2). Risk stratify into low-, moderate-, or high-risk categories (step 3), and employ enhanced recovery pathways specific to the risk category (step 4). ERAS indicates enhanced recovery after surgery; O-NET, opioid-naïve, exposed, and tolerant; O-NET+, opioid-naïve, exposed, and tolerant plus modifiers; ORAE, opioid-related adverse event. Figure reused with the permission of the Perioperative Quality Initiative (POQI). For permission requests, contact info@poqi.org.

and with prolonged use. These topics should be initiated in the surgeon's office and continued throughout the preoperative period at subsequent encounters.

Topic 3: Psychological Optimization

We recommend optimizing management of psychosocial comorbidities before surgery.

No studies were found that measured the impact of psychological treatments on perioperative outcomes of patients on preoperative opioids. However, recognizing the presence of complex psychosocial issues and comorbid psychiatric illness in the patient on chronic opioid therapy is of utmost importance to improve outcomes. Patients on chronic opioid therapy may have relevant accompanying disorders including depression, anxiety, posttraumatic stress disorder, borderline personality disorders, among others.[52–57] Screening and risk stratification for modifiable comorbid conditions in patients on opioids can identify those that might benefit from preoperative interventions to improve resilience and coping skills that could mitigate opioid dose escalation and self-medication of negative emotions with opioids.[56,58–62]

In particular, mindfulness-based training has been proposed as a valid adjunct for the preparation and management of postoperative pain, particularly in surgical patients with chronic forms of pain such as osteoarthritis.[61] Most studies of mindfulness focused on chronic pain for which mindfulness seems to have the greatest benefit in improving the psychological impact and quality of life of the pain experience.[63] The effect of mindfulness meditation on acute pain has been studied less, and the studies are generally of very low to low quality,[64] but demonstrate promise in reducing analgesic requirements, pain intensity, and anxiety.[65] Based on these limited data in patients with acute or chronic pain, mindfulness training has the potential to improve current pain management strategies for patients on opioids who are at risk of suffering after surgery.

Topic 4: Perioperative Pain Specialist Consultation

We recommend identification of and communication with the patient's outpatient opioid prescriber to anticipate discharge needs. We recommend referral to a Perioperative Pain Specialist before surgery for highest risk patients.

There is no direct evidence that preoperative consultation by specialists in pain management improves perioperative outcomes of patients on opioids. This is to say that no study compares the outcome for patients on opioids when a preoperative consultation is obtained with a pain specialist (or a perioperative pain specialist such as an acute pain service consultant) versus no consultation. Only a single observational patient survey was found in our search of this topic.[66] The study surveyed patient satisfaction with a taper schedule provided by an acute pain service to patients who presented for elective surgery already on opioids. Although few studies directly evaluate the impact of consultative services, there is strong evidence for the specialized medical care that is provided by these services (ie, regional anesthesia, multimodal analgesia). A well-planned and communicated strategy for delivering multimodal analgesia, historically the specialty domain of pain management specialists, almost certainly improves the safety, quality, cost, and coordination of care.[67–71] Consultation with a specialized, dedicated acute pain, or perioperative consult service continues to be a strong recommendation from multiple expert panels.[72–75] Enhanced recovery pathways, the perioperative surgical home, and the transitional pain service are organization responses to improve recovery and reduce the prolonged negative outcomes related to surgery (chronic pain and opioid use among them).[76–79] These dedicated, modern services reflect a multidisciplinary approach as teams of specialists provide individualized care to surgical patients, and move away from pain practice as the cottage industry of the solo surgeon or specialist.

Topic 5: Multimodal Pain Management Strategies

For patients on opioids, we strongly recommend that an individualized multimodal analgesia pain management strategy be used, including regional/neuraxial anesthesia when appropriate, to minimize the use of opioids (evidence: Grading of Recommendations, Assessment, Development and Evaluations A). We strongly recommend the routine use of nonopioid options as part of a comprehensive multimodal analgesia perioperative analgesia plan (evidence: Grading of Recommendations, Assessment, Development and Evaluations A). We strongly recommend the use of nonpharmacological treatments of pain (evidence: Grading of Recommendations, Assessment, Development and Evaluations A).

Perioperative Pain Management in Patients on Preoperative Opioids. Our search identified 32 articles, several of high quality (Grading of Recommendations, Assessment, Development and Evaluations A) in which multimodal analgesia was used and the results specifically address the outcome for patients chronically on opioids.[39,80–85] The multimodal analgesia regimens included multiple medications, nonopioid and opioid combinations, to attain pain control while limiting side effects. Hundreds of additional articles, including meta-analyses, demonstrate level-1 evidence to support the efficacy of multimodal analgesia and its widespread use across surgical types. It is the consensus of this panel that multimodal analgesia is even more relevant for the population on chronic opioids.[86–91] Specific nonopioid analgesics that are useful in enhanced recovery pathways have been extensively reviewed elsewhere.[70,86,92]

A primary objective for pain management in patients on preoperative opioids is to treat acute pain while preventing withdrawal and avoiding persistent opioid escalation beyond the baseline dose. Many patients with chronic pain on opioids may already be on a multimodal analgesia pain treatment regimen designed to treat chronic pain. The strategy of maximizing and optimizing a multimodal analgesia regimen could include increased doses, rotation of medication (ie, opioid rotation for better efficacy or reduction in side effects), or addition of medication of another class. Adjustments to dose, frequency, or timing of medications may be needed to assist with postoperative recovery and to prevent side effects such as sedation, delirium, and respiratory depression of concurrent therapies.

Nonopioid multimodal analgesia analgesics commonly used in enhanced recovery pathways include lidocaine and ketamine infusions, the anticonvulsants gabapentin and pregabalin, acetaminophen, nonsteroidal anti-inflammatory drugs including nonselective and selective cyclooxygenase inhibitors, and regional nerve blocks and epidural analgesia using local anesthetics. There is level-1 evidence in specific surgical types for the use of lidocaine infusions to reduce opioid consumption,[93–98] and decrease pain scores,[93,95,96] but when reviewed in combination intraoperative use of lidocaine infusions has not consistently shown benefit for relevant reduction of pain or opioids.[99] There are no randomized controlled trials of lidocaine infusions in patients on chronic opioids.

Ketamine can be a powerful adjunctive therapy for opioid-sparing enhanced recovery pathways, given its *N*-methyl-D-aspartate receptor antagonism. As an infusion, level-1 evidence supports the use of ketamine for opioid-sparing and pain score reduction strategies.[83,85,100–102] Clinical practice guidelines by expert consensus suggest the use of ketamine in many surgical procedures especially in the opioid-tolerant patient.[73] Ketamine is one of the few adjuncts studied in the patient on preoperative opioids. In a recent blinded trial randomized controlled trial, intraoperative ketamine infusion reduced opioid consumption up to 24 h after lumbar fusion in opioid-dependent patients.[80] Ketamine was an effective adjuvant resulting in lower opioid consumption in patients with opioid use disorder undergoing minor procedures and enabled earlier readiness for discharge times.[103] There is, however, a dose dependency or surgery-specific benefit in patients on opioids.[104]

Based on the strength of the literature for multimodal analgesia, and its value for mitigation of opioid-related adverse events and poor surgical outcomes among populations reported, it is this expert panel's consensus recommendation that the data are likely even more relevant for the patient already on opioids before surgery.

Regional Anesthesia. Strong evidence supports the use of regional anesthesia to reduce acute pain and this often results in a reduction of opioid consumption. The effectiveness of the type of regional block may depend on the body location, and the type and invasiveness of the surgery[39,102,105–109]; however, regional anesthesia has been consistently shown to be superior to the use of opioid analgesia.[88,89,91] Multiple clinical guidelines suggest the use of regional anesthesia as part of a thorough multimodal analgesia plan.[72,73] In a retrospective analysis of 198 major lower limb amputation, the use of perineural regional catheters was a significant predictor of lower total postsurgical opioid use even in patients with presurgical chronic pain and opioid use.[110] However, a study of liposomal bupivacaine comparing periarticular injection in the opioid-tolerant patient having total knee arthroplasty did not result in reduced opioid utilization or pain scores.[111]

Nonpharmacological Adjuncts. Many types of complementary nonmedication pain management strategies have been used in patients undergoing surgical procedures. However, these have not been studied specifically in patients who are on opioids before surgery. Therefore, we list only a few of the many options that could be considered and incorporated into an enhanced recovery pathway. Distraction therapy is effective at reducing pain and distress among children undergoing needle-related procedures.[64] Music therapy has been used in patients undergoing surgery to lower pain scores in the short term.[112,113] Hypnosis has been widely documented to reduce distress before a procedure. In a large meta-analysis of adult and pediatric patients undergoing a variety of procedures, hypnosis had a large and beneficial effect on emotional distress related to medical procedures. Schnur et al[114] demonstrated that a single 15-minute hypnosis session was more effective than placebo at lowering scores for emotional upset, depressed mood, and anxiety. Enqvist et al[115] found that women undergoing breast reduction randomized to listen to hypnosis tapes in the days leading up to surgery had reduced opioid consumption, and postoperative nausea/vomiting. Transcutaneous electrical nerve stimulation has been used as a nonpharmacologic adjunct for the treatment of acute pain for the past 30 years. Moderate evidence demonstrates that transcutaneous electrical nerve stimulation reduces analgesic requirements while improving pain, nausea, and pulmonary function in the perioperative period.[116] Given the low cost and relative safety, transcutaneous electrical nerve stimulation should be considered in the armamentarium of nonmedication adjuncts.

Topic 6: Perioperative Opioid Management

We suggest weaning opioids preoperatively to the lowest effective dose depending on the patient's underlying condition. Opioid-free intraoperative management is feasible, and we suggest that it may be appropriate; however, there are insufficient data to recommend it. We recommend the lowest effective opioid dose in the postoperative period. We recommend avoiding opioid dose escalation. We recommend the addition of opioids only in the setting of suboptimal analgesia after first-line administration of nonopioid options. We strongly recommend limiting discharge opioid prescription to the expected duration of pain that is severe enough to require opioids. We recommend postoperative coordination of opioid tapering with the patient's outpatient provider. We recommend the continuation of multimodal therapy throughout the convalescence after surgery, and as long as the patient continues to require additional opioids. We strongly recommend limiting discharge opioid prescription to the expected duration of pain that is severe enough to require opioids, and we recommend postoperative coordination of opioid tapering with the patient's outpatient provider.

Preoperative Opioid Reduction. One reason for developing the O-NET+ classification scheme is to more clearly understand the correlation between preoperative opioid dose and poor outcomes.[3,117,118] It is possible that a protocol-based preoperative opioid reduction strategy for chronic opioid users would improve those outcomes.[119,120] Based on this concept, McAnally[121] proposed delaying elective surgery when feasible for a 10- to 12-week multidisciplinary preoperative optimization program for chronic pain patients. This program would focus on opioid reduction, reducing pain catastrophizing, and prehabilitation.

Preoperative opioid reduction for patients being treated for pain, acute, or chronic (discussion of substance use disorder is reviewed below) has yet to be evaluated in high-quality prospective trials. It may not be easy or ideal to taper opioids in patients being treated for chronic pain or who are on long-acting opioid formulations before surgery. A cohort study in patients undergoing total joint arthroplasty compared patients who successfully weaned opioids (a 50% reduction in morphine equivalent dose) to opioid users that did not wean and to a group of nonopioid users (Grading of Recommendations, Assessment, Development and Evaluations C).[122] They found that the group who successfully weaned preoperatively had significantly better outcomes in disease-specific and generic health outcomes and exhibited similar outcomes to the nonusers. The data being limited to support preoperative tapering, this panel therefore suggests weaning to the lowest effective dose, depending on the patient's underlying condition.

Day of Surgery Opioid Management. Managing opioids on the day of surgery can be complicated, and with little specific evidence to guide clinical practice, most literature is based on expert opinion.[69] Expert consensus, including that of the authors of this article, recommends continuation of a patient's typical dose of prescribed opioid on the morning of surgery with intraoperative analgesia sufficient to treat surgical pain.[69,72,73,117,123] Opioid-free intraoperative analgesia is possible and most common when regional anesthesia is used but is also possible when multimodal protocols are used during general anesthesia.[94,124–127] General anesthesia can be avoided in many surgeries in which effective regional anesthesia blocks are sufficient. This may be true even in the patient on preoperative opioids; however, opioid-free anesthesia has not been specifically evaluated in patients on preoperative opioids. Thus, it is our conclusion that opioid-free intraoperative management is feasible, and we suggest that it may be appropriate; however, there are insufficient data to recommend it.

Postoperative Opioid Management. Given the risks associated with higher opioid dosing as described above, expert consensuses universally recommend opioid-sparing techniques. In an opioid-tolerant patient, the goal may be even more important to limit postoperative opioid escalation and associated increased incidence of opioid-related adverse events.[128] A multimodal analgesic approach may decrease or slow opioid dose escalation,[129,130] reduce the incidence of adverse events,[68,131] and allow more patients to wean off opioids in the postoperative period.[132] In patients on preoperative opioids, there is a balance between adequate pain relief and avoidance of opioid-related adverse events, and recovery should be closely monitored, especially given the potential for high opioid requirements (as high as 3- to 4-fold over opioid-naïve patients).[69,117] Patients on opioids have increased overall risk for suffering if undertreated, and of adverse events if overtreated. Patients of low-socioeconomic status lack resources and access to medical care, increasing the risk of prolonged use of opioids and opioid-related adverse events.[133–135] Transitional pathways should consider the continuum of care to ensure long-term safety and optimal outcomes especially for this group of patients.

While studies examining the dose escalation, duration, and necessity of opioids in the postoperative period for patients on preoperative opioids are limited, postoperative prescribing should provide sufficient pain medication to allow for functional recovery for the duration of severe pain expected for the surgical type while avoiding collateral adversities from overprescribing.[136] Emphasis on function first, and opioids last means that a strategy to treat acute postoperative pain ideally maximizes nonopioid medications and nonmedication options before, or at least concurrent with, prescribing opioids. Therefore, we recommend the lowest effective opioid dose for the shortest duration in the postoperative period. While short-term dose escalation is reasonable to treat perioperative pain, we recommend avoiding persistent escalation of chronic doses of opioids. Deescalation and cessation of opioids when appropriate should be planned.[66] We recommend the addition of opioids only in the setting of suboptimal analgesia following first-line administration of nonopioid options.

Discharge Prescriptions and Opioid Taper. Surgical procedures with expected significant or prolonged postsurgical pain may warrant discharge prescription of opioids above a patient's preoperative dose. The importance of collaborating with preoperative prescribers cannot be understated, especially to ensure optimal recovery from surgery and eventual taper off. Consultation with a psychologist, psychiatrist, pain specialist, or addiction specialist may be necessary if continued opioid use occurs beyond the expected duration of acute postoperative pain.

Clarke[76] reports on the development of a Transitional Pain Service at Toronto General Hospital to address the gaps in the perioperative care continuum with respect to pain and functional recovery.[77] In their experience, approximately 12.5% of patients present to surgery on preoperative opioids and historically were discharged on 100%–300% increase over baseline dose of their original opioid, without a plan to wean.[76] Despite the generally increased awareness of an opioid use epidemic, prescribers tend to provide opioids after surgery in a trend toward increasing morphine equivalents.[137] Opioid weaning guidance after surgery is limited and mostly comes from expert opinion in clinical guidelines.[138,139]

Another significant gap in care is the length of time between discharge and postdischarge follow-up appointments.[76] Ensuring adequate follow-up for postoperative pain management should be a priority, including coordinating care with a patient's opioid prescriber, pain management provider, psychiatrist, and/or psychologist. This panel recommends the continuation of multimodal therapy throughout the convalescence after surgery, and as long as the patient continues to require additional opioids. We also strongly recommend limiting discharge opioid prescription to the expected duration of pain that is severe enough to require opioids. We recommend postoperative coordination of opioid tapering with the patient's outpatient providers.

Topic 7: Substance Dependence (International Statistical Classification of Diseases and Related Health Problems, Tenth Edition), Substance Use Disorder (Diagnostic and Statistical Manual-5)

The International Statistical Classification of Diseases and Related Health Problems, Tenth Edition and the draft International Statistical Classification of Diseases and

Related Health Problems, Eleventh Edition categorizes opioid dependence within the substance dependence master diagnosis.[140] Opioid dependence is the preferred term for opioid addiction in the International Statistical Classification of Diseases and Related Health Problems, tenth edition classification scheme (although it also includes patients with physical dependence that would not necessarily meet criteria for addiction), and opioid use disorder is the preferred term in the Diagnostic and Statistical Manual-5 classification scheme. The International Statistical Classification of Diseases and Related Health Problems, Tenth Edition classification is analogous to, although not entirely concordant with, the Diagnostic and Statistical Manual-5 classification.[140–144] It is estimated that 1.9 million Americans meet criteria for opioid dependence.[145]

We reviewed 9 studies identified by our search that deal directly with the perioperative management of patients with substance use disorder. These include management of patients on methadone or buprenorphine medication-assisted therapy. The level of evidence for these studies ranged from 3 to 4, of moderate to very low quality by Grading of Recommendations, Assessment, Development and Evaluations criteria. This lack of quality data is notable given that the opioid epidemic is defined by a dramatic increase in the prevalence of opioid dependence.

The patient on maintenance opioid agonist therapy (medication-assisted therapy) warrants special consideration in perioperative management.[146] Medication-assisted therapy utilizes controlled doses of long-acting opioids to prevent withdrawal and minimize euphoria. Designed to reduce drug craving and drug misuse, medication-assisted therapy also reduces levels of drug abuse, offending, and overdose risk in patients with opioid dependence. Methadone and buprenorphine are the 2 most commonly used drugs for medication-assisted therapy. Management of patients on methadone and buprenorphine should include a conscientious analgesia regimen including multimodal and adjuvant analgesic agents. Patients on buprenorphine may require high-affinity opioids to help overcome the blocking effect of this partial agonist. Addressing anxiety about pain control, expectation management, and a coordinated multidisciplinary approach that includes the patient's outpatient psychiatrist or pain management provider is critical to successful perioperative pain management.

Unfortunately, there are no guidelines to determine best practice. Clinical consensus recommendations and expert opinion offer several strategies.[69,146–149] Patients on methadone should be continued on their maintenance dose throughout the perioperative period. For patients on buprenorphine, 3 strategies have been recommended: continuation of buprenorphine at the maintenance dose, perioperative escalation for improved pain management, or switching to full agonist opioid therapy before surgery.[146,148,150] Given the complexities involved, it is recommended to coordinate care with the outpatient psychiatrist, psychologist, or other prescriber treating the patient with medication-assisted therapy. There is a significant risk for relapse during times of stress and repeat exposure to opioids in the perioperative period, and the most recent data suggest continuation of medication-assisted therapy in the perioperative period would be preferred.[146,151]

CONCLUSIONS

High-quality evidence for the perioperative management of patients on preoperative opioids is nonexistent. This is a particularly large gap in the medical field in the setting of pain and opioid crises. To guide compassionate care, avoid unnecessary suffering, and improve patient safety for patients on opioids in the perioperative period, the following 6 areas of research focus are needed: (1) to understand the relative risks of preoperative opioid dose, the opioid-naïve, exposed, and tolerant+ classification scheme must be validated; (2) preoperative modifiable risk factors, including psychosocial comorbid conditions must be identified and methods for optimization that improve perioperative outcomes demonstrated; (3) The efficacy of preoperative opioid taper on perioperative outcomes needs to be demonstrated across surgical types in high-quality studies; (4) the efficacy or potential harm of perioperative opioid minimization strategies should be shown in patients on preoperative opioids; (5) the cost–benefit of involving specialist care in the management of complex enhanced recovery pathways for patients on preoperative opioids should be demonstrated given the expense of health care and expansion of bundled care; and (6) the benefit or potential harm of the various options for multimodal analgesia should be demonstrated in studies specifically designed to determine their role for patients on opioids.

In summary, the present opioid epidemic is a complicated multifactorial societal problem. The fourth Perioperative Quality Initiative group offers expert consensus recommendations for key topics crucial to the safe perioperative care of patients on opioids. These recommendations would ideally be incorporated into enhanced recovery pathways that include care pathways for patients identified at increased risk for poor outcomes related to their opioid use. We feel enhanced recovery, multimodal analgesia, and novel applications such as transitional pain clinics offer hope for this at-risk patient population. Clearly, given the magnitude of the current opioid epidemic, a nuanced, patient- and surgery-specific approach must be taken for patients on opioids who are at risk.[152,153]

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