Developing Recommendations for Opioid Prescribing at Discharge After Abdominal-Pelvic Surgery

by

David D. Q. Zhang

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Institute of Health Policy, Management and Evaluation
University of Toronto

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ABSTRACT

The current crisis of opioid-related harms has shed light on the suboptimal nature of existing practices for the prescription of opioids at discharge after abdominal-pelvic surgery. In this thesis, I explore current guidance for surgeons on this issue as well as strategies to modify their behavior. First, I conducted a systematic review of existing recommendations on the prescription of opioids at discharge, the disposal of excess opioids as well as the prevention of chronic pain development after abdominal-pelvic surgery. Second, a systematic review of behavioral interventions to reduce post-surgical opioid prescribing was performed. Lastly, I have initiated the development of recommendations using an agreement-building process. Overall, this thesis summarizes the literature on the existing guidance available to abdominal-pelvic surgeons regarding the prescription of opioids as well as potential strategies that can be implemented to improve these practices.

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Background

The Burden of the Current Opioid Epidemic

North America is in the midst of an epidemic of opioid-related deaths. Between January 2016 and June 2018, more than 9,000 Canadians lost their lives as a consequence of opioid intoxications.[1] In 2017, a staggering 11.1 deaths occurred per 100 000 individuals.[2] Unfortunately, this wave of opioid-related casualties is not showing any sign of a slowdown, as 2,066 apparent opioid-related deaths occurred in the first six months of 2018 alone. In the United States, opioids have caused even more harm, as they were involved in 47,600 drug overdose deaths in 2017 alone,[3] corresponding to 14.9 deaths per 100 000 individuals.[4] The impact of the opioid epidemic on society has been devastating; from 2000 to 2016, unintentional substance-related deaths slowed the increase in Canadian life expectancy by 0.16 years.[5] Comparatively, in the United States, drug poisonings led to a loss of 0.28 years of life expectancy.[6] As the overwhelming majority of casualties were unintentional and involved young and middle aged adults, a potentially productive segment of the population has been lost.[1]

In addition to its effect on mortality, opioid intoxications cause a significant burden on the healthcare system. Data from the United States showed that in 2016, opioid-related visits to the emergency department occurred at an unprecedented rate of 268 events per 100 000 individuals, with more than 300 opioid-related inpatient stays per 100 000 individuals.[7] In Canada, hospitalizations due to opioid intoxication have risen by 27% over the past five years.[8] Between 2016 and 2017, emergency visits for opioid intoxication increased by 73% in Ontario, and an average of 17 Canadians were hospitalized on a daily basis.

The Role of Prescription Opioids

The Centers for Disease Control and Prevention recognizes three waves of opioid-related mortality since the beginning of the millennium: 1) deaths due to the increasing

prescribing of opioids that began in the 1990s, 2) deaths involving heroin that began in 2010 and 3) deaths involving synthetic opioids, particularly illicitly-manufactured fentanyl and analogues, that began in 2013 and is ongoing.[9] The dramatic increase in deaths related to opioid intoxication in the past few years has been largely blamed on fentanyl, an extremely potent type of opioid, as well as fentanyl-analogues such as carfentanil and U-48800.[10] In Canada, 72% of apparent opioid-related deaths were due to fentanyl or fentanyl analogues in 2018.[1] In the United States, illicitly-manufactured fentanyl accounted for almost 19 413 deaths in 2016 alone.[11] Although the majority of opioid-related morbidity and mortality in recent years has been attributed to fentanyl and fentanyl-analogues, prescription opioids - agents that are commonly used in clinical settings - remain a significant contributor to the current crisis. In 2017, prescription opioids such as methadone, oxycodone and hydrocodone were involved in more than 35% of all opioid overdose fatalities, a rate five times higher than at the beginning of the century.[12] Current estimates suggest that 46 people die every day in the United States from drug overdoses involving prescription opioids,[12] and in Canada, a recent population-based study in Ontario reported that one third of all opioid-related mortalities occurred among individuals with an active opioid prescription at the time of death.[13] As commonly used for the treatment of pain in various clinical settings, opioid drugs exert their effect by interacting with four types of opioid receptors (mu(μ), kappa(κ), delta(δ) and nociceptin) in order to modulate the release of neurotransmitters.[14] Due to differences in their location throughout the nervous system and their interaction with neurotransmitters, the binding of opioid drugs with receptors results in various clinical effects ranging to analgesia and euphoria to sedation and respiratory depression.[15] In an overdose of a prescription opioid, acute intoxication usually occurs, which is typically characterized by the clinical signs of depressed mental status, decreased respiratory rate, decreased tidal volume, decreased bowel sounds and constricted pupils, and can be fatal. Given the potential for fatal overdoses of prescription opioids, a recent guideline from the

Centers for Disease Control and Prevention recommended that clinicians keep daily dosages under 50 milligram morphine equivalents (MME) when initiating opioids to treat pain.[16]

In addition to the risk of death from overdose, an increasingly recognized harm associated with prescription opioids is the development of misuse, where opioids are used in a way other than prescribed, mostly for their rewarding properties.[17] Indeed, in the human brain, opioids activates the mesolimbic reward system by interacting with mu receptors, resulting in the release of dopamine in the nucleus accumbens, which generates pleasure.[18] When prescription opioids are misused, they are frequently injected, snorted or combined with other drugs to enhance their effect.[17] Estimates from the National Survey on Drug Use and Health (NSDUH) suggest that more than a third of the non-institutionalized United States adult population used a prescription opioid in 2015, and of them, at least 12.5% reported misuse of their prescribed narcotic.[19] Among individuals who use opioids for chronic pain, the rate of misuse may be as high as 29%.[20] The inappropriate use of prescribed opioids is a risk factor for mortality, as approximately 30% of deaths due to opioids occur among individuals who concomitantly ingested benzodiazepines,[21] a class of medications with sedating effects that, when combined with opioids, depresses the respiratory drive from the central nervous system.[16] Moreover, the long-term misuse of prescription opioids can lead to physical dependence, which manifests with the emergence of withdrawal symptoms when opioids are discontinued.[17] Physical dependence can, in turn, serve as a stepping stone towards the development of an opioid use disorder (also known as opioid addiction) by causing affected individuals to seek opioids to avoid withdrawal symptoms. This predisposes individuals to the risk of opioid-related harms due to the widespread circulation of illegal fentanyl or fentanyl analogues.[22] Using pooled data from the 2002 to 2011 NSDUH, Muhuri *et al.* recently showed that individuals who reported prior non-medical use of a pain reliever use had a 19 times higher rate of heroin initiation when compared to those who did not report non-medical pain reliever

use (0.39% versus 0.02%), and that almost 80% of recent heroin initiates previously used pain relievers non-medically.[23] Risks factors that have been identified for the development of prescription opioid misuse include a personal and family history of substance use disorders, mental health disorders, history of legal problems or incarceration, white race, and age less than 40 years.[24-28]

Issues With Post-Surgical Opioid Prescribing

Opioids are commonly used for the management of pain after surgery. Surgeons prescribe approximately 10% of all opioids in the United States.[29] In Ontario, surgeons were responsible for 6.0% (492,729) of the 8,277,790 opioid prescriptions filled in 2016.[30] Although post-surgical prescribing accounts for a small proportion of the total amount of opioids prescribed, the perioperative period is often a patient's first exposure to opioids and may be the first step in a series of events that eventually end in opioid-related harm. Indeed, in 2016, 56.0% of opioid prescribed by surgeons in Ontario were prescribed to previously opioid-naïve individuals.[30] In light of the ongoing opioid crisis, various initiatives within the surgical community have set out to re-examine the appropriateness of its post-operative opioid prescribing practices, and the results are alarming: existing post-operative opioid prescribing practices are poor.

First, the prescription of opioids at discharge after surgery has been found to be variable. For instance, in a descriptive study by Hill *et al.* examining opioid prescribing practices after outpatient general surgical procedures in an academic medical center in the United States, significant variations were found for the amount of opioids prescribed for opioid-naïve patients after specific operations.[31] For example, after a partial mastectomy with sentinel lymph node biopsy, the amount of opioids prescribed ranged anywhere from 0 to 60 pills, and this variability was even more pronounced for other common procedures such as laparoscopic

cholecystectomy (0 to 100 pills) and open inguinal hernia repair (15 to 120 pills). The authors found that, for any particular operation, the median number of pills prescribed by different providers varied widely, and that even individual providers prescribed a different number of pills to different patients undergoing the same surgery. The authors suggested that this variability could be explained by the differences in the "standard" number of pill surgeons prescribe after any particular operation as well as the perception that some patients may have characteristics that may predispose them to different opioid requirement than others. In the recent literature, other studies have also reported significant variability in post-operative opioid prescribing across different surgical specialties.[32-39]

Second, opioids are frequently over-prescribed at discharge after surgery. Recent systematic reviews have demonstrated that up to 92% of patients report unused opioids after surgery, and only up to 59.1% of prescribed opioids are actually consumed.[40,41] In the above study by Hill *et al.*, the authors also surveyed opioid-naïve patients undergoing outpatient general surgery procedures to examine the relationship between the amount of opioid consumed and the amount prescribed.[31] They found that in total, less than 30% of prescribed pills were taken, ranging from 14.7% after a partial mastectomy to 32.7% after a laparoscopic cholecystectomy. Importantly, 75% of patients did not require any opioids after a partial mastectomy, but only 25% of them were not prescribed any opioids. The proportion of patients who did not require any opioids was also substantial after other procedures despite the fact that an opioid prescription was provided to most: 33% after a partial mastectomy with sentinel lymph node biopsy, 34% after a laparoscopic cholecystectomy, 45% after a laparoscopic inguinal hernia repair and 22% after an open inguinal hernia repair. Several other studies have also found that opioids are frequently over-prescribed after surgery.[36,39,42]

The significant variation found in post-surgical opioid prescribing as well as the tendency to prescribe more opioids than what is often medically necessary indicate that existing

opioid prescribing practices are mostly not evidenced-based. That a number of studies demonstrating the small proportion of opioids consumed relative to the amount of prescribed[32-39,42,43] suggests that surgeons are in general unaware of how much opioids their patients actually need after specific procedures and therefore tend to prescribe an exceedingly large quantity in order to satisfy all potential needs. Moreover, a proportion of patients may not require any opioid for the control of their post-operative pain after specific procedures, but despite this, surgeons prescribe opioids to all their patients after a particular procedure.

In the light of the ongoing epidemic of opioid-related harms, there is increasing recognition that the over-prescription of opioids after surgery may be associated with negative patient outcomes. In a recent retrospective cohort study examining the association between post-surgical opioid prescription and the development of misuse and overdose among opioid-naïve patients, Brat *et al.* showed that the post-operative duration of opioid use was a strong predictor of developing opioid misuse: each additional week of opioid use was associated with a 19.9% increase (95% confidence intervals 18.5% to 21.4%) in the hazard of developing opioid dependence, abuse or overdose.[44] The over-prescription of opioids at discharge after surgery can create a surplus of these medications in the household. A recent systematic review demonstrated that less than 9% of patients with unused opioids after surgery appropriately dispose of their excess medications according to government-recommended methods.[40] After surgery, most excess medications are saved at home,[39] however up to 77% of patients do not store their opioids in locked containers.[40] These numbers are concerning, given that the storage of opioids in unlocked locations may increase accidental overdoses, especially by children. In the United States, the accidental ingestion of prescription opioids was responsible for more than 5,000 visits to the emergency room in 2011.[45] Unused opioids also create opportunities for the inappropriate sharing of these medications with family members and friends and diversions, as over 60% of individuals who use pain relievers nonmedically received it from a

family member or friend.[46] In a recent survey of 647 high school seniors who reported nonmedical use of prescription opioids in the past year, 55.0% of them received their drug for free from a friend or a relative, 37.9% received it in exchange for money from these individuals and 22.2% took it from them without asking.[47]

Chronic Post-Surgical Opioid Use

There is growing recognition that some patients prescribed opioids for the first time after surgery will continue to use them long term after their procedure. Although reports have suggested that this number may be up to 10% (Table 1.1), the current body of literature varies significantly in how "chronic" post-operative opioid use is defined, and this ranges from >90 days to >1 year after surgery.[48-53] Nonetheless, given that long-term use of opioids may lead to the development of an opioid use disorder,[20,27,49,54,55] which in turn can predispose to opioid-related harms in the setting of the current crisis, preventing the development of chronic post-surgical opioid use is important. Several risk factors for chronic post-surgical opioid use have been identified that include younger age, lower household income, pre-operative use of benzodiazepines or antidepressants, substance use disorders, mood disorders and pain disorders,[48-53] but the mechanisms by which opioid naïve patients develop a chronic use of opioids after surgery are currently not well understood and likely multifactorial.[48] Efforts to prevent the development of chronic post-surgical opioid use likely need to start in the immediate post-operative period with the appropriate identification of patients at high risk of this complication. However, as the awareness of this problem is recent in the literature, few validated strategies exist to appropriately predict patients at high risk of opioid-related harm from chronic post-operative opioid use. In a recent systematic review, Klimas *et al* identified five screening tools from high-quality studies that were designed to evaluate the risk of developing an opioid use disorder when initiating opioids for pain.[56] However, using a

definition of clinical usefulness as a positive likelihood ratio greater than 2.5 or a negative likelihood ratio of equal or less than 0.5, the authors did not identify any useful tool in differentiating between high and low risk patients.

Table 1. 1 Major Studies Describing The Incidence of Chronic Post-Surgical Opioid Use Among Opioid-Naïve Patients

Study	Country	Data Source	Study Period	Population	Surgical Procedure	Exclusion criteria	Chronic Use Definition	Incidence (95 % CI)
Alam *et al.*(2012)[52]	Canada	Health administrative	April 1997 – December 2008	391,139 patients ≥ 66 years old	Low-risk surgery (cataract, laparoscopic cholecystectomy, transurethral resection of the prostate, varicose vein stripping)	Prescribed analgesic in the year before, died within 425 days after, admitted for > 3 days, hospitalized within 100 days prior, emergency surgery, using palliative care, cancer diagnosis	Prescription within 60 days of the 1 year anniversary of the surgery	7.7% (NA)
Clarke *et al.*(2014)[53] Soneji *et al.*(2016)[57]	Canada	Health administrative	April 2003 – March 2010	39,140 patients ≥66 years old	Major elective surgery (coronary artery bypass graft surgery, open lung resection surgery, lung resection using video assisted thorascopic surgery, open colon resection surgery, minimally invasive colon resection surgery, open radical prostatectomy, minimally invasive radical prostatectomy, open hysterectomy, and minimally invasive hysterectomy)	Pre-existing pain disorders before surgery (prescribed analgesics within one year prior to surgery), using doctor services for palliative care, did not survive to 90 days before analyzed period[1]	1) Opioid prescription within 1 to 90 days after surgery and within 90 to 180 days after surgery 2) Ongoing therapy 1 year after surgery	1) 3.1% (NA) 2) 0.4% (0.3, 0.5)
Sun *et al.*(2016)[51]	United States	Health insurance claims	January 2001 – December 2013	641,941 patients between 18-64 years old	Total knee replacement, total hip replacement, laparoscopic cholecystectomy, open cholecystectomy, laparoscopic appendectomy, open appendectomy, caesarian delivery, functional endoscopic sinus surgery, cataract surgery, transurethral resection of the prostate, simple mastectomy	Not continuously enrolled with insurer for at least 3 calendar years, underwent ≥ 2 procedures, filled opioid prescription 12 months prior to surgery	≥ 10 prescriptions or > 120 days' supply of opioid within the first year after surgery, excluding the first 90 days	From 0.12% for caesarean delivery (0.10, 0.13) to 1.41% for total knee replacement (1.29, 1.53)

Bateman *et al.*(2016)[58]	United States	Health insurance claims	2003-2011	80,127 patients between 12-55 years old who filled an opioid prescription within 6 days of discharge	Caesarean delivery	Not continuously enrolled with insurer, filled opioid prescription prior to delivery, diagnoses indicating opioid abuse or dependence	Prescription up to 1 year after surgery	0.36% (0.32, 0.40)
Brummett *et al.* (2017)[48]	United States	Health insurance claims	January 2012 – June 2015	36,177 patients between 18-64 years old who filled at least 1 opioid prescription in the perioperative period	Major surgery (ventral incision hernia repair, colectomy, reflex surgery, bariatric surgery, hysterectomy) Minor surgery (varicose vein removal, laparoscopic cholecystectomy, laparoscopic appendectomy, hemorrhoidectomy, thyroidectomy, transurethral resection of the prostate, parathyroidectomy, carpal tunnel release)	No complete medical and prescription drug coverage, filled opioid prescription 12 months to 31 days prior to surgery, underwent subsequent surgical procedures within 6 months, inpatient stay > than 30 days	Prescription between 90 and 180 days after surgery	Major surgery: 6.5% (NA) Minor surgery: 5.9% (NA)
Lee *et al.(*2017)[49]	United States	Health insurance claims	January 2010 – June 2014	68,463 patients ≥ 18 years old who filled an opioid prescription attributed to surgery for cancer	Curative-intent surgery (lumpectomy, mastectomy, wide local excision, colectomy, rectal resection, pancreatectomy, liver resection, gastric resection, esophagectomy, and lung resection)	Not continuously enrolled with insurer, admission > 30 days, subsequent procedure within 180 days, discharged to hospice care, died during admission, filled opioid prescription 12 months to 31 days prior to surgery	Prescription filled 90-180 days after surgery	10.4% (10.1, 10.7)

Abbreviations: CI, confidence intervals; NA, not available
1. Only for analysis at 1 year after surgery

The Need for Guidance

The current epidemic of opioid-related mortality has shed light on suboptimal practices regarding the use of opioids for the treatment of acute pain in the post-surgical setting. Specifically, variable and excessive prescribing of opioids at patient discharge after surgery has been described in numerous studies,[31-39] and the development of chronic opioid use after surgery among opioid-naïve patients is increasingly recognized. In this sense, it is timely that the surgical community re-examines its practices. However, the lack of relevant guidelines is commonly cited as a factor responsible for the suboptimal prescription of opioids at discharge after surgery.[29,31,35,42] Recently, published guidelines by the American Society of Anesthesiologists and the American Pain Society provide general recommendations on the use of opioids in managing pain in the inpatient post-operative period, but they failed to explicitly address how clinicians should prescribe opioids at discharge.[59,60] Guidelines from the Centers for Diseases Control and Prevention recommended that, for the treatment of acute pain, the lowest effective dose of immediate-release opioids should be prescribed for three days or less, and only rarely for more than seven days.[16] However, this recommendation focuses on acute pain and may not be directly relevant to prescribing in the post-surgical setting.

Given the paucity of relevant guidelines, many institutions have developed recommendations for the prescription of opioids at discharge after specific surgical procedures that are mostly based on expert opinion and data from surveys of patient consumption of opioids.[31,61-63] For example, the Michigan Opioid Prescribing Engagement Network (OPEN) developed opioid prescribing recommendations at discharge after common surgical procedures based on patient-reported data of opioid consumption, and they derived their recommendations based on the amount required in order to satisfy the use of at least 75% of patients.[63] Similarly, investigators at the Dartmouth Hitchcock Medical Center developed institutional prescribing recommendations after outpatient general surgery procedures based on the number of pills

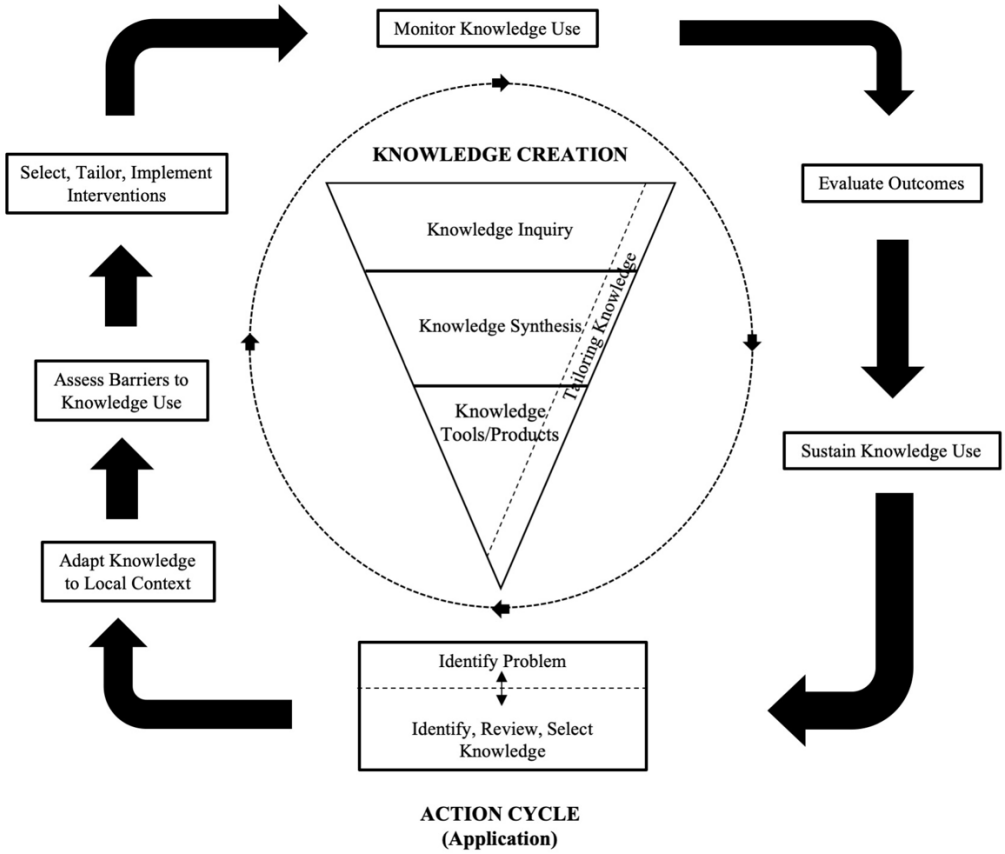
required to satisfy the opioid needs of 80% of patients undergoing each operation.[31,64] Importantly, many studies analyzing the effect of such initiatives on prescriber behavior have demonstrated that the development of these recommendations can successfully decrease the amount of opioid prescribed. For instance, after the dissemination of their prescribing recommendations within their institution through provider education sessions, investigators at the Dartmouth Hitchcock Medical Center observed a total decrease in the number of pills prescribed at discharge after outpatient general surgery procedures by more than 50%.[65] Similarly, other institutional initiatives that involved the developed of local post-surgical prescription recommendations have also observed dramatic decreases in the amount of opioid prescribed,[38,65,66] which indicates that surgeons are receptive to guidance as to how to improve their opioid prescribing practice and are willingly to change their behavior in the setting of the current opioid epidemic.

The Knowledge-to-Action Process

Clearly, current practices for the prescription of opioids at discharge after surgery are suboptimal, and there is an urgent need to improve practice. In 2006, Graham *et al.* developed the knowledge-to-action (KTA) process (Figure 1), a now widely popularized conceptual framework of thinking about moving medical knowledge into action in an effort to improve health care.[67] The KTA process consists of two parts: 1) the creation of knowledge and 2) the action cycle. Regarding the creation of knowledge, it is often depicted graphically as a funnel to represent the distilling process of a large body of information into a concise and usable format for key stakeholders. In the KTA process, knowledge is divided into three generations: the first generation represents the total body of primary studies that is available on a given topic, the second generation represents the results of the aggregation of knowledge (i.e. knowledge synthesis) and the third generation consists of products or tools that builds on knowledge from

the previous generations in order to provide recommendations to influence the behavior of key stakeholders in health care. Importantly, for each generation, knowledge producers can tailor their product in order to meet the specific needs of different types of knowledge users.

Figure 1. 1 The Knowledge-To-Action Process



Adapted from Graham ID, Logan J, Harrison MB, *et al.* Lost in knowledge translation: time for a map? J Contin Educ Health Prof. 2006;26(1):13-24.

After knowledge is created, it is moved on to the action cycle, which depicts a series of phases in order to apply the knowledge with the aim of improving health outcomes. Importantly, each phase can be influenced by feedback from other phases. The action cycle consists in the following phases:

1. Identification of a problem that needs addressing
2. Identification of the knowledge that is relevant to the problem

3. Adapt the knowledge to local context
4. Assess barriers to knowledge use
5. Create and implement interventions that promote the use of knowledge
6. Monitor the use of knowledge
7. Evaluate outcomes from the use of knowledge
8. Sustain ongoing knowledge use.

Clinical Practice Guidelines

In the era of modern medicine, clinical practice guidelines (CPGs) have evolved to provide guidance in clinical decision-making as the body of medical knowledge rapidly increased. In a 2011 publication, the Institute of Medicine (IOM) defined CPGs as "statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options."[68] Specifically, the IOM outlined that, in order to be trustworthy, CPGs should 1) be based on a systematic review of the existing evidence, 2) be developed by a group of experts that represents key affected groups, 3) consider important patient preferences, 4) be transparent and explicit in developing recommendations, 5) clearly explain the relationship between alternative care options and health outcomes and rate both the quality of the evidence and the strength of the recommendations, and 6) be revised when important new evidence emerges that warrants alterations to the document. In the light of these considerations, the IOM has developed a set of standards for the development of trustworthy CPGs (Table 1.2).

Table 1. 2 Institute of Medicine Standards for Developing Trustworthy Clinical Practice Guidelines

Topic	Standard
1. Establishing Transparency	1.1 The processes by which a clinical practice guideline (CPG) is developed and funded should be detailed explicitly and publicly accessible.
2. Management of Conflict of Interest (COI)	2.1 Prior to selection of the guideline development group (GDG), individuals being considered for membership should declare all interests and activities potentially resulting in COI with development group activity, by written disclosure to those convening the GDG. • Disclosure should reflect all current and planned commercial (including services from which a clinician derives a substantial proportion of income), non-commercial, intellectual, institutional, and patient–public activities pertinent to the potential scope of the CPG. 2.2 Disclosure of COIs within GDG • All COI of each GDG member should be reported and discussed by the prospective development group prior to the onset of his or her work. • Each panel member should explain how his or her COI could influence the CPG development process or specific recommendations. 2.3 Divestment • Members of the GDG should divest themselves of financial investments they or their family members have in, and not participate in marketing activities or advisory boards of, entities whose interests could be affected by CPG recommendations. 2.4 Exclusions • Whenever possible GDG members should not have COI. • In some circumstances, a GDG may not be able to perform its work without members who have COIs, such as relevant clinical specialists who receive a substantial portion of their incomes from services pertinent to the CPG. • Members with COIs should represent not more than a minority of the GDG. • The chair or cochairs should not be a person(s) with COI. • Funders should have no role in CPG development.
3. Guideline Development Group Composition	3.1 The GDG should be multidisciplinary and balanced, comprising a variety of methodological experts and clinicians, and populations expected to be affected by the CPG. 3.2 Patient and public involvement should be facilitated by including (at least at the time of clinical question formulation and draft CPG review) a current or former patient, and a patient advocate or patient/consumer organization representative in the GDG. 3.3 Strategies to increase effective participation of patient and consumer representatives, including training in appraisal of evidence, should be adopted by GDGs.
4. Clinical Practice Guideline-Systematic Review Intersection	4.1 Clinical practice guideline developers should use systematic reviews that meet standards set by the Institute of Medicine's Committee on Standards for Systematic Reviews of Comparative Effectiveness Research. 4.2 When systematic reviews are conducted specifically to inform particular guidelines, the GDG and systematic review team should interact regarding the scope, approach, and output of both processes.
5. Establishing Evidence Foundations for and Rating Strength of Recommendations	5.1 For each recommendation, the following should be provided: • An explanation of the reasoning underlying the recommendation, including o a clear description of potential benefits and harms; o a summary of relevant available evidence (and evidentiary gaps), description of the quality (including applicability),

	quantity (including completeness), and consistency of the aggregate available evidence; ○ an explanation of the part played by values, opinion, theory, and clinical experience in deriving the recommendation. • A rating of the level of confidence in (certainty regarding) the evidence underpinning the recommendation • A rating of the strength of the recommendation in light of the preceding bullets • A description and explanation of any differences of opinion regarding the recommendation
6. Articulation of Recommendations	6.1 Recommendations should be articulated in a standardized form detailing precisely what the recommended action is, and under what circumstances it should be performed. 6.2 Strong recommendations should be worded so that compliance with the recommendation(s) can be evaluated.
7. External Review	7.1 External reviewers should comprise a full spectrum of relevant stakeholders, including scientific and clinical experts, organizations (e.g., health care, specialty societies), agencies (e.g., federal government), patients, and representatives of the public. 7.2 The authorship of external reviews submitted by individuals and/or organizations should be kept confidential unless that protection has been waived by the reviewer(s). 7.3 The GDG should consider all external reviewer comments and keep a written record of the rationale for modifying or not modifying a CPG in response to reviewers' comments. 7.4 A draft of the CPG at the external review stage or immediately following it (i.e., prior to the final draft) should be made available to the general public for comment. Reasonable notice of impending publication should be provided to interested public stakeholders.
8. Updating	8.1 The CPG publication date, date of pertinent systematic evidence review, and proposed date for future CPG review should be documented in the CPG. 8.2 Literature should be monitored regularly following CPG publication to identify the emergence of new, potentially relevant evidence and to evaluate the continued validity of the CPG. 8.3 CPGs should be updated when new evidence suggests the need for modification of clinically important recommendations. For example, a CPG should be updated if new evidence shows that a recommended intervention causes previously unknown substantial harm; that a new intervention is significantly superior to a previously recommended intervention from an efficacy or harms perspective; or that a recommendation can be applied to new populations.

Adapted from IOM (Institute of Medicine). 2011. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press.

CPGs are often considered one of the most important tools in improving health care and can affect clinical decision-making.[69] Indeed, when rigorously developed, CPGs represent the combination of the best available research on a given topic and a careful consideration of multiple other factors such as patient preferences and resources by a multidisciplinary group of experts on the topic. In the KTA process, CPGs are usually included as a prime example of a third generation knowledge product that contains clear, concise and usable recommendations

in an accessible format designed to influence the behaviors of key stakeholders.[67] CPGs can then be disseminated and implemented in the action cycle of the framework, where through a series of steps, the knowledge is ultimately applied to improve health outcomes.

Surgeons are in need of guidance as to what constitutes best practices around post-operative opioid prescribing and how to change their behavior. Importantly, appropriate guidance on this topic needs to balance the appropriate controlling post-operative pain while avoiding the harms associated with excessive opioid prescribing. As I have previously described, the lack of useful CPGs on the topic of post-surgical opioid prescribing at discharge has been cited as contributing to suboptimal current practices.[29,31,35,42] The current state of guidance on this topic mostly consists of recommendations developed by consensus or opinion leaders within a specific institution, and, although they have been shown to be effective in changing provider behavior within the institution, they may be limited in their applicability outside of their institution of origin. This may perpetuate or even worsen the existing variability in post-surgical opioid prescribing across North American healthcare institutions. More importantly, many of these institutional initiatives were not based on a systematic review of the literature and may have been mostly driven by strong opinions within the institution, undermining the validity of their recommendations.

After identifying a need for guidance, one of the initial decisions in the development of guidance is whether a suitable CPG is available for use or adaptation. Given the resources required in a de novo development of a CPG and the extensive amount of work need, the Canadian Medical Association recommends the adaptation of an existing document when feasible.[69] To facilitate guideline adaptation, the ADAPTE collaboration has recently developed a framework that organizes the entire process into a series of steps organized into three phases (set-up, adaptation, and final).[70] In the initial set-up phase, investigators seeking to adapt existing guidelines must follow a series of preparatory steps that address the feasibility,

organization, chosen topic, required resources and planning of the project. Then, in the adaptation phase, health questions are defined, guidelines are identified, screened, assessed and selected, and a draft guideline report is produced. The final phase then consists in the external review, plan for update and production of the resulting guidance document.

The Role of Systematic Reviews

Conducting a systematic review is one of the cornerstone steps in the development of a trustworthy guidance document.[71] A systematic review is a type of knowledge synthesis that attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question using explicit, systematic methods that are selected with a view of minimizing bias.[72] Key characteristics of a systematic review include 1) a clearly stated set of objectives with pre-defined eligibility criteria for studies, 2) an explicit, reproducible methodology, 3) a systematic search that attempts to identify all studies that would meet the eligibility criteria, 4) an assessment of the validity of the findings of the included studies, and 5) a systematic presentation and synthesis of the characteristics and findings of the included studies. Systematic reviews may contain meta-analyses, the use of statistical methods to pool the results of independent studies.[73] Given the rapidly growing body of medical literature, systematic reviews have become increasingly important as they represent an effective method to summarize research, distinguish between high and low quality studies, and identify gaps in knowledge.[74] In the current era of evidence-informed health care, systematic reviews allow the judicious use of the available best evidence to inform decision-making at the bedside. Traditional narrative reviews are often written by experts in the field, however this has been shown to lead to products of inferior quality due to prior opinions about the topic and bias towards their own work.[75] Additionally, traditional literature reviews can be limited by issues such as inadequate searches of the literature, selection citation of studies, poor description of

methods and difficulty in differentiating high from low quality research. Systematic reviews, on the other hand, can address these issues using transparent and explicit pre-specified methods to search the literature, select studies and appraise the quality of included research. Given the growing popularity of systematic reviews, the Cochrane Handbook for Systematic Review of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were developed to provide a standard of conducting and reporting these studies.[72,74] In these guidelines, 27 items were developed as part of a checklist that addresses various sections of the study (Table 1.3), and a diagram depicting the flow of information in a systematic review was introduced.[76]

Table 1. 3 PRISMA Checklist of Items to Include When Reporting a Systematic Review or Meta-Analysis

Item #	Section	Description
1	Title	Identify the report as a systematic review, meta-analysis, or both.
2	Structured summary	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.
3	Rationale	Describe the rationale for the review in the context of what is already known.
4	Objectives	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).
5	Protocol and registration	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.
6	Eligibility criteria	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.
7	Information sources	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.
8	Search	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.
9	Study selection	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).
10	Data collection process	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.
11	Data items	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.

12	Risk of bias in individual studies	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.
13	Summary measures	State the principal summary measures (e.g., risk ratio, difference in means).
14	Synthesis of results	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.
15	Risk of bias across studies	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).
16	Additional analyses	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.
17	Study selection	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.
18	Study characteristics	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.
19	Risk of bias within studies	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).
20	Results of individual studies	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.
21	Synthesis of results	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency
22	Risk of bias across studies	Present results of any assessment of risk of bias across studies (see Item 15).
23	Additional analysis	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).
24	Summary of evidence	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).
25	Limitations	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).
26	Conclusions	Provide a general interpretation of the results in the context of other evidence, and implications for future research.
27	Funding	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.

Adapted from Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339:b2535.

Systematic reviews have an important role in the creation of knowledge in the KTA process. Given that they use explicit and reproducible methods to identify, extract, appraise and synthesize research that is relevant to a particular research question, they are frequently employed as a method to distill first generation knowledge into a second-generation product. Furthermore, they form one of the cornerstones in the development of CPGs,[71] which is

represented in the KTA process as the creation of a third-generation knowledge product from a second-generation synthesis of knowledge. Indeed, as CPGs are supposed to be developed in a transparent and rigorous manner, the methodological rigors associated with the conduct of a systematic review are instrumental to create an evidence basis upon which to formulate recommendations that will ultimately guide clinical practice.

Rationale for Current Work

In the context of the prescription of opioids at discharge after surgery, systematic reviews represent a useful initial exercise in improving the quality of care provided. First, as the adaptation of an existing guideline and its recommendations is one of the first considerations in developing guidance for surgeons, the appropriate identification of existing recommendations is of utmost importance. Although a systematic review of guidelines and recommendations has not been mandatory in the guideline adaptation process,[69,70] conducting such a study would provide a rigorous assessment of the body of guidance on the prescription of opioids at discharge after surgery and significantly contribute to the foundational steps in the development of a guidance document.[77] Furthermore, as recommendations within a guideline are typically created based on the best available evidence on a given topic, the identification of guidance documents will provide a source of references that may form the basis of a future guideline development initiative. As surgical procedures performed in the abdomen and pelvis are common, I will perform a systematic review of recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery. This review of recommendations will form the second chapter of this thesis.

Second, as demonstrated in the KTA process, the development of second-generation knowledge through a systematic review has intrinsic value and can be useful in improving quality of health care through the action cycle. Given the acute awareness of poor post-surgical

opioid prescribing raised by the epidemic of opioid overdoses, a systematic review of behavioral interventions designed to improve the prescription of opioids at discharge after surgery would likely serve as a useful point of reference for health care organizations to design future strategies to improve their own opioid prescription practices after surgery. This review of interventions will form the third chapter of this thesis.

Third, building on the body of evidence gathered through my two systematic reviews, I will conduct the preliminary work for the development of a guidance document for the prescription of opioids at discharge after abdominal-pelvic surgery that will contribute to improving opioid prescribing practices at discharge after abdominal-pelvic surgery in Canada. This will include the creation of a guideline panel, the dissemination of the knowledge gathered through my systematic reviews with this panel, and the determination of the scope of the guidance document. This preliminary work will form the fourth chapter of this thesis.

Objectives

1. To systematically review existing recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery
2. To systematically review behavioral interventions to reduce the prescription of opioids at discharge after abdominal-pelvic surgery
3. To initiate the development of a guidance document for the prescription of opioids at discharge after abdominal-pelvic surgery.

Chapter 2

Recommendations for the Prescription of Opioids at Discharge Following Abdominal-Pelvic Surgery: A Systematic Review

This chapter has been accepted for publication by JAMA Surgery.

OVERVIEW

Importance: The prescription of opioids at hospital discharge after abdominal-pelvic surgery is variable and often excessive. A lack of guidance for abdominal-pelvic surgeons may contribute to the suboptimal nature of current prescribing practices.

Objective: To systematically review recommendations on the: 1) prescription of opioids at discharge, 2) appropriate disposal of opioids and 3) prevention of chronic opioid use after abdominal-pelvic surgery.

Evidence Review: I searched MEDLINE, PsycINFO, Healthstar, EMBASE as well as the difficult to locate and unpublished (i.e.grey) literature until December 2018 to identify English-language documents that contained recommendations published by professional societies or healthcare institutions. The quality of clinical practice guidelines (CPGs) was appraised using the Appraisal of Guidelines Research & Evaluation II (AGREE II) tool. A descriptive synthesis of results was performed.

Findings: Of 5,530 citations screened, 41 full-text documents were included. 15 CPGs were identified. AGREE II domain scores varied significantly. I identified 98 recommended interventions for the prescription of opioids at discharge, 8 interventions for the disposal of opioids and 8 interventions for the prevention of chronic post-surgical opioid use. The majority of recommended interventions were not supported by any assessment of evidence, and the amount of prescription opioid recommended varied widely between publications, even for the same procedure.

Conclusion and Relevance: Current guidance for the prescription of opioids at discharge after abdominal-pelvic surgery is heterogenous and seldomly supported by evidence. More research is needed on this topic to guide the development of future recommendations.

INTRODUCTION

The current epidemic of opioid-related mortality has shed light on poor opioid prescribing practices after abdominal surgery. Recent research has demonstrated that significant variations exist in the amount of opioid prescribed at discharge[31,33,35] and that opioid prescriptions are often in excess of actual patient requirements.[31,35,39,78] This is particularly concerning given that over 70% of patients store their excess opioids in unlocked locations and do not properly dispose of them.[41] This easily-accessible supply of prescription opioids may lead to unintended harms, such as opioid misuse[46] and accidental overdoses.[79] Moreover, there is growing awareness that a substantial proportion of opioid-naïve patients will become long-term users of opioids after initial exposure in the immediate post-operative period.[48-50,52,53] As chronic opioid use may lead to physiologic dependence and misuse, prevention in the early phases of perioperative care is important. Abdominal surgeons, however, may not be aware of the risk of chronic opioid use and infrequently perform a risk assessment in their patients.[80]

A lack of guidance for surgeons has been cited as a major factor driving the suboptimal nature of current post-surgical opioid prescribing practices.[31,80,81] Recently published guidelines by the American Society of Anesthesiologists and the American Pain Society provide general recommendations on the use of opioids in managing pain in the inpatient post-operative period, but they failed to explicitly address how clinicians should prescribe opioids at discharge.[59,60] Guidelines from the Centers for Diseases Control and Prevention recommended that, for the treatment of acute pain, the lowest effective dose of immediate-release opioids should be prescribed for three days or less, and only rarely for more than seven days.[16] However, this recommendation focuses on acute pain and may not be directly relevant to prescribing in the post-surgical setting.

In this study, I conducted a systematic review of existing guidance on the prescription of opioids at discharge after abdominal-pelvic surgery. Specifically, I aimed to identify existing

recommendations within three areas of focus: 1) the prescription of opioids at discharge, 2) the appropriate disposal of opioids, and 3) the prevention of chronic post-surgical opioid use after abdominal-pelvic surgery.

METHODS

Review Design

The protocol for this systematic review was designed in accordance with the PRISMA-P guidelines[82] and prospectively registered with PROSPERO (CRD42018093505).[83] The PRISMA statement was followed for the reporting of results (Appendix 2.1).[74]

Eligibility Criteria

I identified all documents published by health care institutions or professional societies that provided recommendations relevant to opioid-naïve adults (≥ 18 years old) undergoing abdominal-pelvic surgery via laparoscopy or laparotomy. Publications with a specific focus on abdominal-pelvic procedures were identified, as well as those that focused on the general post-operative setting or acute pain. Publications were included if they contained recommendations addressing 1) prescription of opioids at discharge, 2) appropriate disposal of excess opioids or 3) prevention of chronic post-surgical opioid use. In order to identify contemporary recommendations relevant to clinical practice in North America, I included documents that were written in English only and published after January 1st 2010. I excluded those that focused on surgical procedures not involving the abdomen or the pelvis or only providing recommendations addressing the prescription of opioids in the inpatient phase of post-operative care.

Data Sources and Search Strategy

I designed a search strategy in MEDLINE, PsycINFO, Healthstar and EMBASE with the assistance of an information specialist using variations of the search terms "opioid" and "surgery" in conjunction with the Canadian Agency for Drugs and Technologies in Health guideline filter (Table 2.1).[84] The search strategy was peer-reviewed by a second information specialist at a separate institution. The initial search was run on March 27th 2018 and subsequently updated on December 13th 2018.

Table 2. 1 Literature Search Strategies

Database	Strategy
MEDLINE	1 exp Narcotics/
	2 exp Opiate Alkaloids/
	3 Pain Management/
	4 Pain/dt [Drug Therapy]
	5 opioid*.mp.
	6 opiate*.mp.
	7 opium*.mp.
	8 narcotic*.mp.
	9 alfentanil.mp.
	10 buprenorphine.mp.
	11 butorphanol.mp.
	12 codeine.mp.
	13 dextropropoxyphene.mp.
	14 fentan?l.mp.
	15 hydrocodone.mp.
	16 hydromorphone.mp.
	17 levorphanol.mp.
	18 meperidine.mp.
	19 methadone.mp.
	20 morphine.mp.
	21 nalbuphine.mp.
	22 normethadone.mp.
	23 oxycodone.mp.
	24 pentazocine.mp.
	25 pethidine.mp.
	26 propoxyphene.mp.
	27 remifentanil.mp.
	28 sufentanil.mp.
	29 tapentadol.mp.
	30 tramadol.mp.
	31 (pain* adj4 (manage* or control*)).tw,kf.
	32 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
	33 Perioperative Care/
	34 Postoperative Care/
	35 Perioperative Period/
	36 exp Postoperative Period/
	37 Pain, Postoperative/

	38 exp Surgical Procedures, Operative/ 39 exp Specialties, Surgical/ 40 Surgeons/ 41 su.fs. 42 (surgery or surgeries or surgical*).tw,kf. 43 postsurg*.tw,kf. 44 operat*.tw,kf. 45 (postop* or post-op).tw,kf. 46 lapar*.tw,kf. 47 postlapar*.tw,kf. 48 resect*.tw,kf. 49 postresect*.tw,kf. 50 perioperative*.tw,kf. 51 peroperative*.tw,kf. 52 ((drug* or medication*) adj4 (discard* or dispos*)).tw,kf. 53 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 54 exp clinical pathway/ 55 exp clinical protocol/ 56 exp consensus/ 57 exp consensus development conference/ 58 exp consensus development conferences as topic/ 59 critical pathways/ 60 exp guideline/ 61 guidelines as topic/ 62 exp practice guideline/ 63 practice guidelines as topic/ 64 health planning guidelines/ 65 (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt. 66 (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf,kw. 67 (standards or guideline or guidelines).ti,kf,kw. 68 ((practice or treatment* or clinical) adj guideline*).ab. 69 (CPG or CPGs).ti. 70 consensus*.ti,kf,kw. 71 consensus*.ab. /freq=2 72 ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf,kw. 73 recommendat*.ti,kf,kw. 74 (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf,kw. 75 (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kf,kw. 76 (algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab,kf,kw. 77 or/54-76 78 32 and 53 and 77 79 limit 78 to yr="2010 -Current"
EMBASE	1 exp narcotic analgesic agent/ 2 pain/dt [Drug Therapy] 3 opioid*.mp. 4 opiate*.mp. 5 opium*.mp. 6 narcotic*.mp. 7 alfentanil.mp. 8 buprenorphine.mp. 9 butorphanol.mp. 10 codeine.mp. 11 dextropropoxyphene.mp.

12 fentan?l.mp.
13 hydrocodone.mp.
14 hydromorphone.mp.
15 levorphanol.mp.
16 meperidine.mp.
17 methadone.mp.
18 morphine.mp.
19 nalbuphine.mp.
20 normethadone.mp.
21 oxycodone.mp.
22 pentazocine.mp.
23 pethidine.mp.
24 propoxyphene.mp.
25 remifentanil.mp.
26 sufentanil.mp.
27 tapentadol.mp.
28 tramadol.mp.
29 (pain* adj4 (manage* or control*)).tw,kw.
30 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31 perioperative period/
32 exp postoperative period/
33 exp surgery/
34 exp surgeon/
35 surgical patient/
36 postoperative pain/
37 (surgery or surgeries or surgical*).tw,kw.
38 postsurg*.tw,kw.
39 operat*.tw,kw.
40 (postop* or post-op).tw,kw.
41 lapar*.tw,kw.
42 postlapar*.tw,kw.
43 resect*.tw,kw.
44 postresect*.tw,kw.
45 perioperative*.tw,kw.
46 peroperative*.tw,kw.
47 ((drug* or medication*) adj4 (discard* or dispos*)).tw,kw.
48 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47
49 exp clinical pathway/
50 exp clinical protocol/
51 exp consensus/
52 exp consensus development conference/
53 exp consensus development conferences as topic/
54 critical pathways/
55 guidelines as topic/
56 exp practice guideline/
57 practice guidelines as topic/
58 health planning guidelines/
59 (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.
60 (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kw.
61 (standards or guideline or guidelines).ti,kw.
62 ((practice or treatment* or clinical) adj guideline*).ab.
63 (CPG or CPGs).ti.
64 consensus*.ti,kw.
65 consensus*.ab. /freq=2
66 ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kw.

	67 recommendat*.ti,kw. 68 (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kw. 69 (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kw. 70 (algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab,kw. 71 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 72 30 and 48 and 71 73 limit 72 to yr="2010 -Current" 74 limit 73 to embase
Healthstar	1 exp Narcotics/ 2 exp Opiate Alkaloids/ 3 Pain Management/ 4 Pain/dt [Drug Therapy] 5 opioid*.mp. 6 opiate*.mp. 7 opium*.mp. 8 narcotic*.mp. 9 alfentanil.mp. 10 buprenorphine.mp. 11 butorphanol.mp. 12 codeine.mp. 13 dextropropoxyphene.mp. 14 fentan?l.mp. 15 hydrocodone.mp. 16 hydromorphone.mp. 17 levorphanol.mp. 18 meperidine.mp. 19 methadone.mp. 20 morphine.mp. 21 nalbuphine.mp. 22 normethadone.mp. 23 oxycodone.mp. 24 pentazocine.mp. 25 pethidine.mp. 26 propoxyphene.mp. 27 remifentanil.mp. 28 sufentanil.mp. 29 tapentadol.mp. 30 tramadol.mp. 31 (pain* adj4 (manage* or control*)).tw,kf. 32 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 33 Perioperative Care/ 34 Postoperative Care/ 35 Perioperative Period/ 36 exp Postoperative Period/ 37 Pain, Postoperative/ 38 exp Surgical Procedures, Operative/ 39 exp Specialties, Surgical/ 40 Surgeons/ 41 su.fs. 42 (surgery or surgeries or surgical*).tw,kf. 43 postsurg*.tw,kf. 44 operat*.tw,kf. 45 (postop* or post-op).tw,kf. 46 lapar*.tw,kf. 47 postlapar*.tw,kf.

	48 resect*.tw,kf. 49 postresect*.tw,kf. 50 perioperative*.tw,kf. 51 peroperative*.tw,kf. 52 ((drug* or medication*) adj4 (discard* or dispos*)).tw,kf. 53 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 54 exp clinical pathway/ 55 exp clinical protocol/ 56 exp consensus/ 57 exp consensus development conference/ 58 exp consensus development conferences as topic/ 59 critical pathways/ 60 exp guideline/ 61 guidelines as topic/ 62 exp practice guideline/ 63 practice guidelines as topic/ 64 health planning guidelines/ 65 (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt. 66 (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf,kw. 67 (standards or guideline or guidelines).ti,kf,kw. 68 ((practice or treatment* or clinical) adj guideline*).ab. 69 (CPG or CPGs).ti. 70 consensus*.ti,kf,kw. 71 consensus*.ab. /freq=2 72 ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,kf,kw. 73 recommendat*.ti,kf,kw. 74 (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf,kw. 75 (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,kf,kw. 76 (algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab,kf,kw. 77 or/54-76 78 32 and 53 and 77 79 limit 78 to yr="2010 -Current"
PsycINFO	1 exp analgesic drugs/ 2 exp narcotic drugs/ 3 pain management/ 4 opioid*.mp. 5 opiate*.mp. 6 opium*.mp. 7 narcotic*.mp. 8 alfentanil.mp. 9 buprenorphine.mp. 10 butorphanol.mp. 11 codeine.mp. 12 dextropropoxyphene.mp. 13 fentan?l.mp. 14 hydrocodone.mp. 15 hydromorphone.mp. 16 levorphanol.mp. 17 meperidine.mp. 18 methadone.mp. 19 morphine.mp. 20 nalbuphine.mp. 21 normethadone.mp.

22 oxycodone.mp.
23 pentazocine.mp.
24 pethidine.mp.
25 propoxyphene.mp.
26 remifentanil.mp.
27 sufentanil.mp.
28 tapentadol.mp.
29 tramadol.mp.
30 (pain* adj4 (manage* or control*)).ti,ab,hw.
31 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32 postsurgical complications/
33 exp SURGERY/
34 surgeons/
35 surgical patients/
36 (surgery or surgeries or surgical*).ti,ab,hw.
37 postsurg*.ti,ab,hw.
38 operat*.ti,ab,hw.
39 (postop* or post-op).ti,ab,hw.
40 lapar*.ti,ab,hw.
41 postlapar*.ti,ab,hw.
42 resect*.ti,ab,hw.
43 postresect*.ti,ab,hw.
44 perioperative*.ti,ab,hw.
45 peroperative*.ti,ab,hw.
46 ((drug* or medication*) adj4 (discard* or dispos*)).ti,ab,hw.
47 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46
48 31 and 47
49 critical pathways/
50 guidelines as topic/
51 practice guidelines as topic/
52 health planning guidelines/
53 exp treatment guidelines/
54 (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.
55 (position statement* or policy statement* or practice parameter* or best practice*).ti,ab,hw.
56 (standards or guideline or guidelines).ti,ab,hw.
57 ((practice or treatment* or clinical) adj guideline*).ab.
58 (CPG or CPGs).ti.
59 consensus*.ti,ab,hw.
60 consensus*.ab. /freq=2
61 ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti,ab,hw.
62 recommendat*.ti,hw.
63 (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,hw.
64 (algorithm* adj2 (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti,ab,hw.
65 (algorithm* adj2 (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti,ab,hw.
66 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65
67 31 and 47 and 66
68 limit 67 to yr="2010 -Current"

As many institution-based recommendations may not be published in the medical literature, I designed an extensive search strategy of the grey literature in consultation with an experienced information specialist (Table 2.2).[72,77] Specifically, I used variations of the search terms "guideline", "opioid", "prescription" and "surgery" to search 1) webpages of major societies in abdominal-pelvic surgery, anesthesia, pain management, 2) theses, 3) grey literature databases (National Guideline Clearinghouse, Canadian Medical Association Clinical Practice Guidelines Infobase, Best Practice Advocacy Centre New Zealand, , National Health and Medical Research Council – Australian Clinical Practice Guidelines, National Institution for Health and Care Excellence and the Scottish Intercollegiate Guidelines Network) and 4) the first 10 pages of Google. The grey literature search was initially run in April-May 2018 and subsequently updated in November 2018. Appendix 2.2 provides a list of the websites searched.

Table 2. 2 Grey Literature Search Strategy

Search Terms	(guideline OR recommendation OR consensus OR position OR best practice OR statement) AND (opioid* OR opiate* OR narcotic*) AND (Prescrib* or Prescription*) AND (postoperat* OR operat* OR surg*)
Sources	1. Webpages of relevant organizations a. Abdominal and pelvic surgical specialties b. Anesthesia c. Pain 2. Theses Canada 3. Grey literature databases a. CMA Infobase - Clinical Practice Guidelines b. Best Practice Advocacy Centre New Zealand – bpacNZ better medicine c. National Guideline Clearinghouse d. National Health and Medical Research Council – Australia's Clinical Practice Guidelines Portal e. National Institute for Health and Care Excellence – NICE Guidelines f. Scottish Intercollegiate Guidelines Network (SIGN) 4. Google (first 10 pages)

Additionally, references of all included publications were manually reviewed to identify any missed document, and I consulted with 7 experts in the field, defined as health care professionals involved in the perioperative pain management of patients undergoing abdominal-pelvic surgery, to identify any potentially missed citation.

Publication Selection and Data Extraction

All citations identified through my search of the medical literature were uploaded to the systematic review software DistillerSR (Evidence Partners, ON, Canada). Publications were screened against my eligibility criteria in two stages: 1) title and abstract and 2) full text. All citations identified from the grey literature search underwent full-text screening. Two reviewers screened all citations independently, and disagreements were resolved by discussion.

For each publication, data were extracted regarding the name of the publishing body, year of publication, type of publication, funding sources, guideline panel disciplines, target surgical procedure, recommendation and associated strength and level of evidence. Data extraction was performed by one review author and verified by a second reviewer for accuracy and completeness. Disagreements between reviewers were resolved by discussion.

Quality Assessment

I assessed the quality of clinical practice guidelines (CPGs) using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) tool,[85] a widely used instrument that evaluates guidelines on 23 key items organized into six domains: scope and purpose, stakeholder involvement, rigour of development, clarity of presentation, applicability, and editorial independence. For each item, four reviewers independently assigned a score on a 7-point scale (1 - Strongly Disagree, 7 – Strongly Agree), and these scores were summed across reviewers for all items included in the domain to generate a scaled domain score. Items where there was a ≥ 3 point discrepancy between reviewers[86] were discussed, and the discrepancy was resolved by consensus.

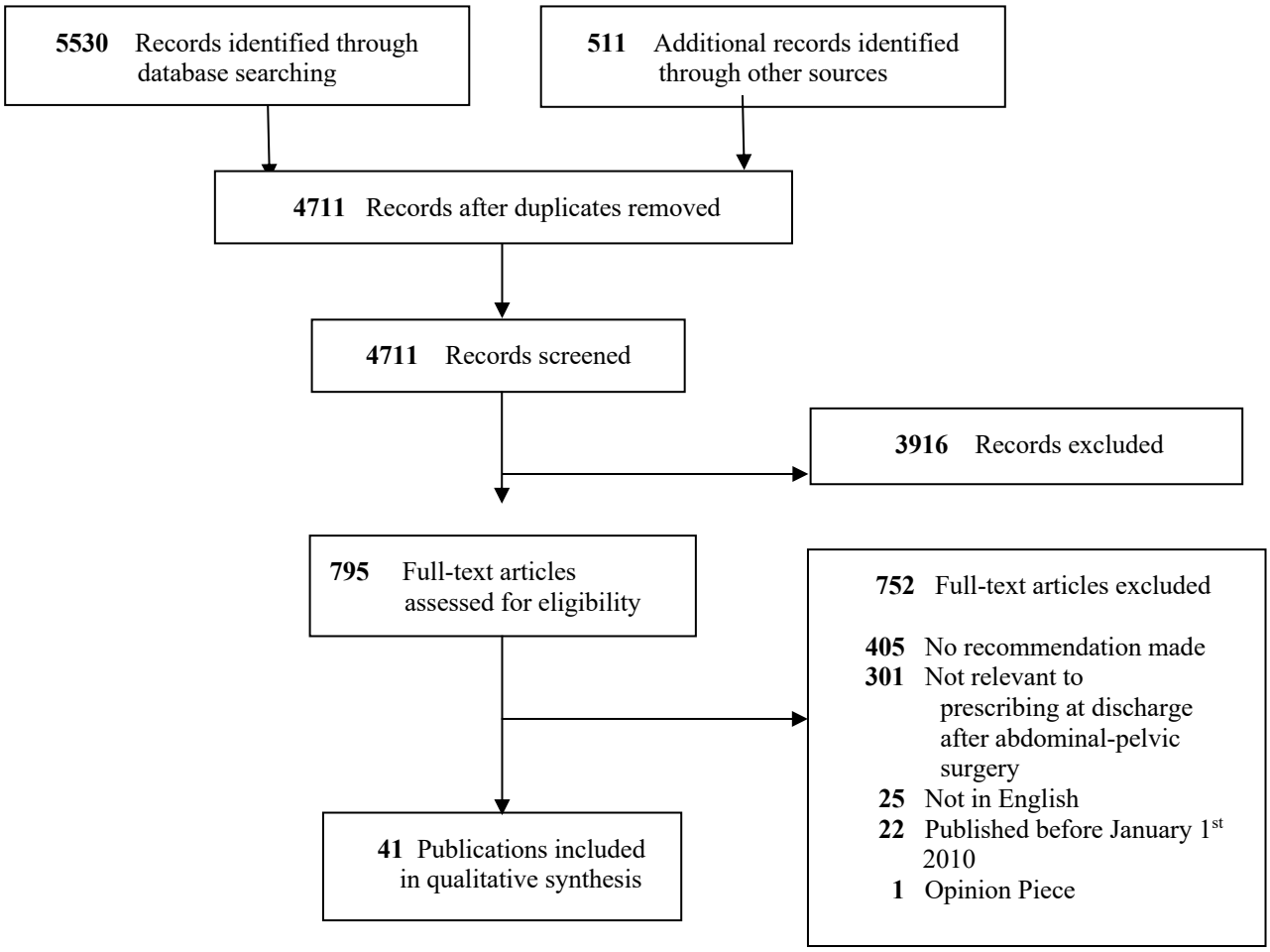
Data Synthesis

I performed a descriptive synthesis of included publications and recommendations. Recommended interventions were summarized according to my three areas of focus: 1) opioid prescribing at discharge, 2) opioid disposal and 3) prevention of chronic opioid use. Due to the heterogeneous natures of recommendations identified for the prescription of opioids at discharge after abdominal-pelvic surgery, they were presented as categories of interventions and divided into general recommendations, recommended co-interventions, and procedure-specific recommendations. To allow for comparison between publications, I converted specific opioid prescription regimens to milligram morphine equivalents (MME) using conversion factors provided the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain.[16] I used the ratio presented in the Interagency Guideline on Prescribing Opioids for Pain to convert tramadol.[87]

RESULTS

I identified 5,530 citations from MEDLINE, PsycINFO, Healthstar, and EMBASE, and 511 citations from the grey literature. After screening, 41 documents were included (Figure 2.1); 18 of which were in the grey literature. No additional documents were identified by manually reviewing references of included publications or through consultation with experts.

Figure 2. 1 PRISMA Flow Chart of Article Selection



Document Characteristics

Characteristics of included documents are presented in Table 2.3. Of the 41 documents, 31 originated from North America, 5 from Europe, 2 from the Middle East, 2 from Australia, 1 from Africa and 1 from Asia. I identified 15 CPGs, 10 original studies, 5 statements, 4 protocols, 3 websites, 2 standards and 2 guides. Information regarding funding was available in only 16 of the 41 documents: 5 were self-funded, 5 were funded by governmental entities, 4 were funded by pharmaceutical companies, 3 were funded by healthcare institutions and 1 received no funding. Seventeen documents provided recommendations that specifically targeted pain management after abdominal-pelvic procedures, 9 addressed pain management in the general post-operative setting and 15 were primarily focused on the management of acute

pain. All but one publication provided recommendations for the prescription of opioids at discharge, whereas only 12 addressed opioid disposal, and 12 addressed the prevention of chronic post-surgical opioid use.

Table 2. 3 Characteristics of Publications Containing Recommendations Relevant to Opioid Prescribing After Abdominal-Pelvic Surgery

Publishing Body (Year)	Country of Origin	Type of Publication	Funding Body	Condition	Recommendations Made		
					Opioid Prescribing At Discharge	Opioid Disposal	Prevention of Chronic Opioid Use
AAGBI (2014)[88]	United Kingdom	Guideline	NA	Postoperative pain	✓		
ABM (2017)[89]	United States	Protocol	NA	Postoperative pain	✓		
ACOEM (2014)[90]	United States	Guideline	NA	Postoperative pain	✓		✓
AMDG-Bree Collaborative (2015)[87,91]	United States	Guideline	State agencies and staff	Abdominal-pelvic surgery	✓	✓	✓
ANZCA (2018)[92]	Australia, New Zealand	Statement	NA	Acute pain	✓		✓
APS-ASRA-ASA (2016)[60]	United States	Guideline	Self-funded	Postoperative pain	✓		
ASA (2012)[59]	United States	Guideline	Self-funded	Postoperative pain	✓		
ASER-POQI (2017)[93]	United States	Statement	Self-funded	Abdominal-pelvic surgery	✓		
AUA (2018)[94]	United States	Statement	NA	Abdominal-pelvic surgery	✓	✓	
Ayad *et al.* (2011)[95]	Egypt, Jordan, Qatar, Saudi Arabia, United Arab Emirates	Guideline	Pfizer	Acute pain	✓		✓
AZDHS (2018)[96]	United States	Guideline	NA	Acute pain	✓	✓	
BWH (2019)[97]	United States	Original study	NA	Abdominal-pelvic surgery	✓		
CDC (2016)[16]	United States	Guideline	Self-funded	Acute pain	✓		
CORE/Overton *et al.* (2018)[62,98]	United States	Original study	NIH, Foundation for Anesthesia Education and Research	Abdominal-pelvic surgery	✓		

CPSBC (2018)[99]	Canada	Standard	NA	Acute pain	✓		
CWC (2018)[100]	Canada	Website	NA	Postoperative pain	✓		
GCOAT (2016)[101]	United States	Guideline	NA	Acute pain	✓	✓	✓
LHSC (2018)[66]	Canada	Original study	NA	Abdominal-pelvic surgery	✓	✓	
DHMC (2017)[31]	United States	Original study	NA	Abdominal-pelvic surgery	✓		
DHMC (2018)[64]	United States	Original study	NA	Abdominal-pelvic surgery	✓		
HQO (2018)[102]	Canada	Standard	NA	Acute pain	✓	✓	
ICSI (2014)[103]	United States	Protocol	Self-funded	Acute pain	✓	✓	✓
ISMP-CPSI (2016)[104]	Canada	Guide	NA	Acute pain	✓	✓	
Mayo Clinic (2018)[61]	United States	Original study	Mayo Clinic	Abdominal-pelvic surgery	✓	✓	
Michigan Medicine (2018)[105]	United States	Original study	NA	Abdominal-pelvic surgery	✓		
Michigan OPEN (2019)[63]	United States	Website	Michigan Department of Health and Human Services, Blue Cross Blue Shield of Michigan Value Partnerships, University of Michigan	Abdominal-pelvic surgery	✓	✓	
NYGH (2018)[43]	Canada	Original study	NA	Abdominal-pelvic surgery	✓		
Pain Working Group (2018)[106]	India	Guideline	Johnson & Johnson	Acute pain	✓		
PSAIT (2018)[107]	Poland	Statement	None	Postoperative pain	✓		
RCoA (2018)[108]	United Kingdom	Website	NA	Acute pain	✓		✓
RPCCC (2018)[109]	United States	Original study	RPCCC, Roswell Park Alliance Foundation, NCI training grant	Abdominal-pelvic surgery	✓		

SA Health (2015)[110]	Australia	Guideline	NA	Acute pain	✓		
Salti *et al.* (2016)[111]	Bahrain, Iraq, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates, Yemen	Guideline	Pfizer	Postoperative pain			✓
SASA (2016)[112]	South Africa	Guideline	MSD Pharmaceuticals	Acute pain	✓		✓
SGO (2017)[113]	United States	Statement	NA	Abdominal-pelvic surgery	✓		✓
SJMHS (2017)[114]	United States	Protocol	NA	Abdominal-pelvic surgery	✓	✓	
SIAARTI (2010)[115]	Italy	Guideline	NA	Postoperative pain	✓		✓
UDOH (2010)[116]	United States	Guideline	Utah State Legislature, Utah Labor Commission, Worker's Compensation Fund of Utah	Acute pain	✓	✓	✓
UPMC (2018)[78]	United States	Original study	NA	Abdominal-pelvic surgery	✓		
University Hospital North Staffordshire NHS Trust (2010)[117]	United Kingdom	Protocol	NA	Abdominal-pelvic surgery	✓		
WCH-ISMP (2017)[118]	Canada	Guide	NA	Acute pain	✓		

Abbreviation: NA: Not Available; ABM, Academy of Breastfeeding Medicine; AMDG, Agency Medical Directors' Group; ACOEM, American College of Occupational and Environmental Medicine; APS, American Pain Society; ASRA, American Society of Regional Anesthesia and Pain Medicine; ASA, American Society of Anesthesiologists; ASER, American Society for Enhanced Recovery; POQI, Perioperative Quality Initiative; AUA, American Urological Association; AZDHS, Arizona Department of Health Services; AAGBI, Association of Anesthetists of Great Britain and Ireland; ANZCA, Australian and New Zealand College of Anaesthetists; BWH, Brigham and Women's Hospital; CDC, Center for Disease Control and Prevention; CORE, Center for Opioid Research and Education; CWC, Choosing Wisely Canada; CPSBC, College of Physicians and Surgeons of British Columbia; DHMC, Dartmouth Hitchcock Medical Center; HQO, Health Quality Ontario; ICSI, Institute for Clinical Systems Improvement; ISMP, Institute for Safe Medication Practices Canada; CPSI, Canadian Patient Safety Institute; Michigan OPEN, Michigan Opioid Prescribing Engagement Network; NYGH, North York General Hospital; GCOAT, Governor's Cabinet Opiate Action Team; PSAIT, Polish Society of Anaesthesiology and Intensive Therapy; SA Health, South Australia Health; SIAARTI, Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva; SGO, Society of Gynecologic Oncology; SJMHS, St. Joseph Mercy Health System; RCoA, Royal College of Anaesthetists; RPCCC, Roswell Park Comprehensive Cancer Centre; NHS, National Health Services; UDOH, Utah Department of Health; UPMC, University of Pittsburgh Medical Center; SASA, South African Society of Anaesthesiologists; WCH, Women's College Hospital

Quality Assessment

An assessment of the quality of the 15 CPGs is presented in Table 2.4. Guidelines scored moderately in domain 4 (clarity of presentation), but highly variably in other domains (scope and purpose, stakeholder involvement, rigor of development, applicability, and editorial independence). For domain 1 (scope and purpose), scores ranged from 22% (SIAARTI) to 93% (CDC). Specifically, SIAARTI did not describe the health questions covered by their guideline and did not clearly define their overall objective and target population. The guideline by SASA was also found to have a low score in this domain (24%) for similar reasons. Regarding the second domain of stakeholder involvement, a wide range of scores was again found: 8% (Salti *et al.*) to 99% (CDC). In their publication, Salti *et al.* did not seek the views and preferences of patients and did not clearly define their target users. For domain 3 (rigor of development), the quality of guidelines was also found to be highly variable, and scores ranged from 2% (GCOAT and SA Health) to 94% (CDC). The lowest scoring guidelines in this domain included the ones by AAGBI (9%), GCOAT (2%), SA Health (2%) and SASA (9%). Specifically, these guidelines did not clearly describe their methods used to search for evidence, criteria for selection of the evidence, assessment of the strengths and limitations of the body of evidence and methods of formulating recommendations. Additionally, details regarding external review and the procedure for update were lacking in these guidelines. The guideline by GCOAT and SA Health also did not provide an explicit link between the recommendations and supporting evidence, and did not explicitly consider health benefits, side effects and risks. The applicability of guidelines was also found to variable, as scores in domain 5 ranged from 2% (Ayad *et al.* and GCOAT) to 73% (CDC). The publications by Ayad *et al.* and GCOAT (2%) did not clearly present tools for application of recommendations, failed to explicitly consider cost implications and did not clearly present criteria for monitoring and auditing purposes. Similarly, the guideline published by the Pain Working Group did not present criteria for

monitoring and auditing and did not clearly discuss tools for application, organizational barriers and cost implications. Lastly, scores for the domain of editorial independence were also found to be highly variable, ranging from 2% (SASA) to 92% (APS/ASRA/ASA). Four guidelines scored below 10% in this domain: GCOAT, SA Health, SASA and SIAARTI. These guidelines did not clearly describe the role of the funding body in the development of their recommendations and did not address conflicts of interest.

Table 2. 4 AGREE II Domain Scores of Identified Clinical Practice Guidelines Relevant to Opioid Prescribing At Discharge After Abdominal-Pelvic Surgery

	Domain* (%)					
Publishing Body	**Scope and Purpose**	**Stakeholder Involvement**	**Rigor of Development**	**Clarity of Presentation**	**Applicability**	**Editorial Independence**
AAGBI[88]	44	49	9	54	29	63
ACOEM[90]	86	38	79	88	51	50
AZDHS[96]	50	38	19	85	56	13
AMDG-Bree Collaborative[87,91]	78	71	54	75	66	79
APS-ASRA-ASA[60]	60	50	73	83	11	92
ASA[59]	72	50	73	88	16	10
Ayad *et al.*[95]	39	17	19	54	2	42
CDC[16]	93	99	94	94	73	88
GCOAT[101]	38	13	2	49	2	6
Pain Working Group[106]	33	24	19	40	7	33
SA Health[110]	40	31	2	63	19	4
Salti *et al.*[111]	36	8	20	68	11	44
SASA[112]	24	29	9	42	27	2
SIAARTI[115]	22	31	31	67	14	6
UDOH[116]	36	50	43	83	10	40

Abbreviation: AAGBI, Association of Anaesthetists of Great Britain and Ireland; ACOEM, American College of Occupational and Environmental Medicine; AZDHS, Arizona Department of Health Services; AMDG; Agency Medical Directors' Group; APS, American Pain Society; ASRA, American Society of Regional Anaesthesia and Pain Medicine; ASA, American Society of Anesthesiologists; ASA, American Society of Anesthesiologists; CDC, Center for Disease Control and Prevention; GCOAT, Governor's Cabinet Opiate Action Team; SA Health, South Australia Health; SASA, South Africa Society of Anaesthesiologists; SIAARTI, Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva

*For each item, four reviewers independently assigned a score on a 7-point scale (1 - Strongly Disagree, 7 – Strongly Agree), and these scores were summed across reviewers for all items included in the domain to generate a scaled domain score. Items where there was a large scoring discrepancy between reviewers, defined as a ≥ 3 points difference,[86] were discussed, and the discrepancy was resolved by consensus.

Recommendations for Opioid Prescribing At Discharge After Abdominal-Pelvic Surgery

General Recommendations

General recommendations relevant to the prescription of opioids at discharge after abdominal-pelvic surgery are presented in Table 2.5. Fourteen publishing bodies recommended a multimodal approach to pain management (using a variety of analgesic medications and techniques combined with nonpharmacological interventions)[59,60,63,65,87,90,94-96,101-103,115,116] and only three documents provided an associated strength or level of evidence: American College of Occupational and Environmental Medicine (ACOEM) (C-level evidence, high confidence),[90] American Society of Anesthesiologists (ASA) (A1 category evidence)[59] and American Pain Society-American Society of Regional Anesthesia and Pain Medicine-American Society of Anesthesiologists (APS-ASRA-ASA) (strong recommendation, high-quality evidence).[60] Eleven documents recommended that clinicians ensure that opioids are appropriately indicated.[92,95,101,103,106,108,110,112,114,115] While many recommendations acknowledged that opioids are generally required for the treatment of moderate to severe pain immediately after surgical procedures (SIAARTI: level A recommendation),[95,101,106,112,115] several documents recommended that the need for opioid treatment should be re-assessed at patient discharge and the prescription should be based on in-hospital opioid use.[92,110,114] Five documents recommended caution when prescribing opioids to special patient populations such as those with concurrent alcohol, benzodiazepines and other drug use (Institute of Clinical Systems Improvement (ICSI): low quality evidence), renal or liver impairment (ICSI: low quality evidence), delirium/dementia/fall risk, psychiatric comorbidities (ICSI: low quality evidence), existing opioid prescription (ICSI: low quality evidence), respiratory insufficiency or sleep apnea, concerns with safe driving, advanced age or breastfeeding.[88,89,101,103,118] Specifically, ACOEM recommended against concurrent opioid use for individuals while performing safety-sensitive jobs (C-level evidence, moderate confidence),[90] such as operating

motor vehicles or other modes of transportation, forklift driving, overhead crane operation, heavy equipment operation, sharps work, work with injury risks and tasks involving high levels of cognitive function and judgment.[119]

Regarding the type of opioid, recommendations were generally consistent in that the least potent type should be prescribed, but most documents did not provide guidance as to specific agents to use.[94,101,102,118] South Australia Health (SA Health) recommended oxycodone as the preferred option of acute pain treatment, whereas SIAARTI suggested that morphine should be the gold standard.[115] The Ohio Governor's Cabinet Opiate Action Team (GCOAT) recommended the use a morphine equivalence chart when choosing opioids.[101] Additionally, SIAARTI specifically recommended against combining tramadol and morphine (level C recommendation).[115] Regarding the opioid formulation, all documents that addressed this recommended immediate-release opioids[16,63,91,93,102,103,110] and against long-acting opioids.[63,96,101,103,112] The dose of opioid should be the lowest possible,[16,91,94,96,100,102] and daily dosages should not exceed 30 MMEs[118] to 50 MMEs (ACOEM: I-level evidence, moderate confidence).[90] The duration of the opioid prescription should be based on the expected duration of pain,[100,104,116] and clinicians should generally prescribe opioids for less than 3 days[16,87,91,100,102,103] or 3-5 days.[63,96]

Table 2. 5 General Recommendations When Prescribing Opioids At Discharge After Abdominal-Pelvic Surgery

Intervention	**Supporting Publishing Body**	**Strength/Level of Evidence Provided**
Multimodal prescribing	AZDHS, ICSI, AMDG-Bree Collaborative, GCOAT, ACOEM, ASA, SIAARTI, APS-ASRA-ASA, Ayad *et al.*, UDOH, Michigan OPEN, DHMC, HQO, AUA	Yes (ACOEM, ASA, APS-ASRA-ASA)
Ensure appropriate indication	SA Health, ICSI, SJMHS, RCoA, ANZCA, GCOAT, Pain Working Group, SIAARTI, SASA, Ayad *et al.*	Yes (SIAARTI)
Prescribe immediate-release opioids	SA Health, CDC, ICSI, AMDG-Bree Collaborative, Michigan OPEN, ASER-POQI, HQO	No
Prescribe lowest effective dose	AZDHS, CDC, CWC, AMDG, HQO, AUA,	No
Prescribe based on opioid requirement in 24 hours before discharge	DHMC, BWH, SJMHS, RPCCC, SA Health	No
Avoid long-acting opioids	AZDHS, ICSI, GCOAT, SASA, Michigan OPEN,	No
Cautious prescribing in special populations	ICSI, WCH-ISMP, GCOAT, AAGBI, ABM	Yes (ICSI)
Prescribe for less than 3 days	ICSI, CDC, CWC, AMDG-Bree Collaborative, HQO	No
Prescribe least potent type	WCH-ISMP, GCOAT, HQO, AUA	No
Prescribe based on expected duration of pain	ISMP-CPSI, CWC, UDOH	No
Prescribe for less than 3-5 days	AZDHS, Michigan OPEN	No
Prescribe less than total allowable dosing	SA Health, AMDG-Bree Collaborative	No
Avoid in patients who perform safety-sensitive jobs	ACOEM	Yes
Do not prescribe refills	GCOAT	No
Prescribe less than 50 mg MED/day	ACOEM	Yes
Prescribe less than 30 mg MED/day	WCH-ISMP	No
Prescribe less than 20 pills of low-dose short-acting opioids	ICSI	No
Prescribe minimum possible quantity	GCOAT	No
Preferentially prescribe morphine	SIAARTI	No
Preferentially prescribe oxycodone	SA Health	No
Prescribe electronically	AUA	No
Prescribe according to specific procedures	AZDHS	No
Legal prescribing	SA Health	No
Avoid combining tramadol and morphine	SIAARTI	Yes
Avoid pre-operative prescribing	Michigan OPEN	No

Abbreviations: MED, morphine equivalent dose, ABM, Academy of Breastfeeding Medicine; AMDG, Agency Medical Directors' Group; ACOEM, American College of Occupational and Environmental Medicine; APS, American Pain Society; ASRA, American Society of Regional Anesthesia and Pain Medicine; ASA, American Society of Anesthesiologists; ASER, American Society for Enhanced Recovery; POQI, Perioperative Quality Initiative; AUA, American Urological Association; AZDHS, Arizona Department of Health Services; AAGBI, Association of Anesthetists of Great Britain and Ireland; ANZCA, Australian and

New Zealand College of Anaesthetists; BWH, Brigham and Women's Hospital; CDC, Center for Disease Control and Prevention; CWC, Choosing Wisely Canada; DHMC, Dartmouth Hitchcock Medical Center; HQO, Health Quality Ontario; ICSI, Institute for Clinical Systems Improvement; ISMP, Institute for Safe Medication Practices Canada; CPSI, Canadian Patient Safety Institute; Michigan OPEN, Michigan Opioid Prescribing Engagement Network; GCOAT, Governor's Cabinet Opiate Action Team; SA Health, South Australia Health; RPCCC, Roswell Park Comprehensive Cancer Centre; SIAARTI, Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva; SJMHS, St. Joseph Mercy Health System; UDOH, Utah Department of Health; SASA, South African Society of Anaesthesiologists; WCH, Women's College Hospital

Co-Interventions

I identified 11 co-interventions relevant to the prescription of opioids at discharge after abdominal-pelvic surgery (Table 2.6). Only two interventions were supported by a recommendation strength and level of evidence: patient education and comprehensive patient assessment. A recommendation strength and level of evidence was provided by APS-ASRA-ASA regarding education on treatment alternatives (strong recommendation, low quality evidence) and the plan for taper and discontinuation (strong recommendation, low quality evidence).[60] Similarly, the Polish Society of Anaesthesiology and Intensive Therapy (PSAIT) provided a grade I recommendation (strongly recommended) regarding education on the plan for taper and discontinuation supported by level C evidence.[107] Nine publications recommended a comprehensive assessment of the patient prior to the prescription of opioids, and only APS-ASRA-ASA provided a strength and level of evidence for this recommendation (strong recommendation, low-quality evidence).[60]

Table 2. 6 Recommended Co-Interventions When Prescribing Opioids At Discharge After Abdominal-Pelvic Surgery

Intervention (Specific Elements)	Supporting Publications	Strength/Level of Evidence Provided
Patient education (benefits, risks, alternatives, side effects, appropriate use, expectations, norms, goals, multimodal treatment, safe storage, safe disposal, activity restrictions, avoid sedating drugs, avoid sharing, reproductive plans, plan for taper and discontinuation, designated responsible provider)	AZDHS, SA Health, ICSI, SJMHS, WCH-ISMP, ISMP-CPSI, AMDG-Bree Collaborative, ANZCA, GCOAT, APS-ASRA-ASA, Ayad *et al.*, UDOH, Michigan OPEN, SGO, DHMC, HQO, AUA, CPSBC, PSAIT, Mayo Clinic	Yes (APS-ASRA-ASA, PSAIT)
Comprehensive patient assessment (medical comorbidities, psychiatric comorbidities, concomitant medications, history of chronic pain, history of substance use, family history of substance use disorder, previous postoperative treatment regimens and responses, physical exam, relevant investigations)	AZDHS, RCoA, GCOAT, ACOEM, APS-ASRA-ASA, Michigan OPEN, HQO, CPSBC	Yes (APS-ASRA-ASA)
PDMP access	AZDHS, SJMHS, GCOAT, Michigan OPEN, HQO, AUA, CPSBC	No
Communication with other providers (primary care, prescribers of benzodiazepines)	SA Health, ICSI, RCoA, ANZCA, GCOAT	No
Provider education (local medical disposal programs, laws, best practices, professional body requirements and recommendations, prescription drug monitoring program, available pain management/addiction medicine/palliative care specialists)	ISMP-CPSI, RCoA, SGO, HQO, AUA	No
Avoid concurrent sedating medications (benzodiazepines/sedative-hypnotics/anxiolytics/CNS depressant)	WCH-ISMP, AMDG-Bree Collaborative, Michigan OPEN, CPSBC	No
Prescribe naloxone for patients at risk of overdose (greater than 90 mg MED/day, on benzodiazepines, history of respiratory impairment, history of overdose, substance use disorder)	WCH-ISMP, Michigan OPEN, CPSBC	No
Pharmacist involvement (assess appropriateness of recommended regimen, create opioid discontinuation plan, patient education)	SJMHS, RCoA	No
Ensure consistent messaging	Michigan OPEN	No
Ensure primary care follow-up in 3-5 days	AZDHS	No
Clear documentation (relevant clinical findings, intended outcomes, choice of drug, formulation, dose, duration of treatment, circumstances for adjustment, plan for taper and discontinuation, follow-up, information given)	RCoA	No

Abbreviation: AMDG, Agency Medical Directors' Group; ACOEM, American College of Occupational and Environmental Medicine; APS, American Pain Society; ASRA, American Society of Regional Anesthesia and Pain Medicine; ASA, American Society of Anesthesiologists; AUA, American Urological Association; AZDHS, Arizona Department of Health Services; ANZCA, Australian and New Zealand College of Anaesthetists; CPSBC, College of Physicians and Surgeons of British Columbia; HQO, Health Quality Ontario; DHMC, Dartmouth Hitchcock Medical Center; ICSI, Institute for Clinical Systems Improvement; ISMP, Institute for Safe Medication Practices Canada; CPSI, Canadian Patient Safety Institute; Michigan OPEN, Michigan Opioid Prescribing Engagement Network; GCOAT, Governor's Cabinet Opiate Action Team; PSAIT, Polish Society of Anaesthesiology and Intensive Therapy; SIAARTI, Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva; SGO, Society of Gynecologic Oncology; SJMHS, St. Joseph Mercy Health System; RCoA, Royal College of Anaesthetists; UDOH, Utah Department of Health; WCH, Women's College Hospital

Procedure-Specific Opioid Prescription Regimens

Fourteen documents provided recommendations for opioid prescriptions after 21 specific abdominal-pelvic procedures (Table 2.7). While the majority of documents recommended a single amount of opioid per procedure, recommendations from the Mayo Clinic stratified prescriptions into low dose, standard dose or high dose,[61] and three documents recommended basing the discharge prescription on inpatient opioid consumption.[64,97,109] Oxycodone was the most commonly recommended type of opioid (10 documents).[31,61,63,64,78,93,97,98,105,109] Only 6 documents included a frequency of administration in their recommended opioid prescriptions.[43,66,93,98,109,117] The majority of documents recommended including non-opioid analgesics in the discharge prescription. The recommended amount of opioid ranged widely between guidelines for many procedures. After a minimally-invasive cholecystectomy, appendectomy, inguinal hernia repair, hysterectomy, nephrectomy, prostatectomy or caesarean section, recommendations ranged from 0 to 150 MMEs per prescription. For minimally-invasive bariatric, benign foregut or adrenal procedures, ventral hernia repair (minimally-invasive or open), colectomy (minimally-invasive or open), open small bowel resection, enterolysis, or radical prostatectomy, this ranged from 0 to 225 MME. However, after a stoma creation/re-siting/closure or an open hysterectomy, recommendations ranged from 12 opioid tablets to a 14-day supply (60-180 MMEs). No recommendation was associated with a formal assessment of strength or level of evidence.

Table 2. 7 Procedure-Specific Opioid Prescription Recommendations At Discharge After Abdominal-Pelvic Surgery

Publishing Body	Prescription Opioid	MME	Frequency	Prescription Non-Opioid	Strength /Level of Evidence Provided
Minimally-Invasive Cholecystectomy					
CORE[98]	• 10 tablets of oxycodone (5 mg) OR • 10 tablets of hydromorphone (2 mg) OR • 10 tablets of tramadol (50 mg)	75 80 50	Q6-8H Q6-8H Q6-8H	Acetaminophen, NSAIDs, lidoderm patch	No
University Hospital North Staffordshire NHS Trust [117]	• 10 tablets of codeine (30)	45	Daily	NSAIDs, acetaminophen	No
DHMC[31]	• 15 tablets of oxycodone (5 mg)	112.5	-	None	No
Michigan OPEN[63]	• 10 tablets of oxycodone (5 mg) OR • 10 tablets of hydrocodone (5 mg)	75 50	-	None	No
AMDG-Bree Collaborative[87,91]	• If necessary, 8 to 12 tablets of short-acting opioids	NA	-	NSAIDs, acetaminophen	No
NYGH[43]	• 20 tablets of morphine (5 mg), dispense 10 tabs every 3 days OR • 20 tablets of hydromorphone (1 mg), dispense 10 tabs every 3 days	100 80	Q4H	NSAIDs, acetaminophen	No
Mayo Clinic[61]	• Low dose: no opioid • Standard dose: 8 tablets of oxycodone (5 mg) OR 12 tablets of tramadol (50 mg) • High dose: 20 tablets of oxycodone (5 mg) OR 30 tablets of tramadol (50 mg)	0 60 60 150 150	-	NSAIDs, acetaminophen	No
LHSC[66]	• 10 tablets of tramadol (50 mg) OR • 10 tablets of codeine (30 mg)	50 45	Q6H	NSAIDs	No
Michigan Medicine[105]	• 15 tablets of hydrocodone (5 mg) OR • 15 tablets of oxycodone (5 mg)	75 112.5	-	NSAIDs, acetaminophen	No
Open Cholecystectomy					
Michigan OPEN[63]	• 15 tablets of oxycodone (5 mg)	112.5	-	None	No
Minimally-Invasive Appendectomy					
Michigan OPEN[63]	• 10 tablets of oxycodone (5 mg) OR	75	-	None	No

	• 10 tablets of hydrocodone (5 mg)	50			
AMDG-Bree Collaborative[87,91]	• If necessary, 8 to 12 tablets of short-acting opioids	NA	-	NSAIDs, acetaminophen	No
NYGH[43]	• 20 tablets of morphine (5 mg), dispense 10 tabs every 3 days OR • 20 tablets of hydromorphone (1 mg), dispense 10 tabs every 3 days	100 80	Q4H	NSAIDs, acetaminophen	No
Mayo Clinic[61]	• Low dose: no opioid • Standard dose: 8 tablets of oxycodone (5 mg) OR 12 tablets of tramadol (50 mg) • High dose: 20 tablets of oxycodone (5 mg) OR 30 tablets of tramadol (50 mg)	0 60 60 150 150	-	NSAIDs, acetaminophen	No
Open Appendectomy					
Michigan OPEN[63]	• 10 tablets of oxycodone (5 mg) OR • 10 tablets of hydrocodone (5 mg)	75 50	-	None	No
Minimally-Invasive Inguinal Hernia Repair					
CORE[98]	• 12 tablets of oxycodone (5 mg) OR • 12 tablets of hydromorphone (2 mg) OR • 12 tablets of tramadol (50 mg)	90 96 60	Q6-8H Q6-8H Q6-8H	NSAIDs, acetaminophen, lidoderm patch	No
DHMC[31]	• 15 tablets of oxycodone (5 mg)	112.5	-	No	No
Michigan OPEN[63]	• 10 tablets of oxycodone (5 mg) OR • 10 tablets of hydrocodone (5 mg)	75 50	-	None	No
AMDG-Bree Collaborative[87,91]	• 8 to 12 tablets of short-acting opioids	NA	-	NSAIDs, acetaminophen	No
Mayo Clinic[61]	• Low dose: no opioid • Standard dose: 8 tablets of oxycodone (5 mg) OR 12 tablets of tramadol (50 mg) • High dose: 20 tablets of oxycodone (5 mg) OR 30 tablets of tramadol (50 mg)	0 60 60 150 150	-	NSAIDs, acetaminophen	No
Minimally-Invasive Bariatric, Benign Foregut or Adrenal Surgery					
Mayo Clinic[61]	• Low dose: no opioid • Standard dose: 8 tablets of oxycodone (5 mg) OR 12 tablets of tramadol (50 mg) • High dose: 20 tablets of oxycodone (5 mg) OR	0 60 60 150	-	NSAIDs, acetaminophen	No

	30 tablets of tramadol (50 mg)	150			
Michigan OPEN[63]	• 10 tablets of oxycodone (5 mg) • 10 tablets of hydrocodone (5 mg)	75 50	-	None	No
DHMC[64]	• Discharge on POD #1: 15 tablets of oxycodone (5 mg) • Discharge on POD #2 or later: no opioid if patient did not take any the day before discharge OR 15 tablets of oxycodone (5 mg) if patient took 1 to 3 tablets the day before discharge OR 30 tablets of oxycodone (5 mg) if patient took 4 or more pills the day before discharge	112.5 0 112.5 225	-	No	No
Minimally-Invasive Solid Organ Resection					
Mayo Clinic[61]	• Low dose: no opioid • Standard dose: 15 tablets of oxycodone (5 mg) OR 25 tablets of tramadol (50 mg) • High dose: 25 tablets of oxycodone (5 mg) OR 40 tablets of tramadol (50 mg)	0 112.5 125 187.5 200	-	NSAIDs, acetaminophen	No
Open Major Abdominal Resection					
Mayo Clinic[61]	• Low dose: no opioid • Standard dose: 30 tablets of oxycodone (5 mg) OR 60 tablets of tramadol (50 mg) • High dose: 50 tablets of oxycodone (5 mg) OR 80 tablets of tramadol (50 mg)	0 225 300 375 400	-	NSAIDs, acetaminophen	No
Open Ventral Hernia Repair					
CORE[98]	• 14 tablets of oxycodone (5 mg) OR • 14 tablets of hydromorphone (2 mg) OR • 14 tablets of tramadol (50 mg)	105 112 70	Q6-8H Q6-8H Q6-8H	NSAIDs, acetaminophen, Lidoderm patch	No
Michigan OPEN[63]	• 10 tablets of oxycodone (5 mg) OR • 10 tablets of hydrocodone (5 mg)	75 50	-	None	No
AMDG-Bree Collaborative[87,91]	• ≤ 42 tablets of short-acting opioids	NA	-	NSAIDs, acetaminophen	No
LHSC[66]	• 10 tablets of tramadol (50 mg) OR • 10 tablets of codeine (30 mg)	50 45	Q6H	NSAIDs	No
DHMC[64]	• Discharge on POD #1: 15 tablets of oxycodone (5 mg)	112.5	-	No	No

	• Discharge on POD #2 or later: no opioid if patient did not take any the day before discharge OR 15 tablets of oxycodone (5 mg) if patient took 1 to 3 tablets the day before discharge OR 30 tablets of oxycodone (5 mg) if patient took 4 or more pills the day before discharge	0 4 112.5 225			
Minimally-Invasive Ventral Hernia Repair					
DHMC[64]	• Discharge on POD #1: 15 tablets of oxycodone (5 mg) • Discharge on POD #2 or later: no opioid if patient did not take any the day before discharge OR 15 tablets of oxycodone (5 mg) if patient took 1 to 3 tablets the day before discharge OR 30 tablets of oxycodone (5 mg) if patient took 4 or more pills the day before discharge	112.5 0 112.5 225	-	No	No
Hepatectomy or Pancreatectomy					
DHMC[64]	• Discharge on POD #1: 15 tablets of oxycodone (5 mg) • Discharge on POD #2 or later: no opioid if patient did not take any the day before discharge OR 15 tablets of oxycodone (5 mg) if patient took 1 to 3 tablets the day before discharge OR 30 tablets of oxycodone (5 mg) if patient took 4 or more pills the day before discharge	112.5 0 112.5 225	-	No	No
Open or Minimally-Invasive Colectomy					
Michigan OPEN[63]	• 15 tablets of oxycodone (5 mg) OR • 15 tablets of hydrocodone (5 mg)	112.5 75	-	None	No
ASER-POQI[93]	• ≤ 3 days of oxycodone (5 mg)	90	Q6h	Gabapentin, acetaminophen, NSAIDs	No
AMDG-Bree Collaborative[87,91]	• ≤ 42 tablets of short-acting opioids	NA	-	NSAIDs, acetaminophen	No
Mayo Clinic[61]	• Low dose: no opioid • Standard dose: 15 tablets of oxycodone (5 mg) OR 25 tablets of tramadol (50 mg) • High dose: 30 tablets of oxycodone (5 mg) OR 45 tablets of tramadol (50 mg)	0 112.5 125 225 225	-	NSAIDs, acetaminophen	No

DHMC[64]	• Discharge on POD #1: 15 tablets of oxycodone (5 mg) • Discharge on POD #2 or later: no opioid if patient did not take any the day before discharge OR 15 tablets of oxycodone (5 mg) if patient took 1 to 3 tablets the day before discharge OR 30 tablets of oxycodone (5 mg) if patient took 4 or more pills the day before discharge	112.5 0 112.5 225	-	No	No
Open Small Bowel Resection or Enterolysis					
Michigan OPEN[63]	• 20 tablets of oxycodone (5 mg) OR • 20 tablets of hydrocodone (5 mg)	150 100	-	None	No
AMDG-Bree Collaborative[87,91]	• ≤ 42 tablets of short-acting opioids	NA	-	NSAIDs, acetaminophen	No
Mayo Clinic[61]	• Low dose: no opioid • Standard dose: 15 tablets of oxycodone (5 mg) OR 25 tablets of tramadol (50 mg) • High dose: 30 tablets of oxycodone (5 mg) OR 45 tablets of tramadol (50 mg)	0 112.5 125 225 225	-	NSAIDs, acetaminophen	No
Ileostomy/Colostomy Creation, Re-Siting or Closure					
Michigan OPEN[63]	• 15 tablets of oxycodone (5 mg) OR • 15 tablets of hydrocodone (5 mg)	112.5 75	-	None	No
AMDG-Bree Collaborative[87,91]	• ≤ 14 days of short-acting opioids	NA	-	NSAIDs, acetaminophen	No
Minimally-Invasive Hysterectomy					
CORE[98]	• 10 tablets of oxycodone (5 mg) OR • 10 tablets of hydromorphone (2 mg) OR • 10 tablets of tramadol (50 mg)	75 80 50	Q6-8H Q6-8H Q6-8H	NSAIDs, acetaminophen, Lidoderm patch	No
Michigan OPEN[63]	• 15 tablets of oxycodone (5 mg) OR • 15 tablets of hydrocodone (5 mg)	112.5 75	-	None	No
AMDG-Bree Collaborative[87,91]	• ≤ 42 tablets of short-acting opioids	NA	-	NSAIDs, acetaminophen	No
RPCCC[109]	• ≤ 5 doses of opioid required in the 24 hours before discharge: no opioid • > 5 doses of opioid required in the 24 hours before discharge: 12 tablets of hydrocodone (5 mg) OR	05 60	Q6H	NSAIDs, acetaminophen	No

	12 tablets of oxycodone (5 mg)	90			
Open Hysterectomy					
CORE[98]	• 15 tablets of oxycodone (5 mg) OR • 15 tablets of hydromorphone (2 mg) OR • 15 tablets of tramadol (50 mg)	112.5 120 75	Q6-8H Q6-8H Q6-8H	NSAIDs, acetaminophen, lidoderm patch	No
Michigan OPEN[63]	• 15 tablets of oxycodone (5 mg) OR • 15 tablets of hydrocodone (5 mg)	112.5 75	-	None	No
AMDG-Bree Collaborative[87,91]	• ≤ 14 days of short-acting opioids	NA	-	NSAIDs, acetaminophen	No
RPCCC[109]	• ≤ 5 doses of opioid required in the 24 hours before discharge: 12 tablets of hydrocodone (5 mg) OR 12 tablets of oxycodone (5 mg) • > 5 doses of opioid required in the 24 hours before discharge: 24 tablets of hydrocodone (5 mg) OR 24 tablets of oxycodone (5 mg)	 60 90 120 180	Q6H	NSAIDs, Acetaminophen	No
Caesarean Section					
CORE[98]	• 10 tablets of oxycodone (5 mg) OR • 10 tablets of hydromorphone (2 mg)	75 80	Q6-8H Q6-8H	NSAIDs, acetaminophen, lidoderm patch	No
Michigan OPEN[63]	• 15 tablets of oxycodone (5 mg) OR • 15 tablets of hydrocodone (5 mg)	112.5 75	-	None	No
AMDG-Bree Collaborative[87,91]	• ≤ 42 tablets of short-acting opioids	NA	-	NSAIDs, acetaminophen	No
BWH[97]	• No opioid required post-delivery: no opioid • No opioid required in the 24 hours before discharge: ≤ 10 tablets of oxycodone (5 mg) • Opioid required in the 24 hours before discharge: ≤ 20 tablets of oxycodone (5 mg)	0 75 150	-	None	No
Minimally-Invasive Nephrectomy					
Michigan OPEN[63]	• 10 tablets of oxycodone (5 mg) OR • 10 tablets of hydrocodone (5 mg)	75 50	-	None	No
UPMC[78]	• 20 tablets of oxycodone (5mg)	150	-	None	No
Open Nephrectomy					

UPMC[78]	• 22 tablets of oxycodone (5mg)	165	-	None	No
Minimally-Invasive Prostatectomy					
CORE[98]	• 10 tablets of oxycodone (5 mg) OR • 10 tablets of hydromorphone (2 mg) OR • 10 tablets of tramadol (50 mg)	75 80 50	Q6-8H Q6-8H Q6-8H	NSAIDs, acetaminophen, lidoderm patch	No
Michigan OPEN[63]	• 10 tablets of oxycodone (5 mg) OR • 10 tablets of hydrocodone (5 mg)	75 50	-	None	No
UPMC[78]	• 17 tablets of oxycodone (5mg)	127.5	-	None	No
Radical Prostatectomy					
UPMC[78]	• 23 tablets of oxycodone (5mg)	172.5	-	None	No
Michigan OPEN[63]	• 10 tablets of oxycodone (5 mg) OR • 10 tablets of hydrocodone (5 mg)	75 50	-	None	No

Abbreviations: MME, milligram morphine equivalent; NSAID, non-steroid anti-inflammatory drug; NA, Not Applicable; CORE, Center for Opioid Research and Education; DHMC, Dartmouth Hitchcock Medical Center; Michigan OPEN, Opioid Prescribing Engagement Network; AMDG, Agency Medical Directors' Group; NYGH, North York General Hospital; ASER, American Society for Enhanced Recovery; POQI, Perioperative Quality Initiatve; UPMC, University of Pittsburgh Medical Center; BWH, Brigham and Women's Hospital; LHSC, London Health Sciences Centre; RPCCC, Roswell Park Comprehensive Cancer Centre

Recommendations for Opioid Disposal

Eight interventions were identified that are relevant to the disposal of opioids (Table 2.8). No recommendation was accompanied by a strength or level of evidence. Although twelve documents recommended the education of patients regarding appropriate opioid disposal,[61,63,87,94,96,101-103,114,116,118] few provided details regarding specific methods of disposal. A take-back program was the most commonly recommended option for opioid disposal,[87,113,118] and recommendations by the Food and Drug Administration (FDA) suggested to flush opioids down the toilet if there is no readily available take-back option and the medication is on the FDA flush list.[87,103] If the medication was not on the flush list, then the FDA recommended to combine it with unpalatable substances and dispose of in the garbage.[87,103] On the other hand, the Institute of Safe Medication Practices Canada and the Canadian Patient Safety Institute (ISMP-CPSI) recommended against flushing opioids in the toilet or throwing out unused doses in the garbage unless there is a compelling safety need.[118] ICSI also recommended opioid disposal in anonymous drop-boxes.[103] Importantly, ISMP-CPSI and the American Urological Association recommended that clinicians should educate themselves regarding appropriate disposal options that are relevant to their area of practice.[94,118]

Table 2. 8 Recommendations For Opioid Disposal After Abdominal-Pelvic Surgery

Intervention	Number of Supporting Publications	Strength or Level of Evidence Provided
Patient education	AZDHS, ICSI, SJMHS, ISMP-CPSI, AMDG-Bree Collaborative, GCOAT, UDOH, Michigan OPEN, HQO, AUA, Mayo Clinic, SGO	No
Take-back programs	ISMP-CPSI, AMDG-Bree Collaborative, SGO	No
Provider education	ISMP-CPSI, AUA	No
Flush down the toilet if no readily available take-back option and the medication is on the FDA flush list	ICSI, AMDG-Bree Collaborative	No
Combine with unpalatable substances and throw away if no readily available take-back option and the medication is not on the FDA flush list	ICSI, AMDG Bree Collaborative	No
Anonymous drop-box	ICSI	No
Do not throw out unused doses in the garbage	ISMP-CPSI	No
Do not flush in the toilet unless there is a compelling safety need	ISMP-CPSI	No

Abbreviation: FDA, Food and Drug Administration; AMDG, Agency Medical Directors' Group; AUA, American Urological Association; AZDHS, Arizona Department of Health Services; HQO, Health Quality Ontario; ICSI, Institute for Clinical Systems Improvement; ISMP, Institute for Safe Medication Practices Canada; CPSI, Canadian Patient Safety Institute; Michigan OPEN, Michigan Opioid Prescribing Engagement Network; GCOAT, Governor's Cabinet Opiate Action Team; SGO, Society of Gynecologic Oncology; SJMHS, St. Joseph Mercy Health System; UDOH, Utah Department of Health

Recommendations for Preventing Chronic Post-Operative Opioid Use

I identified 8 recommended interventions for the prevention of chronic post-surgical opioid use (Table 2.9). Six documents recommended that providers reassess patients with pain that persists beyond the anticipated duration after surgery.[87,90,96,108,113,116] GCOAT and ACOEM recommended that this reassessment be performed at 14 days after onset of pain (ACOEM: I-level evidence, high confidence).[90,101] Four documents recommended the use of preventive analgesia, such as regional anesthesia, gabapentin, pregabalin and ketamine, to prevent the development of chronic opioid use.[95,111,112,115] This was associated with a level A evidence in the publication by Salti *et al.*[111] and level C evidence by SIAARTI.[115] Following the prescription of opioids, clinicians should also have a plan for the taper and discontinuation of opioids among patients who exceed the anticipated duration of post-operative opioid use.[87,90,94] Three documents recommended screening patients for risk factors of persistent post-surgical pain,[87,92,95] and two recommended referral of patients with persistent opioid use to specialists in mental health, palliative care, or substance misuse.[101,108] Two documents recommended providers screen patients for risk factors of opioid misuse (ICSI: low quality evidence),[103,113] and ICSI also recommended screening for risk factors of opioid use disorder (low quality evidence).[103] Salti *et al.* recommended establishing clear communication channels between the surgeon and the anesthesiologist to reduce the development of chronic postsurgical pain (Level B evidence).[111]

Table 2. 9 Recommendations For Preventing Chronic Opioid Use After Abdominal-Pelvic Surgery

Intervention	Supporting Publications	Strength or Level of Evidence Provided
Reassess persistent pain	AZDHS, AMDG-Bree Collaborative, RCoA, ACOEM, UDOH	Yes (ACOEM)
Preventive analgesia	Salti *et al.*, SIAARTI, SASA, Ayad *et al.*	Yes (Salti *et al*., SIAARTI)
Have a plan for taper and discontinuation	AMDG-Bree Collaborative, ACOEM, AUA	No
Screen for risk factors for persistent pain	AMDG-Bree Collaborative, AZNCA, Ayad *et al.*	No
Referral to specialists	RCoA, GCOAT	No
Screen for risk factors for opioid misuse	ICSI, SGO	Yes (ICSI)
Surgeon-anesthetist communication prior to surgery	Salti *et al.*	Yes
Screen for risk factors for opioid use disorder	ICSI	Yes

Abbreviation: AMDG, Agency Medical Directors' Group; ACOEM, American College of Occupational and Environmental Medicine; AZDHS, Arizona Department of Health Services; ANZCA, Australian and New Zealand College of Anaesthetists; ICSI, Institute for Clinical Systems Improvement; GCOAT, Governor's Cabinet Opiate Action Team; SIAARTI, Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva; SGO, Society of Gynecologic Oncology; RCoA, Royal College of Anaesthetists; UDOH, Utah Department of Health; SASA, South African Society of Anaesthesiologists; AUA, American Urological Association

DISCUSSION

I systematically reviewed existing recommendations regarding the use of opioids for the outpatient treatment of pain after abdominal-pelvic surgery. Of the 41 included documents, I identified 98 recommendations for the prescription of opioids at discharge, 8 recommendations for the disposal of opioids, and 8 recommendations for the prevention of chronic post-surgical opioid use. For the prescription of opioids at discharge, I identified 25 interventions that provided general guidance, 11 co-interventions, and 62 prescription regimens after 21 specific abdominal-pelvic surgical procedures. Few recommended interventions were supported by an explicit assessment of the body of evidence, and the amount of opioid recommended in procedure-specific regimens varied substantially. Furthermore, I found the quality of CPGs to be highly variable.

The suboptimal nature of current post-operative opioid prescribing practices has been attributed in part to a lack of guidance for surgeons,[31,80,81] and my systematic review has identified several limitations in the existing body of recommendations. Out of 41 included documents, 15 CPGs were identified, but their quality varied widely across all domains of the AGREE II tool. Few CPGs scored consistently well across all AGREE II domains,[16,59,60,90,91] but the guidance provided mostly addressed inpatient post-operative pain management and were not targeted at specific surgical procedures. The CPG with the highest domain scores was the CDC Guideline for Prescribing Opioids for Chronic pain. Although this document provides some guidance for the treatment of acute pain, the majority of its recommendations focused on the management of chronic pain, which may have hindered its dissemination among providers managing post-operative pain.[16]

Additionally, although I have identified a large number of recommended interventions when prescribing opioids at discharge after abdominal-pelvic surgery, few interventions were

supported by an explicit assessment of the supporting evidence, which may limit the implementability of the recommendation. Moreover, the recommended interventions at times lacked specificity to be directly actionable for surgeons. For example, several documents recommended that the least potent type of opioid should be prescribed,[94,101,102,118] and that the dose should be the lowest possible.[16,91,94,96,100,102] Although these statements provide an overarching guidance of how to best prescribe opioids, they lack actionable details to guide surgical practice. Similarly, despite the fact that patient education was recommended in 21 of 43 documents, few recommendations provided specific details regarding the timing and the method by which patient education should occur. A potentially crucial element of patient education that might reduce post-discharge opioid consumption is setting appropriate expectations for post-operative pain, which was recommended in several documents.[61,63,87,94-96,99,101] As the current epidemic of opioid-related harms has been partially attributed to the surge in the prescription of opioids since the designation of pain as the fifth vital sign, surgeons should set the expectation that some degree of pain will be a normal part of surgical recovery as long as it does not interfere with function.

In the light of the growing awareness of opioid over-prescription at discharge after surgery, many surgeons may seek guidance regarding the optimal amount to prescribe to their patients at discharge. However, my systematic review has demonstrated that there are variations in the recommended amount of opioid after specific procedures. For example, the recommended prescription amount at discharge after an abdominal hysterectomy ranged from 12 tablets to a 14-day supply of opioids. This heterogeneity may be explained by the lack of evidence supporting any specific amount of opioid at the time of guideline development, however recent studies using patient-reported opioid consumption data indicate that approximately 100 MMEs is consumed after an abdominal hysterectomy, which corresponds to approximately 14 tablets of 5-mg

oxycodone.[120,121] As more evidence emerges regarding the requirement for opioids after specific surgical procedures, future guidelines should incorporate new evidence to guide clinical practice. Moreover, current guidance is conflicting regarding the prescription of opioids at discharge after an inpatient post-surgical stay, as several publications now recommend to tailor the discharge prescription based on inpatient opioid consumption in the 24 hours to discharge.[64,97,109] This is in contrast to traditional prescribing practices, where a fixed amount of opioid is often prescribed at discharge for all patients undergoing the same procedure. Although a few studies have shown that the tailoring of the discharge prescription based on inpatient opioid consumption can decrease amount of opioid prescribed without affecting the control of post-operative pain,[97,109] more research is needed to rigorously evaluate the effectiveness and the safety of this novel approach to discharge prescribing.

Regarding opioid disposal, several documents recommended the education of patients,[61,63,87,94,96,101-103,114,116,118] although few provided specific details on how to do so.[87,103,113,118] However, recent research has shown that appropriate patient education regarding disposal by surgeons is rather uncommon. In a recent survey of 101 general surgery residents at an academic medical centre in the United States, less than 10% of respondents reported providing any education to their patient regarding opioid disposal.[80] The appropriate disposal of excess prescription opioids may play an important role in preventing unintended deleterious consequences, and abdominal-pelvic surgeons and surgical trainees need to ensure that all their patients receive appropriate disposal instructions. This can be facilitated by the distribution of a pamphlet at discharge detailing appropriate methods of disposal, as there is emerging evidence that opioid disposal rates can be significantly improved with this simple intervention among surgical patients.[122,123]

While I described several deficiencies in the current body of recommendations on the prescription of opioids at discharge following abdominal-pelvic surgery, I would like to acknowledge that these should not be interpreted to indicate a lack of usefulness of these documents. Given the urgency associated with the ongoing crisis of opioid-related mortality, surgeons should strive to improve their prescribing practices as of now and could implement recommendations from guidance documents that they consider sensible and appropriate to the specific circumstances of their practice. Future research on this topic should focus on providing higher-quality evidence to support the proposed guidance, however I believe that it is reasonable to adopt current recommendations into practice while waiting for new evidence to surface.

A strength of my review is the broad scope of my eligibility criteria. As formal CPGs may not contain recommendations regarding the prescription of opioids specifically at discharge after abdominal-pelvic surgery, I included more informal recommendations that were produced by professional organizations that have not undergone peer-review. In order to capture these documents, I performed an extensive search of the grey literature. Additionally, my study included not only documents that specifically addressed pain management after abdominal-pelvic surgery, but also those that focused on the general post-operative setting as well as the acute pain setting. This approach allowed us to perform a more comprehensive analysis of the existing body of recommendations that are relevant to abdominal-pelvic surgery. However, I recognize that this may have introduced some heterogeneity in the body of identified recommendations, as the guidance from acute pain documents may have been developed for pain management in the primary care or emergency room setting. In addition, it was at times difficult to identify recommendations from non-CPG documents that originated from the grey literature. This was mitigated by the involvement of at least two reviewers with clinical experience in the screening

and data extraction processes to capture recommendations that are relevant to prescribing at discharge after abdominal-pelvic surgery. However, it remains plausible that some recommendations may still have been missed. Also, the National Guideline Clearinghouse was discontinued in July 2018 due to a lack of funding, and I were therefore unable to access this database beyond this time. Finally, although our strategy to search the medical literature was peer-reviewed, I did not use the recommendations from the PRESS guidelines[124] to do so, which may have undermined the quality of our search strategy.

CONCLUSION

I identified existing guidance on the prescription of opioids at discharge after abdominal-pelvic surgery, the appropriate disposal of opioids, and the prevention of chronic post-surgical opioid use. Despite a large number of suggested interventions, few recommendations were supported by an explicit assessment of evidence, and the quality of existing CPGs was highly variable. Many recommendations were not directly actionable for abdominal-pelvic surgeons, and procedure-specific recommendations of opioid regimens were often conflicting for the same procedure. Additional guidelines with specific and actionable recommendations supported by a systematic assessment of evidence are needed.

Chapter 3

A Systematic Review of Behavioral Interventions to Decrease Opioid Prescribing After Surgery

This chapter has been published as:

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OVERVIEW

Objective: To summarize strategies to reduce post-surgical opioid prescribing at discharge.

Summary Background Data: Current practices for the prescription of opioids at discharge after surgery are highly variable and often excessive. I conducted a systematic review to identify behavioral interventions designed to improve these practices.

Methods: I searched MEDLINE, EMBASE, CINAHL and PsycINFO until December 14th 2018 to identify studies of behavioral interventions designed to decrease opioid prescribing at discharge among adults undergoing surgery. Behavioral interventions were defined according to the Cochrane Effective Practice and Organisation of Care (EPOC) taxonomy. I assessed the risk of bias of included studies using criteria suggested by Cochrane EPOC and the Newcastle-Ottawa scale.

Results: Of 8,048 citations that were screened, 24 studies were included in my review. Six types of behavioral interventions were identified: local consensus-based processes (18 studies), patient-mediated interventions (2 studies), clinical practice guidelines (1 study), educational meetings (1 study), inter-professional education (1 study) and clinician reminder (1 study). All but one study reported a statistically significant decrease in the amount of opioid prescribed at discharge after surgery, and only two studies reported evidence of increased pain intensity. Reductions in prescribed opioids ranged from 34.4 to 212.3 milligram morphine equivalents. All studies were found to have medium-to-high risks of bias.

Conclusion: I identified six types of behavioral strategies to decrease opioid prescription at discharge after surgery. Despite the risk of bias, almost all types of intervention appeared effective in reducing opioid prescriptions at discharge after surgery without negatively impacting pain control.

INTRODUCTION

Opioids are commonly used for the treatment of acute pain after surgery. However, recent research has demonstrated that the prescription of opioids at discharge after surgery is highly variable and often exceeds actual patient requirements.[31,35,125] For example, up to 92% of patients report unused opioids after surgery,[40] with only up to 59.1% of prescribed opioids being actually consumed.[41] As the safe storage and appropriate disposal of unused opioids is uncommon,[40,126] the over-prescription of opioids can lead to unintended harms, such as diversion and accidental overdoses.[79,127] Moreover, there is increasing recognition that a significant proportion of patients will become long-term users of opioid after initial exposure in the post-operative period,[49,52,53] which can predispose to opioid dependence and/or opioid use disorder. As the risks of opioid misuse, use disorder and overdose increase with the duration of the initial post-operative opioid prescription,[44] preventing the over-prescription of opioids may play an important role in preventing subsequent harms.

The prescription of opioids after surgery has been generally based on traditions and routines rather than actual patient requirements. However, the ongoing epidemic of opioid-related mortality and the increasing awareness of harms associated with opioids has resulted in many surgeons re-evaluating their prescribing practices. In an effort to change practice, many institutions have developed interventions specifically designed to improve opioid prescribing behaviors at discharge after surgery.[38,65,128] Although many of these interventions have been developed and implemented according to specific institutional circumstances, they may serve as a useful model for healthcare institutions seeking to improve post-operative opioid prescribing practices. I therefore systematically reviewed the literature to summarize existing behavioral interventions designed to reduce post-surgical opioid prescribing.

METHODS

Review Design

The protocol for this systematic review was designed in accordance with the PRISMA-P guidelines[82] and prospectively registered with PROSPERO (CRD42018093521).[129] The PRISMA statement was followed for the reporting of results (Appendix 3.1).[74]

Eligibility Criteria

I included all primary studies published in the medical literature evaluating a behavioral intervention implemented within a health care institution to decrease opioid prescribing at discharge after surgery. Eligible studies included randomized controlled trials (RCT), non-randomized trials, pre-post studies, interrupted-time-series studies, cohort studies, case-control studies, historically controlled studies and cross-sectional studies. Studies involving adults (≥ 18 years old) undergoing any type of surgery were included. Behavioral interventions were defined according on the Cochrane Effective Practice and Organisation of Care (EPOC) taxonomy of health system interventions.[130] In this taxonomy, Cochrane EPOC provides a categorization of implementation strategies targeted at healthcare workers to change their behavior such as audit and feedback, educational meetings, local consensus processes, public release of performance data, etc. A full list of the EPOC categories and their definitions is presented in Table 3.1. The primary outcome was the amount of opioid prescribed at hospital discharge after surgery, expressed as the number of opioid tablet or milligram morphine equivalent (MME). Studies that only reported the proportion of patients discharged with any opioid-containing prescription were also included. Due to the potential for inadequate pain control associated with a decreased amount of prescribed opioid, the secondary outcome consisted of post-operative pain control, measured by prescription refills,

pain scores or overall satisfaction with pain management. Due to the rapidly increasing scientific interest in this area, I included conference abstracts captured through database searches that met my inclusion criteria.

I excluded studies that reported the effect of specific surgical techniques or perioperative anesthetic interventions on post-operative opioid consumption. Studies that exclusively involved pediatric patients were excluded due to differences in pain management compared to the adult population. Studies that evaluated the effect of policy-level interventions were excluded as these are outside the scope of this review.

Table 3. 1 Cochrane EPOC Taxonomy of Implementation Strategies Targeted at Healthcare Workers

Intervention	Definition
Audit and feedback	A summary of health workers' performance over a specified period of time, given to them in a written, electronic or verbal format. The summary may include recommendations for clinical action
Clinical incident reporting	System for reporting critical incidents
Monitoring the performance of the delivery of healthcare	Monitoring of health services by individuals or healthcare organisations, for example by comparing with an external standard
Communities of practice	Groups of people with a common interest who deepen their knowledge and expertise in this area by interacting on an ongoing basis
Continuous quality improvement	An iterative process to review and improve care that includes involvement of healthcare teams, analysis of a process or system, a structured process improvement method or problem solving approach, and use of data analysis to assess changes
Educational games	The use of games as an educational strategy to improve standards of care
Educational materials	Distribution to individuals, or groups, of educational materials to support clinical care, i.e., any intervention in which knowledge is distributed. For example this may be facilitated by the internet, learning critical appraisal skills; skills for electronic retrieval of information, diagnostic formulation; question formulation
Educational meetings	Courses, workshops, conferences or other educational meetings
Educational outreach visits, or academic detailing	Personal visits by a trained person to health workers in their own settings, to provide information with the aim of changing practice

Clinical practice guidelines	Clinical guidelines are systematically developed statements to assist healthcare providers and patients to decide on appropriate health care for specific clinical circumstances' (US IOM)
Inter-professional education	Continuing education for health professionals that involves more than one profession in joint, interactive learning
Local consensus processes	Formal or informal local consensus processes, for example agreeing a clinical protocol to manage a patient group, adapting a guideline for a local health system or promoting the implementation of guidelines
Local opinion leaders	The identification and use of identifiable local opinion leaders to promote good clinical practice
Managerial supervision	Routine supervision visits by health staff
Patient-mediated interventions	Any intervention aimed at changing the performance of healthcare professionals through interactions with patients, or information provided by or to patients
Public release of performance data	Informing the public about healthcare providers by the release of performance data in written or electronic form
Reminders	Manual or computerized interventions that prompt health workers to perform an action during a consultation with a patient, for example computer decision support systems
Routine patient-reported outcome measures	Routine administration and reporting of patient-reported outcome measures to providers and/or patients
Tailored interventions	Interventions to change practice that are selected based on an assessment of barriers to change, for example through interviews or surveys

From Effective Practice and Organisation of Care (EPOC). EPOC Taxonomy; 2015. Available at: https://epoc.cochrane.org/epoc-taxonomy.

Data Sources and Search Strategy

In April 2018, a literature search strategy was designed in collaboration with an information specialist using variations on the search terms "opioid", "surgery" and "prescription" (Table 3.2). The following databases were searched: MEDLINE, EMBASE, CINAHL, PsycINFO, the Database of Abstracts of Reviews of Effectiveness (DARE) and the Cochrane Central Register of Controlled Trials (CENTRAL). I also searched ClinicalTrials.gov, the International Standard Randomized Controlled Trial Number (ISRCTN) registry and the first 10 pages of Google Scholar to identify any unpublished studies. Citation tracking was performed for all included studies, and the references of all included studies were manually reviewed to identify any additional citation.

No language or date restriction was imposed. The initial search was run on April 20th 2018 and subsequently updated on December 14th 2018.

Table 3. 2 Literature Search Strategies

Database	Strategy
MEDLINE	1 exp Narcotics/
	2 exp Opiate Alkaloids/
	3 opioid*.mp.
	4 opiate*.mp.
	5 opium*.mp.
	6 narcotic*.mp.
	7 alfentanil.mp.
	8 buprenorphine.mp.
	9 butorphanol.mp.
	10 codeine.mp.
	11 dextropropoxyphene.mp.
	12 fentan?l.mp.
	13 hydrocodone.mp.
	14 hydromorphone.mp.
	15 levorphanol.mp.
	16 meperidine.mp.
	17 methadone.mp.
	18 morphine.mp.
	19 nalbuphine.mp.
	20 normethadone.mp.
	21 oxycodone.mp.
	22 pentazocine.mp.
	23 pethidine.mp.
	24 propoxyphene.mp.
	25 remifentanil.mp.
	26 sufentanil.mp.
	27 tapentadol.mp.
	28 tramadol.mp.
	29 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28
	30 Perioperative Care/
	31 Postoperative Care/
	32 Perioperative Period/
	33 exp Postoperative Period/
	34 Pain, Postoperative/
	35 exp Surgical Procedures, Operative/
	36 exp Specialties, Surgical/
	37 Surgeons/
	38 su.fs.
	39 (surgery or surgeries or surgical* or surgeon*).tw,kf.
	40 postsurg*.tw,kf.
	41 (operate* or operative* or operation or operations).tw,kf.
	42 (postop* or post-op).tw,kf.
	43 resect*.tw,kf.
	44 postresect*.tw,kf.

	45	perioperative*.tw,kf.
	46	peroperative*.tw,kf.
	47	30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46
	48	29 and 47
	49	Drug Therapy/
	50	Drug Dosage Calculations/
	51	exp Drug Prescriptions/
	52	Inappropriate Prescribing/
	53	Practice Patterns, Physicians'/
	54	prescription*.tw,kf.
	55	prescrib*.tw,kf.
	56	((drug* or medication*) adj4 (discard* or dispos*)).tw,kf.
	57	49 or 50 or 51 or 52 or 53 or 54 or 55 or 56
	58	29 and 47 and 57
EMBASE	1	exp narcotic analgesic agent/
	2	opioid*.mp.
	3	opiate*.mp.
	4	opium*.mp.
	5	narcotic*.mp.
	6	alfentanil.mp.
	7	buprenorphine.mp.
	8	butorphanol.mp.
	9	codeine.mp.
	10	dextropropoxyphene.mp.
	11	fentan?l.mp.
	12	hydrocodone.mp.
	13	hydromorphone.mp.
	14	levorphanol.mp.
	15	meperidine.mp.
	16	methadone.mp.
	17	morphine.mp.
	18	nalbuphine.mp.
	19	normethadone.mp.
	20	oxycodone.mp.
	21	pentazocine.mp.
	22	pethidine.mp.
	23	propoxyphene.mp.
	24	remifentanil.mp.
	25	sufentanil.mp.
	26	tapentadol.mp.
	27	tramadol.mp.
	28	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27
	29	perioperative period/
	30	exp postoperative period/
	31	exp surgery/
	32	exp surgeon/
	33	surgical patient/
	34	postoperative pain/
	35	su.fs.
	36	(surgery or surgeries or surgical* or surgeon*).tw,kw.
	37	postsurg*.tw,kw.
	38	(operate* or operative* or operation or operations).tw,kw.
	39	(postop* or post-op).tw,kw.
	40	resect*.tw,kw.

	41 postresect*.tw,kw. 42 perioperative*.tw,kw. 43 peroperative*.tw,kw. 44 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 45 dose calculation/ 46 drug misuse/ 47 prescription/ 48 exp inappropriate prescribing/ 49 clinical practice/ 50 drug utilization/ 51 prescription*.tw,kw. 52 prescrib*.tw,kw. 53 ((drug* or medication*) adj4 (discard* or dispos*)).tw,kw. 54 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 55 28 and 44 and 54 56 limit 55 to embase
CINHAL	1. (MH “Narcotics+”) 2. (MH “Analgesics, Opioid+”) 3. (MH “Narcotic Antagonists+”) 4. TX opioid* 5. TX opiate* 6. TX opium* 7. TX narcotic* 8. TX alfentanil 9. TX buprenorphine 10. TX butorphanol 11. TX codeine 12. TX dextropropoxyphene 13. TX fentan?l 14. TX hydrocodone 15. TX hydromorphone 16. TX levorphanol 17. TX meperidine 18. TX methadone 19. TX morphine 20. TX nalbuphine 21. TX normethadone 22. TX oxycodone 23. TX pentazocine 24. TX pethidine 25. TX propoxyphene 26. TX remifentanil 27. TX sufentanil 28. TX tapentadol 29. TX tramadol 30. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 31. (MH “Perioperative Care”) 32. (MH “Postoperative Care+”) 33. (MH “Postoperative Period”) 34. (MH “Postoperative Pain”)

	35. (MH “Surgery, Operative+”) 36. (MH “Specialties, Surgical+”) 37. (MH “Surgeons”) 38. MW “SU” 39. S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 40. (MH “Drug Therapy”) 41. (MH “Prescriptions, Drug”) 42. (MH “Inappropriate Prescribing”) 43. (MH “Prescribing Patterns”) 44. TI prescription* OR AU prescription* 45. TI prescrib* OR AB prescrib* 46. TI (((drug* or medication*) N4 (discard* or dispos*))) AND AB (((drug* or medication*) N4 (discard* or dispos*))) 47. S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 48. S30 AND S39 AND S47
PsycINFO	1 exp analgesic drugs/ 2 exp narcotic drugs/ 3 opioid*.mp. 4 opiate*.mp. 5 opium*.mp. 6 narcotic*.mp. 7 alfentanil.mp. 8 buprenorphine.mp. 9 butorphanol.mp. 10 codeine.mp. 11 dextropropoxyphene.mp. 12 fentan?l.mp. 13 hydrocodone.mp. 14 hydromorphone.mp. 15 levorphanol.mp. 16 meperidine.mp. 17 methadone.mp. 18 morphine.mp. 19 nalbuphine.mp. 20 normethadone.mp. 21 oxycodone.mp. 22 pentazocine.mp. 23 pethidine.mp. 24 propoxyphene.mp. 25 remifentanil.mp. 26 sufentanil.mp. 27 tapentadol.mp. 28 tramadol.mp. 29 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 30 postsurgical complications/ 31 exp SURGERY/ 32 surgeons/ 33 surgical patients/ 34 (surgery or surgeries or surgical* or surgeon*).ti,ab,hw. 35 postsurg*.ti,ab,hw. 36 (operate* or operative* or operation or operations).ti,ab,hw. 37 (postop* or post-op).ti,ab,hw. 38 resect*.ti,ab,hw.

	39	postresect*.ti,ab,hw.
	40	perioperative*.ti,ab,hw.
	41	peroperative*.ti,ab,hw.
	42	30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41
	43	drug therapy/
	44	drug dosages/
	45	prescription drugs/
	46	exp "prescribing (drugs)"/
	47	prescription*.ti,ab,hw.
	48	prescrib*.ti,ab,hw.
	49	((drug* or medication*) adj4 (discard* or dispos*)).ti,ab,hw.
	50	43 or 44 or 45 or 46 or 47 or 48 or 49
	51	29 and 42 and 50
DARE	1	Narcotics.kw.
	2	Analgesics, Opioid.kw.
	3	Opiate Alkaloids.kw.
	4	opioid*.tw.
	5	opiate*.tw.
	6	opium*.tw.
	7	narcotic*.tw.
	8	alfentanil.tw.
	9	buprenorphine.tw.
	10	butorphanol.tw.
	11	codeine.tw.
	12	dextropropoxyphene.tw.
	13	fentan?l.tw.
	14	hydrocodone.tw.
	15	hydromorphone.tw.
	16	levorphanol.tw.
	17	meperidine.tw.
	18	methadone.tw.
	19	morphine.tw.
	20	nalbuphine.tw.
	21	normethadone.tw.
	22	oxycodone.tw.
	23	pentazocine.tw.
	24	pethidine.tw.
	25	propoxyphene.tw.
	26	remifentanil.tw.
	27	sufentanil.tw.
	28	tapentadol.tw.
	29	tramadol.tw.
	30	1 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
	31	Perioperative Care.kw.
	32	Postoperative Care.kw.
	33	Perioperative Period.kw.
	34	Postoperative Period.kw.
	35	Pain, Postoperative.kw.
	36	Surgical Procedures, Operative.kw.
	37	Specialties, Surgical.kw.
	38	Surgeons.kw.
	39	su fs.kw.
	40	(surgery or surgeries or surgical* or surgeon*).tw.
	41	postsurg*.tw.
	42	(operate* or operative* or operation or operations).tw.

	43	(postop* or post-op).tw.
	44	resect*.tw.
	45	postresect*.tw.
	46	perioperative*.tw.
	47	peroperative*.tw.
	48	31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47
	49	Drug Therapy.kw.
	50	Drug Dosage Calculations.kw.
	51	Prescription Drug Misuse.kw.
	52	Drug Prescriptions.kw.
	53	Inappropriate Prescribing.kw.
	54	Practice Patterns, Physicians'.kw.
	55	prescription*.tw.
	56	prescrib*.tw.
	57	((drug* or medication*) adj4 (discard* or dispos*)).tw.
	58	49 or 50 or 52 or 53 or 54 or 55 or 56 or 57
	59	30 and 48 and 58
CENTRAL	1	exp Narcotics/
	2	exp Opiate Alkaloids/
	3	opioid*.tw.
	4	opiate*.tw.
	5	opium*.tw.
	6	narcotic*.tw.
	7	alfentanil.tw.
	8	buprenorphine.tw.
	9	butorphanol.tw.
	10	codeine.tw.
	11	dextropropoxyphene.tw.
	12	fentan?l.tw.
	13	hydrocodone.tw.
	14	hydromorphone.tw.
	15	levorphanol.tw.
	16	meperidine.tw.
	17	methadone.tw.
	18	morphine.tw.
	19	nalbuphine.tw.
	20	normethadone.tw.
	21	oxycodone.tw.
	22	pentazocine.tw.
	23	pethidine.tw.
	24	propoxyphene.tw.
	25	remifentanil.tw.
	26	sufentanil.tw.
	27	tapentadol.tw.
	28	tramadol.tw.
	29	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28
	30	Perioperative Care/
	31	Postoperative Care/
	32	Perioperative Period/
	33	exp Postoperative Period/
	34	Pain, Postoperative/
	35	exp Surgical Procedures, Operative/
	36	exp Specialties, Surgical/
	37	Surgeons/

	38 su.fs. 39 (surgery or surgeries or surgical* or surgeon*).ti,ab,hw. 40 postsurg*.ti,ab,hw. 41 (operate* or operative* or operation or operations).ti,ab,hw. 42 (postop* or post-op).ti,ab,hw. 43 resect*.ti,ab,hw. 44 postresect*.ti,ab,hw. 45 perioperative*.ti,ab,hw. 46 peroperative*.ti,ab,hw. 47 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 48 Drug Therapy/ 49 Drug Dosage Calculations/ 50 exp Prescription Drug Misuse/ 51 exp Drug Prescriptions/ 52 Inappropriate Prescribing/ 53 Practice Patterns, Physicians'/ 54 prescription*.ti,ab,hw. 55 prescrib*.ti,ab,hw. 56 ((drug* or medication*) adj4 (discard* or dispos*)).ti,ab,hw. 57 48 or 49 or 51 or 52 or 53 or 54 or 55 or 56 58 29 and 47 and 57
ClinicalTrials.gov	prescribing OR prescription|opioid
ISRCTN	(opioid OR narcotic) AND (prescribing OR prescription)
Google Scholar	(opioid OR narcotic) AND (prescribing OR prescription) AND (surgery OR surgical OR surgeon OR operative OR operate

Study Selection and Data Extraction

All citations identified through my literature search were uploaded to the systematic review software DistillerSR (Evidence Partners, ON, Canada). Two reviewers independently reviewed each citation against my eligibility criteria in a two-stage process: 1) title and abstract and 2) full-text. Data extraction was performed by one reviewer using pre-specified Cochrane EPOC data collection forms,[131] and a second reviewer verified all entries. The following data were extracted for each study: general information, population and setting, study period, methods, participants, intervention group, outcomes, results and applicability. During all stages of study selection and data extraction, disagreements between reviewers were resolved through discussion.

Quality Assessment

The risk of bias in individual studies was assessed according to study design using criteria suggested by the Cochrane EPOC group.[132] Two reviewers independently appraised all studies. All disagreements were resolved through discussion and consensus.

For randomized controlled trials (RCT), I assessed the risk of bias on the domains of random sequence generation, allocation concealment, similar baseline outcome measurements, similar baseline characteristics, incomplete outcome data, knowledge of the allocated interventions adequately prevented during the study, protection against contamination, selective outcome reporting and other risks of bias. The risk of bias in each domain was rated as low, unclear or high. A summary risk of bias was derived for each study as suggested by Cochrane EPOC: low if all domains were at a low risk of bias, unclear if one or more domain had an unclear risk of bias and high if one or more domain had a high risk of bias.[133]

For pre-post studies and interrupted time series, I assessed the risk of bias on the domains of intervention independent of other changes, shape of the intervention pre-specified, intervention unlikely to affect data collection, knowledge of the allocated interventions adequately prevented during the study, incomplete outcome data, selective outcome reporting and other risks of bias. The risk of bias for each domain was rated as low, unclear or high. An overall risk of bias was assigned based on current practices in the literature: an overall low risk of bias if all individual domains were rated to be low, an overall medium risk of bias if one or two criteria were rated as high or unclear and an overall high risk of bias if more than two criteria were scored as high or unclear.[134-136]

The risk of bias in cohort studies was assessed using the Newcastle-Ottawa Quality Assessment Scale for cohort studies.[137] Domains assessed included the representativeness of the

exposed cohort, the selection of the non-exposed cohort, the ascertainment of exposure, the demonstration that the outcome of interest was not present at the start of the study, the comparability of the two cohorts on the basis of the design or analysis, the assessment of outcome, the length of follow-up and the adequacy of follow-up. The risk of bias in individual domains was represented in the allocation of stars. A maximum of one star could be awarded to each individual item, except on the domain of comparability where two stars could be awarded.

Data Synthesis

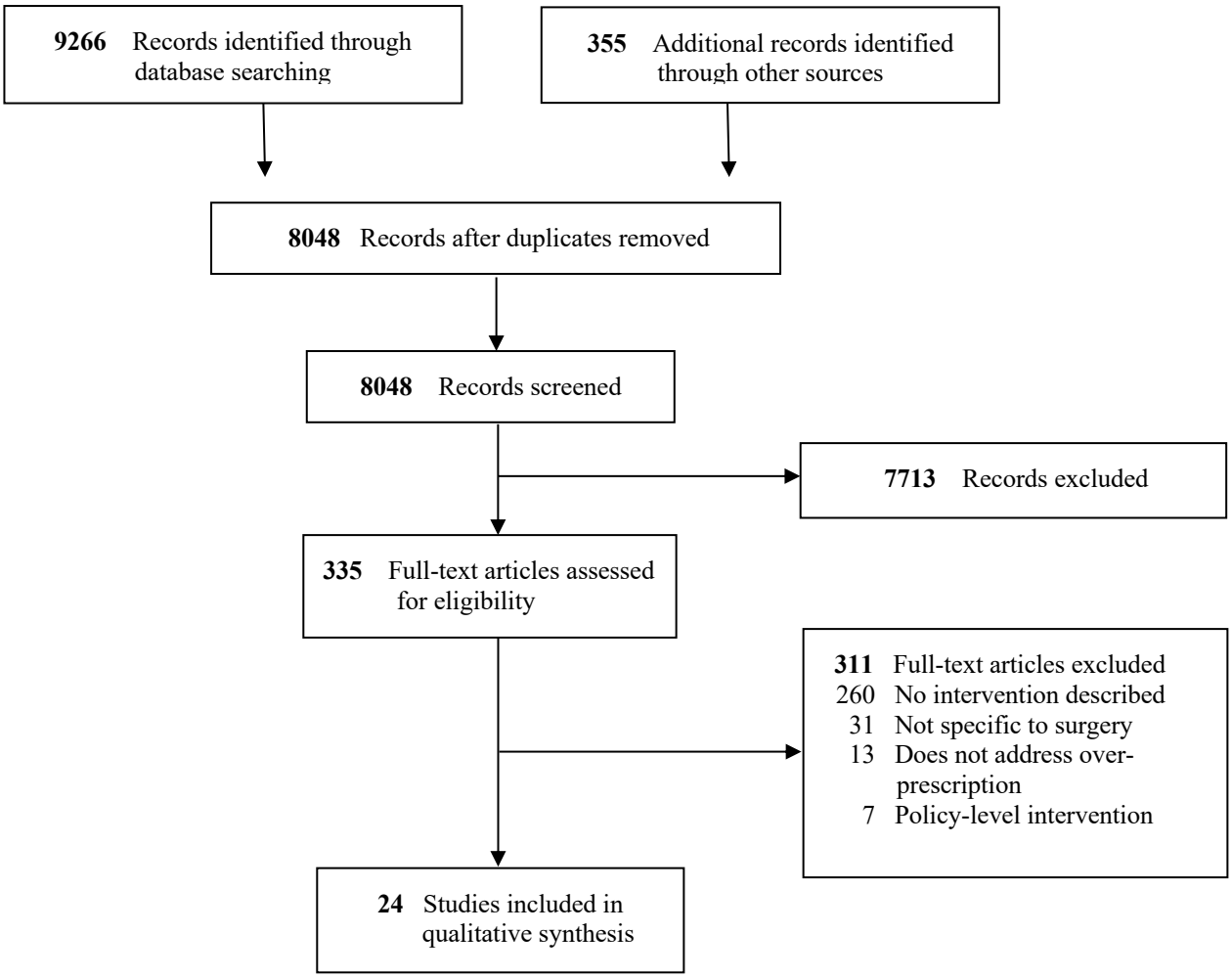
I performed a descriptive synthesis of identified interventions and their effectiveness in reducing the amount of opioid prescribed at discharge after surgery. For each study, I calculated the absolute change in the average amount of opioid prescribed with associated 95% confidence intervals (CI). In order to standardize opioid prescriptions across studies, I converted the amount prescribed to milligram morphine equivalents (MME) using conversion factors provided in the 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain.[138] When only a number of opioid tablets was reported, I calculated MMEs assuming that these represented 5-mg tablets of oxycodone. When means were not reported, they were estimated based on available statistics using the methods proposed by Wan *et al.*[139] In order to compare changes in mean prescribed MME, two-sample t tests were conducted using summary measures in SAS 9.4 (Cary, NC, USA). Given the anticipated heterogeneity in study populations and the natures of intervention, quantitative synthesis was not performed.

RESULTS

I identified 9,266 citations from MEDLINE, EMBASE, CINAHL, PsycINFO, DARE and CENTRAL (Figure 3.1). An additional 355 citations were retrieved from Google Scholar, Clinical

Trials.gov and ISRCTN. After de-duplication, the titles and abstracts of 8,048 unique citations were screened against my eligibility criteria, from which 7,713 were excluded. Subsequently, the full-text publications of 335 citations were retrieved and assessed for inclusion. Twenty-four studies were retained for my descriptive synthesis. No additional study was identified through tracking citations and by manually reviewing the references of included studies.

Figure 3. 1 PRISMA Flow Chart of Article Selection



Study Characteristics

Characteristics of included studies are presented in Table 3.3. I identified 6 types of behavioral interventions: local consensus-based processes (18 studies), patient-mediated interventions (2 studies), clinical practice guidelines (1 study), inter-professional education (1 study), educational meetings (1 study) and clinician reminder (1 study). All studies were written in English. Most studies were published within the past 3 years from tertiary care academic medical centers in the United States. Two studies originated from Canadian institutions[43,66], and 1 study originated from Australia[140]. Only one RCT was identified.[141] Of the remaining 23 non-randomized studies, 19 were uncontrolled pre-post studies, 2 were interrupted time series studies, and 2 were cohort studies. 3 studies were conference abstracts.[43,142,143] In total, post-surgical opioid prescribing at discharge for 21 204 patients was evaluated (11 585 pre-intervention/control, 9 619 post-intervention/exposed). Included participants underwent a variety of procedures including plastic, general, obstetric, gynecologic, thoracic, urologic, oral and maxillofacial, vascular and orthopedic surgery. The majority of studies excluded patients with a history of chronic pain or opioid use prior to surgery. Patients who developed post-operative complications were often excluded as well as those who had any contra-indications to the use of non-opioid pain medication.

Table 3. 3 Characteristics of Studies Evaluating Behavioral Interventions to Decrease Opioid Over-Prescribing After Surgery

Author	Year of Publication	Country	Design	Setting	Study Period	No. of Participants (pre-intervention/control, post-intervention/treatment)	Type of Surgery	Exclusion Criteria
Local Consensus Processes								
Dwyer *et al.*	2018	United States	Uncontrolled pre-post[1]	Hospital-based practice	04/2016 – 09/2016	381 (236, 145)	Plastic	< 18 years old Open fracture Chronic opioid use History of opioid abuse or pain syndrome
Earp *et al.*	2018	United States	Uncontrolled pre-post	Academic trauma center	10/2015 – 12/2016	518 (231, 287)	Orthopedic	Post-operative admission Non-protocol procedure Polytrauma Chronic opioid therapy < 18 years old
Gerrish *et al.*	2018	United States	Retrospective cohort	Academic tertiary care center	11/2014 – 11/2016	775 (451, 324)	General	NA
Hartford *et al.*	2018	Canada	Uncontrolled pre-post	Academic tertiary care center	07/2017 – 04/2018	416 (224, 192)	General	Pre-operative opioid use Chronic pain conditions Chronic kidney disease or nephropathy Active peptic ulcer disease
Hill *et al.*	2018	United States	Uncontrolled pre-post	Academic center	06/2016 – 09/2016	915 (692, 223)	General	Pre-op opioid use History of opioid abuse Postoperative complications

Holland *et al.*	2019	United States	Uncontrolled pre-post	Academic tertiary care center	10/2017 – 04/2018	372 (191, 181)	Obstetric	Contraindication to acetaminophen or NSAIDs History of opioid dependence General anesthesia Complex surgery Non-English-speaking
Howard *et al.*	2018	United States	Interrupted time series	Academic center	01/2015 – 03/2017	370 (170, 200)	General	NA
Howard *et al.*	2018	United States	Uncontrolled pre-post	Academic center	01/2016 – 08/2017	1153 (558, 595)	General	Postoperative complication Presentation to emergency department within 30 days after operation
Kim *et al.*	2018	United States	Uncontrolled pre-post	Houston Methodist Hospital	NA	106 (NA, 106)[1]	Thoracic	Urgent or emergent operation
Lee *et al.*	2018	United States	Interrupted time series	Academic center	07/2016 – 09/2017	847 (240, 607)	General	NA
Mark *et al.*	2018	United States	Uncontrolled pre-post	Tertiary care cancer center	07/2016 – 06/2018	1231 (626, 605)	Gynecologic	NA
Rojas *et al.*	2018	United States	Retrospective cohort	Maimonides Medical Center	09/2017 – 02/2018	157 (67, 90)	General	Diabetes with peripheral neuropathy Substance dependence
Srikandarajah *et al.*	2018	Canada	Uncontrolled pre-post	University-affiliated community teaching hospital	04/2017 – 01/2018	238 (129, 109)	General	NA
Stanek *et al.*	2015	United States	Uncontrolled pre-post	Academic center	2011 - 2013	159 (63, 96)	Plastic	> 1 procedure Prescribed opioids preoperatively

Starks *et al.*	2018	United States	Uncontrolled pre-post	University Hospitals Case Medical Center	NA	80 (20, 60)	Urologic	NA
Stepan *et al.*	2018	United States	Uncontrolled pre-post	Academic center	07/2016 – 01/2018	1348 (435, 913)	Plastic	Overnight stay in hospital Procedure that could not be categorized into guidelines Prescription involving high-dose opioids
Thiels *et al.*	2017	United States	Uncontrolled pre-post	Mayo Clinic	11/2015 – 09/2016	45 (23, 22)[2]	General	NA
Wagner *et al.*	2018	United States	Uncontrolled pre-post	University of Minnesota	02/2016 – 10/2016	8071 (5279, 2792)	Oral and maxillofacial	NA
Patient-Mediated Intervention								
Sugai *et al.*	2013	United States	Randomized controlled trial	University of Hawai'i	01/2008 – 10/2011	135 (66, 69)	Plastic	Chronic pain History of substance abuse History of opioid use Allergy to acetaminophen, COX-2 inhibitors, gabapentin, hydrocodone
Prabhu *et al.*	2017	United States	Uncontrolled pre-post	Academic center	04/2016 – 06/2016	50 (NA, 50)[1]	Obstetric	History of chronic pain or chronic opioid use Age < 18 years Non–English-speaking Post-op stay > 7 days Use of oral opioids other than oxycodone Contraindications to

								acetaminophen or NSAIDs
Clinical Practice Guidelines								
Karst *et al.*	2018	United States	Uncontrolled pre-post	Nashville Veterans Affairs Medical Center	07/2015 – 03/2018	60 (24, 36)	Vascular	Chronic opioid use or abuse Hospitalization > 72 hours Reoperation
Inter-Professional Education								
Tran *et al.*	2017	Australia	Uncontrolled pre-post	Academic hospital	02/2014 – 06/2014	661 (320, 341)	Orthopedic General Plastic Other	Patients discharged on weekends
Educational Meetings								
Chiu *et al.*	2018	United States	Uncontrolled pre-post	Tertiary care academic center	07/2016 – 07/2017	206 (93, 113)	General	NA
Reminder								
Chiu *et al.*	2018	United States	Uncontrolled pre-post	Multicenter health system	02/2017 – 08/2017	2910 (1447, 1463)	General Urologic Orthopedic Gynecologic	Pediatric patient Patients with missing data

Abbreviations: NA, Not Available; NSAID, non-steroidal anti-inflammatory drug; COX, cyclooxygenase

Risk of Bias Within Studies

All pre-post and interrupted time series studies were found to have at least an overall medium risk of bias, and an overall high risk of bias was found in seven studies (Tables 3.4, 3.5 and 3.6).[65,80,128,143-146] Among these studies, an unclear or high risk of bias was found regarding the prevention of the knowledge of the studied intervention. Moreover, a high risk of bias was found regarding the independence of the intervention from other changes (12 studies), the incomplete reporting of outcome data (5 studies), the lack of pre-specified shape of the intervention effect (1 study) and the selective reporting of outcomes (1 study). In the only RCT evaluating the effect of pre-operative patient education on requests for hydrocodone prescriptions,[141] an overall high risk of bias was found due to dissimilar baseline characteristics, different baseline outcomes and a lack of allocation concealment, blinding and protection against contamination (Table 3.5). For the two cohort studies evaluating the effect of enhanced post-surgical recovery protocols on opioid prescriptions,[147,148] six stars (out of a maximum of nine) were assigned to each of the study due to a lack of representativeness of the exposed cohort, a lack of demonstration that the outcome of interest was not present at the start of the study and a lack of comparability of the studied cohorts (Table 3.6).

Table 3. 4 Risk of Bias of Pre-Post Studies And Interrupted Time Series Evaluating Behavioral Interventions to Decrease Opioid Prescribing After Surgery

Study	Intervention independent of other changes	Shape of the intervention effect pre-specified	Intervention unlikely to affect data collection	Knowledge of the allocated interventions adequately prevented during the study	Incomplete outcome data	Selective outcome reporting	Other risks of bias	Overall risk of bias*
Local Consensus Processes								
Dwyer *et al.* 2017	High	Low	Low	High	Low	Low	Low	Medium
Earp *et al.* 2018	Low	Low	Low	High	Low	Low	Unclear	Medium
Hartford *et al.* 2018	Low	Low	Low	High	High	Low	Low	Medium
Hill *et al.*, 2018	High	Low	Low	High	High	Low	Low	High
Holland *et al.* 2018	Low	Low	Low	High	Low	Low	Low	Medium
Howard *et al.* 2017	Low	Low	Low	High	Low	Low	Low	Medium
Howard *et al.* 2018	High	Low	Low	High	Low	Low	Low	Medium
Kim *et al.* 2018	High	Unclear	Low	High	Low	Low	Unclear	High
Lee *et al.* 2018	Low	Low	Low	High	Low	Low	Low	Medium
Mark *et al.* 2018	High	Low	Low	High	Low	Low	Low	Medium
Srikandarajah *et al.* 2018	High	Low	Low	High	Low	Low	Low	Medium
Stanek *et al.* 2015	High	Low	Low	High	Low	Low	Low	Medium
Starks *et al.* 2018	High	Low	Low	High	High	Low	Low	High
Stepan *et al.* 2018	Low	Low	Low	High	Low	Low	Unclear	Medium

Thiels *et al.* 2017	High	Low	Low	High	Low	Low	Low	Medium
Wagner *et al.* 2018	Unclear	Unclear	Low	High	Unclear	Unclear	Unclear	High
Patient-Mediated Intervention								
Prabhu *et al.* 2017	High	Low	Low	High	High	Low	Low	High
Clinical Practice Guidelines								
Karts *et al.* 2018	High	Low	Low	High	High	Low	Low	High
Inter-Professional Education								
Tran *et al.* 2017	High	Low	Low	Unclear	Low	Low	Low	Medium
Educational Meetings								
Chiu *et al.* 2018	High	High	Unclear	High	Low	High	Low	High
Reminder								
Chiu *et al.* 2018	Low	Low	Low	High	Low	Low	Low	Medium

* An overall risk of bias was assigned based on current practices in the literature: an overall low risk of bias if all individual domains were rated to be low, an overall medium risk of bias if one or two criteria were rated as high or unclear and an overall high risk of bias if more than two criteria were scored as high or unclear.[134-136]

Table 3. 5 Risk of Bias of Randomized Controlled Trial Evaluating Behavioral Interventions to Decrease Opioid Prescribing After Surgery

Study	Random Sequence Generation	Allocation Concealment	Baseline Outcome Measurements Similar	Baseline Characteristics Similar	Incomplete Outcome Data	Knowledge of the Allocated Interventions Adequately Prevented During the Study	Protection Against Contamination	Selective Outcome Reporting	Other Risks of Bias	Overall Risk of Bias*
Sugai *et al.* 2013	Low	Unclear	Unclear	High	Low	High	High	Low	Low	High

*An overall risk of bias was determined based on methods suggested by Cochrane EPOC: low if all domains were at a low risk of bias, unclear if one or more domain had an unclear risk of bias, and high if one or more domains had a high risk of bias.

Table 3. 6 Risk of Bias of Cohort Studies Evaluating Behavioral Interventions to Decrease Opioid Prescribing After Surgery

Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Total Stars
Gerrish *et al.* 2018	-	1 star	1 star	-	1 star	1 star	1 star	1 star	6
Rojas *et al.* 2018	-	1 star	1 star	-	1 star	1 star	1 star	1 star	6

Summary of Evidence by Intervention

Local Consensus-Based Processes

18 studies evaluated the effect of institutional opioid prescribing recommendations developed through local consensus and its effect on opioid prescribing (Table 3.7). Various methods were used to develop opioid prescribing recommendations, although few studies provided a detailed description of the development process, and no institution based their recommendations on a formal systematic review of the literature. Patient survey data on post-discharge opioid consumption were commonly used to guide the recommendation development process.[31,105,109,149,150] For example, using patient-reported data on post-operative opioid consumption and pain control after common outpatient general surgical procedures, Hill *et al.* calculated an "ideal" number of tablets to satisfy the consumption need for 80% of patients after each procedure.[31] Other studies based their recommendations on data derived from a review of institutional prescription practices.[38,145,151] In an effort to standardize opioid prescriptions after hand surgery at their institution, Stanek *et al.* preferentially used the mode of the observed distribution of prescription amounts to derive their recommendation.[38] Although a local opioid prescribing protocol was the main intervention in all of these studies, a number of co-interventions were described: provider education (8 studies), patient education (6 studies), shared decision-making (1 study), distribution of memory aid (1 study) and electronic order set default change (1 study).

The overwhelming majority of studies describing a local opioid prescribing consensus reported a decrease in the mean amount of opioid prescribed at discharge immediately after the intervention (Table 3.7). This reduction in narcotic prescription ranged from 34.4 to 212.3 MMEs,

which corresponds to a decrease of 4 to 28 tablets of 5-mg oxycodone. The greatest reduction in prescribed opioid was observed in a report by Howard *et al.*, who developed post-operative prescribing guidelines based on patient survey data regarding opioid consumption, use of non-opioids and pain intensity after elective laparoscopic cholecystectomy.[105] The authors then communicated these guidelines to surgical providers at their institution using video and oral presentations. Using an interrupted time series analysis, the authors demonstrated that, despite a preintervention trend towards a decreasing amount of opioid per prescription, the implementation of their guidelines was associated with a further decrease of 212.3 MMEs (95% CI 186.0, 239.3) and an increase in prescriptions for acetaminophen or ibuprofen (48.5% postintervention versus 21.2% preintervention, $p < 0.001$). Importantly, no difference was found regarding refill requests or pain scores when compared to the preintervention period.

Two studies specifically assessed whether this reduction in the prescription opioid at discharge was sustained long-term (Table 3.7).[38,152] In a study evaluating a multi-faceted intervention consisting of a multimodal pain management plan, provider education, distribution of memory aid and electronic order set default change, Stanek *et al.* found that opioid prescriptions after hand surgery were significantly reduced at one year after the implementation of the prescribing protocol compared to pre-protocol amounts, and this finding was present among all patients except those who underwent trigger finger releases. Importantly, similar rates of prescription refill were demonstrated at one year. A separate study by Stepan *et al.* studied the development of opioid prescribing recommendations and provider education after plastic surgery. In this study, the authors also demonstrated a sustained reduction in the amount of opioid prescribed at 11 months after guideline dissemination when compared to pre-guideline amounts (-161.8 MMEs, 95% CI -173.1, -150.4).

Few studies reported no reduction in prescribed opioids at discharge following the implementation of their recommendations (Table 3.7). Gerrish *et al.* assessed the effect of an enhanced recovery protocol after colorectal surgery on the amount of opioids prescribed at discharge, and they found that these patients were discharged with an average surplus of 64.9 MMEs compared to their off-protocol counterparts (95% CI 26.4 – 103.4). The authors theorized that an early discharge among patients treated on the enhanced recovery protocol may be associated with a higher level of pain at discharge that necessitated more opioids. Two other studies described reductions in opioid prescription that were not statistically significant among patients undergoing breast biopsy, lumpectomy, releases of the first dorsal compartment or trigger finger.[38,150] In both of these studies, however, a statistically significant reduction in opioid prescription was observed among patients undergoing other included surgical procedures.

The majority of studies describing a behavioral intervention involving local prescription recommendations did not demonstrate any increase in post-operative pain associated with a reduced amount of opioid prescribed (Table 3.7). However, there was evidence that post-operative pain was inadequately controlled in three studies.[142,149,153] In an interrupted time series analysis of opioid prescription trends after the development of institutional prescribing recommendations for laparoscopic cholecystectomy, Howard *et al.* observed that prescribed amounts also decreased after laparoscopic appendectomy by 87.9 MMEs (95% CI 68.0, 107.8). However, this was associated with an increased proportion of prescription refill in this patient subgroup (6.6% post-intervention versus 0.8% pre-intervention, p=0.01), which suggests that reductions in prescribed opioid at discharge must be done cautiously. A similar phenomenon was observed in two other studies among patients undergoing mastectomy with tissue expander reconstruction[142] or distal radius volar locked plating[153], although the difference observed in prescription refill did not reach

statistical significance. An increased proportion of requests for prescription refills was also observed in a cohort study by Gerrish *et al.* among patients treated on an enhanced recovery after surgery protocol (28.7% versus 18.9%, p=0.001).[147] However, patients treated on the protocol were discharged earlier and with a higher amount of opioid than their off-protocol counterparts (307.4 MMEs versus 242.5 MMEs, p=0.001), suggesting that the increased pain post-discharge was likely not a result of a decreased amount of opioid prescribed.

Patient-Mediated Intervention

Two studies evaluated the effect of interventions that aimed to change the behavior of health care providers through interactions with patients (Table 3.7). In a RCT, Sugai *et al.* studied the effect of pre-operative patient education on patient request of opioid prescription for use after aesthetic surgery.[141] In this study, patients were educated regarding endogenous opioids and the negative consequences associated with using synthetic opioids. The authors found that only 10% of patients who underwent education sessions requested opioids compared to 100% in the control group, and they experienced a lower intensity and duration of pain post-operatively. A second type of patient-mediated intervention was described by Prabhu *et al.*, who used a computer-based decision aid to help patients determine the amount of opioid they would be prescribed after cesarean delivery.[128] During a shared decision-making session involving verbal physician counselling and review of the decision aid, patients received information regarding anticipated pain, expected opioid use, benefits and risks of opioids and non-opioids as well as disposal and access of refill. Compared to a pre-intervention institutional standard of 40 opioid tablets per prescription, the authors found that the shared-decision making session resulted in a significant decrease in the amount of opioid prescribed by 150.0 MMEs (95% CI 133.5, 166.5). Post-

intervention, 8% of patients obtained a refill prescription and 90% of patients were satisfied or very satisfied with their pain management.

Clinical Practice Guidelines

One study examined trends in opioid prescribing after vascular surgery following the publication of the Centers for Disease Control and Prevention (CDC) opioid prescribing guidelines, which recommended 3 days or less of opioid therapy for acute pain (Table 3.7).[16] In their study, Karst *et al.* found that, compared to the pre-guideline publication period, the average amount of opioid prescribed decreased by 135.2 MMEs following guideline publication (95% CI 46.1, 224.3).[146] The authors further assessed the effect of monthly surgical resident education using the CDC guidelines, however they did not find any further statistically significant reduction in opioid prescribing (-21.4 MMEs, 95% CI -142.4, 185.2).

Educational Meetings

In a study by Chiu *et al.*, the effect of educating surgical interns regarding post-operative analgesia prescribing was assessed (Table 3.7).[80] All incoming surgical interns starting at an academic tertiary medical center underwent a resident-led educational presentation about the current opioid epidemic and a review of the literature on opioid over-prescribing, as well as recommendations for the dosing of opioid and non-opioid medications. Using a pre-post design, the authors then compared prescriptions written by surgical interns in their first two months of clinical duty to prescriptions written over the same period one year before and found a significant reduction in the amount of opioid per prescription by 83.0 MMEs (95% CI 51.8, 115.8).

Inter-Professional Education

Tran *et al.* described the effect of an inter-professional intervention involving pharmacist assistance in prescription preparation and its effect on the amount of opioid prescribed (Table 3.7).[140] Using a pre-post design, the authors compared prescriptions prepared by a pharmacist to those prepared by a junior physician for patients discharged from a surgical ward. When the pharmacists prepared discharge prescriptions and reviewed them with the physician prior to finalization, the average amount of opioid prescribed per patient decreased by 110.3 MMEs (95% CI 90.8, 129.0). Importantly, despite a reduced amount of opioid prescribed and supplied, no increase in hospital visit for post-operative pain was observed after the intervention.

Clinician Reminders

Finally, a recent study by Chiu *et al.* demonstrated that a simple electronic reminder targeted towards surgeons can effectively change their behavior (Table 3.7).[154] In their study, the authors changed the default number of opioid pills from 30 to 12 when prescribing within an electronic medical records system and assessed its effect on the amount of opioid prescribed after common surgical procedures. Following the implementation of the new default, a mean of 34.4 MMEs were prescribed less per patient (95% CI 27.5, 41.4), and this was not associated with any increase in the proportion of prescription refill (1.5% post-intervention versus 3.0% pre-intervention, p=0.41).

Opioid-Free Prescribing

In this review, I have identified a number of studies which showed that an opioid-free prescription at the time of discharge may be safe for certain surgical patients. In an uncontrolled

pre-post evaluation of a quality improvement initiative that involved prescribing opioids at discharge only to patients who required opioids during their hospital stay, Holland *et al.* found that 59.7% of patients were discharged home after a cesarean delivery without any prescription opioid, and no statistically significant change in requirement for additional prescriptions, pain scores and patient satisfaction post-intervention was observed.[97] In this study, the in-hospital elements of the quality improvement initiative involved the use of opioids only when requested by the patient, standing use of acetaminophen and non-steroidal anti-inflammatory drugs for 72 hours post-operatively and patient education. A separate report by Rojas *et al.* demonstrated that the use of an enhanced recovery after surgery protocol could completely eliminate the prescription of opioids at discharge after breast lumpectomy.[148] Pain management elements of this protocol involved pre-operative counseling regarding pain expectations and plan, pre-operative administration of acetaminophen and gabapentin, long-acting local analgesia infiltration prior to incision and prior to closure, administration of ketorolac during closure and the use of standing ibuprofen and acetaminophen for 4-5 days post-operatively. In this study, the prescription of opioids at discharge was eliminated for 90 patients treated on the protocol, and no significant difference was observed in pain scores compared to the off-protocol patients who were prescribed a median of 54.5 MMEs at discharge. Finally, Sugai *et al.* reported that post-operative pain could be managed without opioids in more than 90% of patients undergoing outpatient aesthetic surgery after undergoing pre-operative opioid education, and these patients did not appear to demonstrate any increased pain intensity or duration compared to patients who were prescribed opioids.[141] Among patients who were not prescribed any opioid at discharge, nearly a third were administered celecoxib and gabapentin pre-operatively, and all had access to acetaminophen on an as needed basis post-operatively.

Table 3. 7 Summary of Behavioral Interventions to Decrease Opioid Over-Prescribing At Discharge After Surgery

Study	Intervention	Prescription Outcome	Absolute Change in Prescription Outcome (95% CI)	Pain Control Outcome	Pain Control Post-Intervention (pre-intervention/control, p-value)	Risk of bias
Local Consensus Processes						
Dwyer *et al.* 2017[153]	1) Opioid prescribing recommendations 2) Patient education	Opioid tablet	CTR: -90.0 MME (-106.5, -73.5) VLP: -105.0 MME (-150.0, -60.0)	1) PR (%) 2) PS (%)	1) CTR: 1.7 (2.0, NA) VLP: 25.0 (9.4, 0.15) 2) CTR : 96.0 (NA) VLP : 88.0 (NA)	Medium
Earp *et al.* 2018[151]	Opioid prescribing protocol	ME	Tier 1: -74.4 MME (-88.9, -59.9) [1] Tier 2: -109.7 MME (-155.5, -63.9) [1] Tier 3: -98.4 MME (-143.5, -52.3) [1] Tier 4: -56.7 MME (-102.8, -10.6) [1] Tier 5: -123.0 MME (-203.5, -42.5)[1]	PR (%)	1.7 (6.5, <0.001)	Medium
Gerrish *et al.* 2018[147]	ERAS protocol	ME	64.9 MME (26.4, 103.4)	1) PR within 30 days (%) 2) PR between 30 and 60 days (%)	1) 28.7 (18.9, 0.001) 2) 11.1 (9.8, 0.54)	6 stars[2]
Hartford *et al.* 2018[66]	1) Postoperative pain management strategy 2) Intraoperative pain management strategy 2) Patient education 3) Provider education	ME	-47.0 MME (-51.3, -42.7)	1) Mean PL in 7 days 2) Good/very good pain control (%) 3) PR (%)	1) 2.3 (2.1, 0.10) 2) 85.0 (69.0, <0.001) 3) 2.6 (3.5, 0.62)	Medium
Hill *et al.* 2018[65]	1) Opioid prescribing recommendations 2) Provider education	Oxycodone tablet (5 mg)	PM: -110.3 MME (-124.5, -96.8) PM SLNB: -105.8 MME (-122.3, -89.3) LC: -118.5 MME (-140.3, -97.5) LIH: -108.8 MME (-137.3, -80.3) IH: -111.8 MME (-152.3, -71.3)	PR (%)	0.4 (NA)	High
Holland *et al.* 2019[97]	1) Opioid prescribing recommendations 2) Provider education 3) Shared decision-making	1) Patient discharged with opioids (%) 2) ME	1) –50.3 (NA) 2) -52.5 MME (-61.6, -43.5)	1) Number of additional prescription 2) Mean daily PL 3) PS (%)	1) 0 (2.1, 0.12) 2) 1.8-3.5 (2.0-3.3, NS) 3) 88.0 (90.0, 1.00)	Medium
Howard *et al.* 2017[105]	1) Opioid prescribing recommendations	1) Opioid tablet	1) -212.3 MME (-239.3, -186.0)	1) PR (%) 2) Median PL	1) 2.5 (4.1, 0.40) 2) 5.0 (5.0, 0.80)	Medium

	2) Provider education	2) Patients discharged with opioids (%)	2) -7.5 (NA)			
Howard *et al.* 2018[149]	1) Opioid prescribing recommendations 2) Provider education	ME	LSG : -155.7 MME (-177.9, -133.5) LA : -87.9 MME (-107.8, -68.0) LIHR : -77.1 MME (-105.8, -48.4) T/P : -38.9 MME (-46.3, -31.5)	PR (%)	LSG : 7.9 (5.2, 0.37) LA : 6.6 (0.8, 0.01) LIHR : 5.6 (1.7, 0.23) T/P : 2.0 (2.1, 0.94)	Medium
Kim *et al.* 2018[144]	ERAS protocol	Patients prescribed schedule II narcotics (%)	-94.4 (NA)	NA	NA	High
Lee *et al.* 2018[155]	1) Evidence-based prescribing guidelines 2) Prescriber education 3) Patient education	Oxycodone tablet (5 mg)	SM/WLE: -97.5 MME (-185.3, -9.8) L/BB: -90.0 MME (-187.5, 7.5)	PR (%)	SM/WLE: 13.0 (14.0, 0.80) L/BB: 4.0 (5.0, 0.70)	Medium
Mark *et al.* 2018[109]	1) Opioid prescription protocol 2) Patient education	ME	-197.6 MME (-212.9, -182.3)	1) Mean PL 2) PR (%)	1) 1.1 (1.3, 0.06) 2) 16.5 (16.6, 0.99)	Medium
Rojas *et al.* 2018[148]	ERAS protocol	ME	-57.3 MME (-63.5, -51.0)	1) Day 1 median PL 2) Week 1 median PL	1) 1.0 (3.0, 0.19) 2) 1.0 (1.0, 0.26)	6 stars[2]
Srikandarajah *et al.* 2018	Standardized prescription	Opioid tablet prescribed over 3 months	-56% (NA)	1) Mean PL 2) Mean satisfaction score	1) 3.85 (3.87, NA) 2) 4.4 (4.4, NA)	
Stanek *et al.* 2015[38]	1) Multimodal pain management plan 2) Provider education 3) Distribution of memory aid 3) Electronic order set default change 4) Patient education	Opioid tablet	FDC: -52.5 MME (-168.0, 62.9) WG: -52.5 MME (-96.8, -8.3) MF: -60.0 MME (-114.8, -5.3) TF: -15.0 MME (-48.8, 18.8) <u>Late Postprotocol[3]</u> FDC: -37.5 MME (-71.3, -3.8) WG: -37.5 MME (-71.3, -3.8) MF: -67.5 MME (-124.5, -10.5) TF: -15.0 MME (-49.5, 19.5)	PR (%)	FDC: 11.0 (17.0, NA) WG: 6.0 (12.0, NA) MF: 8.0 (29.0, NA) TF: 0.0 (4.0, NA) <u>Late Postprotocol[3]</u> FDC: 13.0 (17.0, NA) WG: 19.0 (12.0, NA) MF: 24.0 (29.0, NA) TF: 4.0 (4.0, NA)	Medium
Starks *et al.* 2018[145]	1) Pain management protocol 2) Patient education	Opioid tablet	-93.8 MME (-122.3, -65.3)	1) PR (%) 2) Mean PL 3) Mean worst PL	1) 1.7 (NA) 2) 3.4 (NA) 3) 4.9 (NA) 4) 3.6 (NA)	High

				4) Mean number of days until pain consistently mild without opioids 5) PS (%)	5) 88.3 (NA)	
Stepan *et al.* 2018[156]	1) Opioid prescribing recommendations 2) Provider education	ME	-138.1 MME (-149.6, -126.6) <u>Intermediate postguidelines</u>[4] -161.8 MME (-173.1, -150.4)	NA	NA	Medium
Thiels *et al.* 2017[142]	Opioid prescribing recommendations	ME[5]	Decreased	1) PR (%)[5] 2) PS (%)[5]	1) 22.7 (4.3, 0.10) 2) 72.7 (82.6, 0.49)	Medium
Wagner *et al.* 2018[143]	Opioid prescribing protocol	Opioid tablet	-52.5 MME (NA)	NA	NA	High
Patient-Mediated Intervention						
Sugai et al, 2013[141]	Patient education	Patient request of opioid prescription (%)	-91.3% (NA)	1) Mean PL for first 5 days 2) Duration of pain in days	1) 2.6-3.0 (3.1-3.2, NA) 2) 1.9-3.1 (4.2-4.9, NA)	High
Prabhu *et al.* 2017[128]	Shared decision-making	Oxycodone tablet (5 mg)	-150.0 MME (-166.5, -133.5)	1) PR (%) 2) PS (%)	1) 8.0 (NA) 2) 90.0 (NA)	High
Clinical Practice Guidelines						
Karst et al, 2018[146]	1) CDC opioid prescribing guidelines 2) Prescriber education	ME prescribed	<u>Post guideline publication</u> -135.2 MME (-224.3, -46.1) <u>Post prescriber education</u> -21.4 MME (-142.4, 185.251)	NA	NA	High
Educational Meetings						
Chiu *et al.* 2018[80]	Surgical intern education	ME prescribed	-83.0 MME (-115.8, -51.8)	NA	NA	High
Inter-Professional Education						
Tran *et al.* 2017[140]	Preparation of discharge prescription by pharmacists	Oxycodone (mg)	-110.3 MME (-129.0, -90.8)	PR (%)	0.0 (0.0, NA)	Medium
Reminder						

Chiu *et al.* 2018[154]	1) Electronic order set default change 2) Provider education	ME	-34.4 MME (-41.4, -27.5)	PR (%)	1.5 (3.0, 0.41)	Medium

Abbreviations: CI, confidence interval; CTR, carpal tunnel release; VLP, distal radius volar locked plating; MME, morphine milligram equivalent; ERAS, enhanced recovery after surgery; OME, oral morphine equivalent; NA, not available; PM, partial mastectomy; PM SLNB, partial mastectomy sentinel lymph node biopsy, LC, laparoscopic cholecystectomy; LIH, laparoscopic inguinal hernia repair; IH, inguinal hernia repair; NS, not significant; LSG, laparoscopic sleeve gastrectomy; LA, laparoscopic appendectomy; LIH, laparoscopic inguinal hernia repair; T/P, thyroidectomy/parathyroidectomy; SM/WLE, simple mastectomy/wide local excision for melanoma; L/BB, lumpectomy/breast biopsy; FDC, release of first dorsal compartment; WG, excision of wrist ganglion; MF, open reduction internal fixation of meta-carpal fracture; TF, trigger finger release; CDC, Center for Disease Control and Prevention; PR, prescription refill; PL, pain level; PS, patient satisfaction; ME, morphine equivalent

[1] Tier 1: carpal tunnel release, trigger finger release, DeQuervain's release, ganglion/mucous cyst excision
Tier 2: cubital tunnel in situ release
Tier 3: closed reduction pinning metacarpal/phalanx, extensor/flexor tendon repairs, tenolysis for lateral epicondylitis, cubital tunnel release with transposition
Tier 4: distal radius open reduction internal fixation, finger/carpometacarpal arthroplasty, Darrach procedure, elbow arthroscopy, shoulder arthroscopy without repairs
Tier 5: shoulder arthroscopy with rotator cuff/labral repair; elbow/shoulder open reduction internal fixation, wrist full/limited fusion, elbow arthroplasty

[2] Based on the Newcastle-Ottawa scale

[3] 1 year after protocol implementation

[4] 9 to 11 months after guideline dissemination

[5] Based on phases 2 and 3 of the quality initiative

DISCUSSION

I systematically reviewed the literature to identify effective behavioral strategies to reduce post-surgical opioid prescriptions at patient discharge. Using the framework of behavioral interventions proposed by the Cochrane EPOC group[130], I identified six types of interventions: local consensus-based processes, patient-mediated interventions, clinical practice guidelines, educational meetings, inter-professional education and clinician reminders. All six types of interventions have been shown to be effective in reducing the amount of opioid prescribed at discharge after surgery, and the majority of studies did not demonstrate that the control of post-operative pain was compromised. Importantly, the reductions in opioid prescription associated with the development and implementation of local prescribing recommendations were shown to be sustained at the hospital-level even at one-year post-implementation.

Our results suggest that, in the light of the ongoing epidemic of opioid-related harms, surgeons can change their opioid prescription practices at patient discharge, and that a number of strategies can be implemented at an institutional level to help them modify their behavior. These strategies can range from a simple alteration of the electronic prescribing default to more complex interventions involving the development of local post-surgical opioid prescribing recommendations by consensus. The current evidence indicates that the development of local opioid prescribing recommendations is the most common strategy reported in the literature and may lead to as much as 212.3 less MMEs prescribed at discharge after surgery, which translates into a reduction of approximately 28 tablets of 5-mg oxycodone. However, the wide range in the reduction in prescription opioid (-34.4 to -212.3 MMEs) associated with local prescription consensus suggests that the effectiveness of this strategy may be influenced by several factors such as the characteristics of the study population, the type of surgery evaluated, the pre-intervention

prescription amounts and the presence of additional components to the intervention. Nonetheless, the similar direction of effect among almost all studies evaluating a local prescribing consensus indicates that surgeons are in need of guidance for their opioid prescription practices and can readily change their behavior. Based on the strategies described in the included studies, institutions seeking to improve their practice could develop post-surgical opioid prescription recommendations that are informed by patient data on post-discharge opioid consumption or by existing prescription practice patterns. Consensus can then be achieved among all relevant providers, and the recommendations disseminated through formal educational sessions. Additional interventions, such as shared decision-making, memory aid distribution or electronic order set default change, can also be considered to provide further stimulus for behavior change.

Few studies were identified that evaluated the effectiveness of strategies that primarily involved a patient-mediated intervention, a clinical practice guideline, inter-professional education, an educational meeting or a clinician reminder. Although the reductions in prescription opioid associated with these strategies were less than those observed with a local prescribing consensus, these studies present effective novel approaches to prescribing that challenge traditional surgical practice. For example, involving the patient in a shared decision-making prescription process may improve patient autonomy in post-operative care and positively impact the post-discharge surgical recovery experience.[128]

However, reductions in the amount of opioid prescribed after surgery must be done with caution, as my review has identified instances where a decreased size of the discharge prescription may be associated with worse post-operative pain control. This was observed most prominently among patients undergoing laparoscopic appendectomy after the implementation of institutional opioid prescribing recommendations for laparoscopic cholecystectomy.[149] In this study, the

spillover effect of the guidelines led to a decrease in the amount of opioid prescribed for patients undergoing laparoscopic appendectomy by 87.9 MMEs (95% CI 68.0, 107.8), but also an increase in the proportion of prescription refill (6.6% post-intervention versus 0.8% pre-intervention, p=0.01). Although the refill rates remained overall low, this study demonstrated an unintended consequence of a local opioid prescribing consensus in that surgeons, stimulated by the implementation of a behavioral intervention, attempted to reduce their prescriptions for other surgical procedures without guidance, which resulted in the under-prescription of analgesia for patients undergoing appendectomy. While decreasing opioid over-prescribing is an important endeavor in light of the current opioid epidemic, we must not forget the importance of providing adequate post-operative analgesia and balance this with risks of excessive opioid prescribing. To this end, future strategies involving the development of post-surgical opioid prescription recommendations need to be clear and explicit regarding the patient population and surgical procedures they encompass, and surgeons should be cautious when trying to decrease the amount of opioid they prescribe when no good evidence or guidance exists.

In this review, I have also gathered evidence that an opioid-free prescription at the time of discharge may be safe for certain patients undergoing caesarean delivery, breast lumpectomy or outpatient aesthetic procedures. In these studies, elements that were common to the described interventions included the education of patients regarding expectations surrounding post-operative pain and the standing use of non-opioid analgesia. Although the success of an opioid-free post-operative pain management plan likely depends on a number of factors, such as the type of surgery, specific patient characteristics and the extent of long-acting intra-operative or inpatient anesthesia, my findings challenge the traditional belief that opioids are absolutely necessary after surgery.

Our systematic review is limited by the significant risks of bias of individual studies. Uncontrolled pre-post studies present with several inherent methodological issues that limit their internal validity, importantly the inability to control for underlying secular trends.[157] It is possible that the reductions observed in opioid prescribing were not directly related to the described interventions, but are rather due to a growing awareness of the over-prescription of opioids among surgical providers. Although several studies used an interrupted time series analysis to control for the secular trend in opioid prescribing, this does not eliminate the possibility that some event other than the intervention caused the observed decrease in prescribed opioid.[158] Additionally, as many of the identified studies described a multi-faceted complex intervention, the effectiveness of each specific component could not be directly determined. Finally, I need to acknowledge the risk for publication bias in this body of literature. Given that most of the existing studies were conducted using an uncontrolled pre-post design, those with negative results may have had a reduced likelihood of publication. In this light, I recommend that future research evaluating the effectiveness of interventions identified in my review use more robust study designs such as RCTs. Given the nature of the interventions, a stepped wedge cluster design may be considered with the institution as the primary unit of analysis.

Limitations of the review process include the lack of pilot-testing and calibration of my screening, data extraction and risk of bias assessment processes. However, at least two review authors independently participated in all stages of the review, and all disagreements were resolved by consensus. Also, the application of the Cochrane EPOC taxonomy to classify behavioral interventions was imperfect in the setting of the studies identified in my review. For example, the only type of multi-disciplinary intervention described by Cochrane EPOC was that of inter-professional education, however the study by Tran *et al.* identified in my review did not explicitly

describe an educational component to their intervention.[140] A significant limitation of the applicability of my review lies in the exclusion of patients with chronic pain or opioid use in most of the included studies. The prescription of opioids in the post-operative setting can prove to be challenging for these patients, and more research is needed to evaluate strategies to avoid opioid over-prescription in this patient population. Finally, while recent behavioral interventions implemented at the policy level, such as prescription drug monitoring programs (PDMP), may also be effective in decreasing post-surgical opioid prescriptions,[159,160] they were excluded in my review as I specifically sought to identify strategies to improve practice at the institution level.

In conclusion, I have identified several types of behavioral interventions designed to reduce opioid prescribing at after surgery. Despite the significant risks of bias, the reductions in opioid prescription at discharge were generally consistent across studies and resulted in little to no harm. Additionally, the interventions described were overall not resource-intensive. In this light, institutions seeking to reduce post-surgical opioid prescribing can likely be successful by adapting strategies identified in my review.

Chapter 4

Development of Practice Recommendations for the Prescription of Opioids at Discharge After Abdominal-Pelvic Surgery: Preliminary Steps

OVERVIEW

Introduction: I have previously identified existing recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery as well as strategies to change provider behavior. These existing guidelines were also found to be of variable quality, with few recommendations being supported by a formal assessment of evidence. Despite this, guidance is needed for abdominal-pelvic surgeons across Canada to improve their practice on the use of opioids for the treatment of acute post-surgical pain

Methods: I plan to develop consensus-based recommendations using a modified Delphi technique. A guideline panel involving key stakeholders across Canada was assembled. I used webinars and summary documents to familiarize my panelists with the results of my systematic reviews and initiated discussions on priorities for recommendations. A web-based survey was then used to reach agreement on the preliminary scope of my recommendations.

Results: A 50-member guideline panel was assembled that included general surgeons, urologists, obstetrician-gynecologists, vascular surgeons, anesthesiologist/pain management experts, family physicians, emergency physicians, nurses, pharmacists and patients. A 34-member provider panel participated in a 1.5-hour webinar where I presented the results of my reviews and initiated discussions on ideas for recommendation. Documents summarizing my systematic reviews were distributed to the participants before and after the webinars. Based on the discussions from the webinars, I developed a survey targeted at health care providers of the guideline panel to help define the scope of my recommendations. 69% of providers participated in the survey.

Conclusion: With the goal of developing recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery, I have assembled a guideline panel and started defining the scope of my recommendations.

INTRODUCTION

The lack of useful guidelines for the prescription of opioids at hospital discharge following surgery has been cited as an important factor that may explain the suboptimal nature of current practices among surgeons.[29,31,35,42] In Chapter 2, I reported the results of a systematic review demonstrating that, for patients undergoing abdominal-pelvic surgery, existing recommendations for the prescription of opioids at discharge are limited. While a large number of recommendation types were identified (98 for the prescription of opioids, 8 for the disposal of opioids and 8 for the prevention of chronic post-operative opioid use), the majority were not supported by high quality evidence. The amount of prescription opioid recommended varied widely between the recommendations, even for the same procedure. Moreover, the quality of the 15 clinical practice guidelines (CPG) was found to be highly variable, which may limit their uptake and implementation.

In Chapter 3, I conducted a systematic review of behavioral interventions to reduce opioid prescribing at discharge after surgery. I found that, in recent years, many health care institutions across North America developed institutional recommendations based on local agreement to guide the prescription of opioids at discharge after surgery. Based on the results of mostly uncontrolled pre-post studies, these initiatives appeared effective in reducing the amount of opioid prescribed while having minimal effect on the adequate control of post-operative pain. These results indicate that surgeons are likely receptive to the development of guidance on this topic and can alter their practice in response to such initiatives. However, these recommendations were mostly institution-based, and the methods by which they were developed were often unclear. As different institutions may have developed different recommendations for the prescription of opioids after the same

procedure, this may have contributed to the variations in the amount of opioid prescribed at discharge after surgery I observed in Chapter 2.

With the goal of improving the prescription of opioids at discharge after abdominal-pelvic surgery in Canada, I will initiate the development of practice recommendations in this chapter. By adopting a national perspective, I hope to minimize variations in opioid prescribing practices across Canada. I will inform this process with the results of the evidence reviews conducted in the previous two chapters.

The GRADE Approach

The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach is an increasingly used framework for the development of clinical practice guidelines. Steps involved with this approach include 1) framing the health care questions, 2) selecting and rating the importance of outcomes, 3) summarizing the evidence, 4) rating the quality of evidence and 5) going from evidence to recommendations.[161] Each step is outlined below in relation to my project.

Step 1: Framing the health care question

The initial step of the GRADE approach involves defining of the scope of the recommendations by the guideline panel in terms of the healthcare questions the recommendations are intended to address. Specifically, the panel defines the patient population, intervention, comparison and outcome of each health care question for which recommendations will be developed.

Step 2: Selecting and rating the importance of outcomes

The guideline panelists are tasked to consider all outcomes related to a healthcare question and to determine the relative importance of these outcomes as "critical for decision making", "important but not critical for decision making" or "of limited importance". Members of the guideline panel typically rate the importance of a particular outcome on a 1 to 9 scale (9 being of most importance, 1 being of least importance), and the mean of the ratings can be used to indicate the group judgement. Based on the scale proposed by GRADE, a mean rating of less than 4 indicates an outcome of limited importance, a mean rating of 4 or greater and less than 7 indicates an important, but not critical outcome, and a mean rating of 7 or greater indicates a critical outcome.

Step 3: Summarizing the evidence

GRADE recommends that systematic reviews form the basis for the development of health care recommendations and that the evidence identified in these reviews be presented using standardized evidence tables. Only outcomes judged as critical or important should be included in evidence tables, which present information about the body of evidence, the judgments about the underlying quality of evidence, key statistical results, and the quality of evidence rating for each outcome. Specifically, GRADE evidence profiles contain 1) a list of outcomes, 2) the number of studies and study designs, 3) the judgements about each of the quality of evidence factors assessed, 4) the assumed risk, 5) the corresponding risk, 6) the relative effect, 7) the absolute effect, 8) the overall quality of evidence, 9) the importance of each outcome and 10) footnotes to provide extra information such as elaboration on judgements made.

Step 4: Rating the quality of evidence

The quality of the supporting evidence for each outcome is appraised across all studies. GRADE defines the quality of evidence as the extent to which a guideline panel's confidence in an estimate of the effect is adequate to support a particular recommendation. It recommends rating the quality of evidence as high (very confident), moderate (moderately confident), low (limited confidence) or very low (very little confidence). The process begins by determining an initial rating of the quality of evidence of studies that form the body of evidence for outcomes that are critical or important but not critical. For randomized controlled trials without important limitations, a high-quality evidence rating is typically assigned. For observational studies without special strengths or important limitations, a low-quality evidence rating is typically assigned. Subsequently, the body of evidence needs to be considered in the light of eight factors, each of which may either increase or decrease the quality of evidence (Table 4.1).

4. 1 Factors Determining the Quality of Evidence According to GRADE

Factor	Definition	Effect
Risk of bias	Limitations in the study design and execution	Downgrade by 1 or 2 levels
Inconsistency	Unexplained heterogeneity of results	Downgrade by 1 or 2 levels
Indirectness	Uncertainty about the applicability of the evidence to the question	Downgrade by 1 or 2 levels
Imprecision	Resulting uncertainty about the results of studies due to small sample size and low number of events	Downgrade by 1 or 2 levels
Publication bias	Systematic under-estimation or over-estimation of the underlying beneficial or harmful effect due to the selective publication of studies	Downgrade by 1 or 2 levels
Large magnitude of effect	For observational studies without serious problems regarding the risk of bias or precision only: relative risk greater than 2 (large) or 5 (very large)	Upgrade by 1 or 2 levels

Effect of plausible residual confounding	All plausible residual confounders would result in an underestimate of an apparent treatment effect.	Upgrade by 1 level
Dose-response gradient	For observational studies only: relationship between dose and response	Upgrade by 1 level

Following the appraisal of the quality of evidence for individual outcomes, the guideline panel are tasked with appraising the overall quality of evidence, which is the combined rating of quality across all outcomes considered critical for answering a health care question. GRADE suggests that, if the quality of evidence is the same for all critical outcomes, then this becomes the overall rating for this health care question. However, if the quality differs for all critical outcomes, the lowest rating becomes the overall quality of evidence.

Step 5: Going from evidence to recommendation

In this final step, the guideline panel determines the strength of a recommendation, defined as the extent to which a guideline panel is confident that the desirable effects of the studied intervention outweigh undesirable effects. Two categories for the strength of recommendations is proposed by GRADE: strong or weak. Strong recommendations reflect a panel's confidence in that the desirable effects of an intervention outweigh its undesirable effects or that the undesirable effects outweigh the desirable effects. Weak recommendations indicate that the desirable effects of an intervention probably outweigh its undesirable effects or that the undesirable effects probably outweigh the desirable effects, but considerable uncertainty exists regarding this judgement. Four factors have been proposed by GRADE that influence the strength of a recommendation: 1) balance between desirable and undesirable outcomes, 2) overall quality of evidence for the healthcare question, 3) confidence in the values and preferences and their variability and 4) use of

resources. A strong recommendation is more likely when there is a larger difference between the desirable and the undesirable consequences, a higher quality of evidence, a smaller variability in the values and preferences and a less costly intervention. Similarly, a weak recommendation is warranted when there is a smaller difference between the desirable and undesirable consequences, a lower quality of evidence, a higher variability in the values and preferences and a higher cost associated with the intervention are present.

After the judgement of the guideline panel regarding the strength of a recommendation has been made, the recommendation is then worded in a manner that reflects its strength. For strong recommendations, GRADE recommends the use of "we recommend…" or "clinicians should…" at the start of the recommendation sentence. For weak recommendations, the terminology "we suggest…" or "clinicians might…" is used instead.

Limitations to the Application of the GRADE Approach

A major limitation in the potential application of the GRADE approach in developing recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery is the paucity of evidence in the literature on this topic. Indeed, in Chapter 2, only 11 of 114 interventions for the prescription of opioids at discharge, disposal of unused opioids or prevention of chronic opioid use after abdominal-pelvic surgery were accompanied by a recommendation strength or level of evidence (9.6%). Among the recommendations that were accompanied by an assessment of evidence, only three interventions were supported by the highest level of evidence within the grading scale of their respective document: multimodal analgesia (American Society of Anesthesiologists (ASA), A1 category evidence; American Pain Society – American Society of Regional Anesthesia and Pain Medicine – American Society of Anesthesiologists (APS-ASRA-

ASA), high-quality of evidence),[60] the use of opioids for moderate to severe pain (SIAARTI, level A recommendation)[115] and preventive analgesia (Salti et al, level A evidence).[111] Of these three guidelines, only the documents making a recommendation on the use of multimodal analgesia (ASA and APS-ASRA-ASA) scored well on the AGREE-II instrument and may be used for the purpose of my guidance document. Based on this body of evidence, the use of the GRADE approach to develop recommendations is theoretically possible; however, it would likely result in the generation of recommendations that are mostly supported by a very low-quality rating of the body of evidence. Indeed, according to GRADE, the absence of high-quality randomized controlled trials assessing prescription of opioids at discharge after abdominal-pelvic surgery would indicate that the initial rating of the quality of evidence is very likely to be low, at best. However, despite this paucity of high-quality evidence, guidance is needed to help Canadian abdominal-pelvic surgeons to improve their practices.

METHODS

Study Design

I plan to develop consensus-based recommendations using a modified Delphi technique. An agreement-based or consensus-based approach was chosen given the paucity of evidence supporting the existing guidance identified through my systematic review. Consequently, the use of agreement-building methods, in conjunction with the available evidence I identified, was thought to be necessary in developing the appropriate guidance. Approval from Research Ethics Boards was obtained at St Michael's hospital and at the University of Toronto.

Agreement-Building Methods

The modified Delphi technique is an iterative process that uses repeated rounds of voting in a systematic manner to achieve agreement in a group of experts. As the name implies, it is a modified version of the original Delphi method, which was originally developed by the RAND corporation in forecasting technological and social developments.[162] In the original Delphi, experts are surveyed individually and anonymously with self-administered questionnaires, and this is repeated for several rounds. After each round, the results of the survey are tabulated and reported to the group, and the experts have an opportunity to revise their answer in the next round of survey. This process is repeated until a high level of agreement is achieved.[163] The advantages associated with the original Delphi method are that it allows participants to express their views in an impersonal manner and avoid some of the detrimental effects of unstructured face-to-face interactions, such as the tendency for people to conform to the judgment of others in a group setting, even against their better judgement.[164] In addition, it allows the participation of a geographically diverse group of individuals through the use of mailed questionnaires, and it often allows the statistical aggregation of numerical estimates.[164]

The modified Delphi technique typically involves an additional face-to-face meeting to the rounds of surveys described in the original Delphi method.[165-167] The modified version was developed in the 1970s[164] and is now widely used in studies where expert agreement is needed. In contrast to the original technique, the modified Delphi provides participants an opportunity to discuss their judgements and to clarify reasons for disagreements in a group setting.

Another common method to build agreement consists of the nominal group technique (NGT). The NGT involves a structured meeting in order to reach agreement between individuals with potentially differing views in a group.[168] In this method, participants are first asked to list

their opinion individually regarding a given question without prior discussion. Each participant then presents, in a round-robin format, the most important element in their list until all lists from all individuals are exhausted. The presented elements are listed in front of the group by the facilitator. Participants then engage in discussions around the each of the listed elements and ask for clarifications if needed. After discussions, participants then rank the elements privately and in writing, and the results are aggregated statistically to derive the group judgement. Compared to informal group meetings to develop agreement, the structured format of the NGT was thought to prevent the influence of dominant opinions, allowing all participants to share their opinions more freely.[168] Also, the NGT avoids too much emphasis on one specific item and allows all items on the agenda to be discussed in turn.[164]

Other methods of building agreement include consensus development conferences, staticised groups and social judgement analysis. Consensus development conferences have been run by the United States National Institutes of Health on a variety of topics.[169] They typically involve a selected group of individuals that are brought together at a conference to participate in a chaired meeting over course of a few days where evidence is presented by various groups not involved in the decision-making group. After presentation of the evidence, the group retires into a chaired private meeting and attempts to reach agreement on the question. Staticised groups involve individuals who work on a question independently with no interaction, and their opinions are then aggregated statistically to create a group view. Compared to the accuracy of individual judgements, judgements from staticised groups have been shown to be superior on tasks involving little in-depth analysis. For example, in an experiment involving two hundred students tasked with arranging a series of ten weights from the heaviest to the lightest, Gordon showed that the correlation of the group ranking with the true ranking increased with an increasing size of the

group used as the unit of analysis.[170] Finally, social judgement analysis is a technique that focuses on the logic behind individual judgements. In this method, participants are given instructions to reflect on specific elements in the rationale behind their judgement and to discuss them in a group setting.[171] It provides feedback on the importance that individuals attach to information and how they relate this information to their judgements. Discussion is structured around the feedback, and this technique is often useful when trying to understand why there is a lack of agreement on a given topic.[164] Table 4.2 presents a summary of the described methods of agreement-building.

4. 2 Characteristics of Common Formal Agreement Development Methods

Method	Description	Advantage	Disadvantage
Delphi[162-164]	1. Participants complete a questionnaire indicating their judgement on specific items. 2. Responses are collected, summarized and sent back to participants in an anonymized summary form. 3. Participants can revise their judgements in a subsequent round of questionnaire. 4. Process is repeated until agreement is achieved.	• Allows statistical combination of individual judgements. • Allows participation of individuals from dispersed geographical backgrounds. • Allows participants to express their views impersonally and prevent the influence of dominant opinions.	• Prevents potentially beneficial effects of interaction (e.g. clarify reasons of disagreement). • Panelists often fatigue after two or three rounds.
Modified Delphi[165-167,172]	1. Process similar to the steps described above for the Delphi technique. 2. Also involves a face-to-face meeting of participants.	• Allows for potentially beneficial effects of interaction.	• Panelists often fatigue after two or three rounds.
Nominal Group Technique[164,168]	1. Participants present their own ideas regarding a specific question in a round-robin format.	• Allows each participant to speak freely and share their ideas. • Allows all items on the agenda to be discussed.	• Success is dependent on the skills of a highly trained leader and on the willingness of the group to work together.

	2. Facilitator lists those ideas in front of the group. 3. Each idea is discussed in turn by the group. 4. Individuals privately record their judgements regarding each idea. 5. Judgements are statistically aggregated to derive the group judgement.		
Consensus Development Conference[164,169]	1. Select group of participants are convened at an open meeting. 2. Evidence is presented to them by various individuals not involved in the decision-making process. 3. The group of participants then retires into a closed meeting and attempts to reach agreement.	• Has been used to develop agreement on a wide range of topics.	• Requires large scale organizational abilities.
Staticised Group[164,170]	1. Participants work on a problem independently with no interaction. 2. Their judgements are aggregated statistically to form the group view.	• Outperforms methods that require interaction for problems that need little in-depth analysis.	• Prevents potentially beneficial effects of interaction.
Social Judgement Analysis[164,171]	1. Participants make private decisions regarding a problem. 2. Feedback is provided to them regarding the logic they used to formulate their judgement. 3. Discussion is structured around the logic used.	• Useful when seeking to understand why there is a lack of agreement on a topic.	• More of a form of feedback rather than a comprehensive agreement method

In the light of these different methods to build agreement, I have decided to use the modified Delphi technique to develop recommendations for the prescription of opioids at hospital discharge after abdominal-pelvic surgery. Given the multidisciplinary nature of this topic, I plan

to seek the opinion of a large group of individuals representing various healthcare disciplines involved in the pain management of patients undergoing abdominal-pelvic surgery. Additionally, representation from experts across Canada would be needed to increase the uptake of my document on a national basis. Also, as I are planning to develop recommendations, I expect that face-to-face discussions around issues such as the wording of recommendations would be necessary to clarify disagreements. Given that the modified Delphi technique allows the participation of a large group of individuals and facilitates the clarification of disagreement between panel members, I chose this method to achieve agreement in developing my guidance document.

Panel Assembly

In their definition of trustworthy CPGs, the Institute Of Medicine outlined that they should be developed by a group of experts that represent key affected groups.[68] In accordance with this, I assembled a 50-member multidisciplinary panel of individuals with expertise in the care of patients treated with opioids at discharge after abdominal-pelvic surgery. The different disciplines involved in my guideline panel were specified a priori. This panel involves general surgeons, urologists, obstetrician-gynecologists, and vascular surgeons since they are the surgical providers responsible for the management of patients undergoing abdominal-pelvic procedures. As many of the discharge prescriptions are prepared by resident physicians in academic institutions, surgical residents were included. Given the important role that anesthesiologists and pain management experts play in the pain management of these patients, they were also recruited. Furthermore, I included family physicians and emergency physicians (who are often involved in the pain management of these patients after hospital discharge), as well as nurses and pharmacists (in order to incorporate the opinion of allied health providers). Additionally, I recruited individuals from

Health Quality Ontario, an advisory body on the quality of healthcare delivery in Ontario, and the Canadian Medical Protective Association, an organization that provides legal and risk management services to physicians in Canada. Lastly and importantly, this panel includes a group of patient representatives, including several individuals with experience in the use of opioids post-operatively. Specifically, I planned to recruit patients who were briefly treated with opioids in the post-operative setting, those who develop de novo long-term opioid requirements after surgery, and who were using opioids chronically prior to undergoing surgery. In order to increase the uptake and dissemination of my guidance document among Canadian abdominal-pelvic surgeons, I included individuals in executive positions at three major Canadian surgical societies; the Canadian Association of General Surgeons, Canadian Urologic Association, and the Society of Obstetrics and Gynecology of Canada.

Although there is general agreement in the literature that guideline panels should be multidisciplinary and include all relevant stakeholders,[68,173,174] no specific agreement exists regarding the optimal size of the panel. However, an important consideration in determining the group size is the need to balance the increase reliability in judgements associated with a large guideline panel and the potential for coordination challenges.[164,175] my research group has previous experience facilitating and coordinating agreement building involving large groups of individuals, and therefore a 50-member panel was chosen to define the scope of my guidance document. For feasibility purposes, 25 members from the panel will be selected to attend the in-person meeting, and I will ensure an adequate representation of all previously described disciplines.

Participants to the guideline panel were recruited by purposive and snowball sampling. I used a purposeful sampling strategy in order to include experts involved in the pain management of patients undergoing abdominal-pelvic surgery because they would provide useful information

towards the objective of my study. I used snowball sampling for feasibility purposes to identify individuals who could provide rich information.[176] Individuals who declined to participate in my study were invited to nominate another potentially interested participant. The email templates used for the recruitment of providers and patients can be found in Appendix 4.1.

Knowledge Dissemination

In order to familiarize the guideline panel with the results of my systematic reviews and initiate discussions on the guideline development process, I held 10 1.5-hour webinars with the provider members of my guideline panel. All providers were invited to participate in one of the 10 webinars. A document summarizing the results of my systematic reviews were sent to the participants one week prior to the webinar. The content presented during the webinars included introductions, methods, and results of both systematic reviews as well as the plan for guideline development. During the webinar, discussions were initiated on current practices regarding the management of pain with opioids after discharge following abdominal-pelvic surgery as well as gaps for practice improvement and ideas for recommendations. Conflicts of interest were disclosed at the beginning of the webinars. One investigator recorded the discussions regarding current practices and topics for recommendations. A post-webinar package was prepared that included the document summarizing the results of my systematic reviews, as well as individual studies requested by participants of the webinars, and this package was distributed to the entire guideline panel 2 weeks following the end of the webinars.

Defining the Scope of the Guideline

Following the dissemination of knowledge identified through my systematic reviews, I proceeded to solicit the opinion of health care providers on my guideline panel regarding the intended scope of my recommendations. Based on the interventions identified through my systematic reviews and through the discussions during the webinars, I designed a survey to solicit the opinion of my panel on the scope of my guidance document. Given that this is a preliminary step to the modified Delphi method to achieve agreement on the scope of recommendations, agreement was defined by majority rule. The survey was distributed to the providers via the web-based platform Survey Monkey (https://www.surveymonkey.com/r/DNPWY26), and reminders to complete the survey were sent at 2 and 4 weeks after the initial survey was sent.

RESULTS

Multidisciplinary Panel

A total of 77 individuals were invited to participate in the guideline panel and 50 individuals accepted the invitation (Table 4.3). Of these participants, 28 were surgeons (14 general surgeons, 6 urologists, 6 obstetricians-gynecologists and 2 vascular surgeons), 7 were anesthesiologists/pain management experts, 1 was a family physician, 1 was an emergency physician, 4 were allied health providers (3 nurses and 1 pharmacist), 2 were individuals from Health Quality Ontario and 1 was from the Canadian Medical Protective Association. Five patients were recruited, including one representative from Chronic Pain Support Services, an organization that aims to support individuals with chronic pain, as well as 4 patients with experience in using opioids for the treatment of acute pain after surgery. Although the majority of individuals

originated from Ontario, I included participants from British Columbia, Alberta, Manitoba, Quebec, Nova Scotia and Newfoundland and Labrador.

4. 3 Panel For Developing Recommendations For The Prescription of Opioids at Discharge After Abdominal-Pelvic Surgery

Discipline	Number of Participant	Province of Origin
General Surgery	14	Quebec, Ontario, Nova Scotia, Alberta, British Columbia, Manitoba
Urology	6	Ontario
Obstetrics-Gynecology	6	Ontario
Vascular Surgery	2	Ontario
Anesthesia and Pain Management	7	Ontario, British Columbia
Family Medicine	1	Ontario
Emergency Medicine	1	Ontario
Nursing	3	Ontario, Newfoundland and Labrador
Pharmacy	1	Ontario
Health Quality Ontario	2	Ontario
Canadian Medical Protective Association	1	Ontario
Patients	5	Ontario

Webinars

Ten webinars were held from January to March 2019, which were attended by 34 out of the 45 providers from the guideline panel (76%). Table 4.4 summarizes major topics of discussion during the webinars, including current clinical practices and ideas for inclusion into the future recommendations. After participating in the webinar, one panelist withdrew his/her participation due to other commitments and was replaced by another individual of the same discipline.

Topics for recommendations generated through discussions during the webinars included:

- The use of prescription drug monitoring programs when patients present for postoperative opioid refills.
- The disposal of excess unused opioids after surgery by bringing them back to a pharmacy.

- Patient education materials in a written format to be given at the time of patient discharge, including instructions for appropriate disposal, expectations for post-operative pain, and use of multimodal analgesia.
- The need for surgeons to encourage the appropriate disposal of excess unused opioids after surgery in their patients.
- Different recommendations of opioid prescription regimens for outpatient and inpatient surgery. The relevant procedures can be identified by soliciting surgeons on the guideline panel.
- The appropriate education of medical trainees with regards to opioid prescribing.
- The prescription of postoperative opioids in small doses and having the patient go back to the pharmacy for refills, if needed.
- The involvement of patients in shared decision-making when prescribing opioids.
- Adjusting the amount of The prescription of opioids at discharge after inpatient surgery based on consumption in the 24 hours prior to discharge.
- Increased communication between surgeons and acute pain services, as well as providers in the community that care for their patient.
- The prescription of non-opioids to maximize their use by patients.
- The consideration of the issues related to the risk of gastro-intestinal anastomotic leaks with using non-steroidal anti-inflammatory medications.
- The use of a checklist to ensure that surgeons comprehensively assess the risk of opioid-related harms in their patient.
- The need to focus the management of patients at high risk of chronic opioid use at the time of opioid refill.

- The use of an opioid-free pain regimen in select outpatient procedures.
- The development of a knowledge translation plan for the guideline document.

4. 4 Summary of Discussions From the Knowledge Dissemination Webinars

Topic	Current Practice	Discussions
Accessing prescription drug monitoring programs when prescribing opioids	In Ontario, only used by emergency physicians and pain. Typically not done for first opioid prescriptions. Surgeons were mostly unaware of these programs.	It may be appropriate to recommend providers to access prescription drug monitoring programs when patient present for opioid refills.
Appropriate disposal	No instruction provided by surgeons, sometimes by family physicians and emergency physicians.	Bringing excess medications back to pharmacies would the most appropriate method of disposal (Health Canada recommendation). It would be useful to incorporate disposal instructions in the discharge summary of surgical patients or provide specific instructions in the form of a handout. Surgeons should encourage patients to return any leftover opioids at follow-up and encourage appropriate disposal. Should other providers (e.g., pharmacists) also perform this education? Surgeons could consider having a medication drop-box in their clinic for excess opioids.
Patient education at the time of discharge	Rarely done by surgeons.	It would be an important part of our guideline. It may be useful in the format of a written document for patients. Setting appropriate expectations regarding pain is very important at patient discharge.
Procedure-specific opioid prescription recommendations	Surgical residents have reduced the amount of opioid they prescribe in the past few years; however, they have no clear guidance regarding this.	It would be important to make separate recommendations for outpatient versus inpatient surgery. The research team could solicit from guideline panelists the procedures to be included. The research team could then solicit prescription recommendations by proposing scenarios. It would be important to educate residents regarding appropriate prescribing.
Prescribing opioids at discharge	NA	The panel could recommend prescribing opioids in small doses and having the patient go back to the pharmacy for refills. It may be beneficial to involve the patient in a shared decision-making process when prescribing opioids.

		It would be reasonable to recommend prescribing opioids at discharge based on inpatient consumption in the 24 hours prior to discharge. The panel needs to be aware of the "addiction to pain scales" when prescribing opioids based on the patient's inpatient consumption.
Communication between providers	Mostly poor.	Appropriate communication between the acute pain service and the surgical team when transitioning pain management responsibility is an important issue to address. Surgeons should communicate with family physicians regarding the management of patients at high risk of chronic opioid use.
Multimodal prescribing	The education around the use of non-opioids first is rarely provided by surgeons.	Will need to consider the issues around the use of non-steroidal anti-inflammatories in gastrointestinal surgery. Would be an important element of patient education. Prescribing non-opioids would likely increase their consumption by patients.
Comprehensive patient assessment	Not routinely done by surgeons.	The questions to ask patients would need to be specific enough to be useful for surgeons. The panel could consider including a short checklist for important elements when assessing patients. However, even if patients are assessed comprehensively, there is the possibility that they could hide their chronic opioid use. Need to specifically include any history of recent opioid prescription.
Management of patients at high risk of chronic opioid use	Not currently done by surgeons, mostly done by anesthesiologists and pain management physicians.	It is difficult to identify which patients are at high risk of chronic opioid use. The optimal time to intervene may be when patients present for opioid refills.
Opioid-free prescriptions	NA	We need to be careful in completely removing opioids from postoperative pain management prescriptions, as inadequate pain control is one of the top causes for readmission. However, select patients, likely those who are undergoing day surgery, may not need opioids. Potential procedures: minimally-invasive hysterectomies, trans-urethral resection of the prostate, kidney stone surgery, and robotic prostatectomy. In Europe, opioids are rarely used or mentioned to patients.
Guideline dissemination	NA	Could consider alternate mediums for dissemination of guideline (e.g., Youtube, Twitter).

	Knowledge translation needs to be planned ahead of time. Need to keep the message simple for surgeons.

Abbreviation: NA, not available

Defining the Guideline Scope

I started to define the scope of my guideline using a series of web-based surveys to solicit the opinion of the providers on the panel. The first survey was designed based on the results of my systematic reviews, as well as the discussions during the webinars (Appendix 4.2), and it was completed by 31 of 45 health care providers on the panel (69%).

Target Population

There was 100% agreement that opioid-naïve patients should be the target population of this guidance document. Respondents also indicated that patients using opioids prior to surgery (81%) as well as previously opioids-naïve patients at high risk of developing chronic opioid use after surgery (87%) would be relevant target populations for this guideline. As well, 42% and 19% of respondents indicated that the target population of this document should include patients with chronic pain or patients on opioid agonist therapy, respectively. A further 84% of respondents indicated that a separate section of recommendations should be developed for each target patient population.

Patient Education

All respondents agreed that the guideline should include recommendations on patient education. Additionally, the majority of respondents (83%) indicated that the guidance document

should incorporate specific patient education materials. Proposed specific elements to include in patient education were summarized and include:

- Rationale for treatment with opioids
- Use of alternatives to opioids (non-opioid pharmacologic and/or non-pharmacologic strategies) as first-line therapy
- Removal of stigma surrounding opioids
- How much and how often each medication should be taken
- Opioid tapering strategies
- Expectation management for degree of post-operative pain
- Importance of adequate pain control and need to seek help if pain management is ineffective
- Neuropathic pain
- Risk of dependence/addiction to opioids
- Difference between tolerance versus dependency versus addiction
- Side effects of opioids
- Dangers of concurrent use of alcohol and sedatives with opioids
- Safety concern to individuals in the surrounding of the one using opioid (e.g. children)
- Potential harms resulting from sharing opioids
- Resources to obtain help for addiction concerns
- Dangers of disregarding MD directions

Prescription of Non-Opioid Therapies

There was unanimous agreement that non-opioid therapies should be prescribed at the time of hospital discharge after abdominal-pelvic surgery.

Development of Chronic Post-Surgical Opioid Use

Most (97%) of the respondents indicated that the guideline should recommend screening of risk factors for the development of chronic post-surgical opioid use. Specifically, the majority of the respondents indicated that the guideline should make recommendations regarding specific risk factors to screen for (100%) as well the timing of the screening process (67%). However, no agreement was reached regarding whether the guideline should recommend which specific provider ought to perform the screening (50%).

Prescription Drug Monitoring Programs

More than half (61%) of the respondents indicated that the guideline panel should recommend the use of prescription drug monitoring programs (PDMP) when prescribing opioids at discharge for all patients undergoing abdominal-pelvic surgery.

Management at the Time of Prescription Refill

The majority of respondents indicated that the panel should make recommendations on the management of patients when they present for opioid prescription refills. Specific components proposed for this recommendation include:

- Reassessment of pain and need for opioid
- Defining the responsible provider for refills

- Consultation of the PDMP
- Prescription of non-opioid alternatives
- Duration of refill prescription
- Establishment of an opioid contract
- Development of a strategy for opioid taper
- Plan for follow-up after refill
- Screening for risk factors for developing chronic opioid use
- Screening for dependence to opioid
- Urine drug testing
- When to refer to chronic pain/addiction
- Communicating with the patient's other providers

Practices to Avoid

The majority (90%) of the respondents indicated that the guideline should provide recommendations on which practices to avoid. Specifically, over 80% of respondents indicated that the panel should recommend against the concurrent prescription of opioids with sedative medications, against the prescription of long-acting opioids and against the pre-operative preparation of discharge prescriptions. Additional elements that were suggested include not prescribing large quantities "just in case", not being unavailable when questions arise regarding the discharge prescription and not prescribing the same amount of opioids to all patients.

Communication Between Providers

Almost three quarters (74%) of the respondents indicated that the appropriate communication between surgeons and other providers involved in the care of their patient should be recommended.

Best Practices for Opioid Prescribing

There was unanimous agreement that the guideline should include recommendations on how to best write opioid prescriptions (e.g., limiting the initial dispensing with the ability for patients to get more).

Relevant Procedures

Relevant procedures for specific opioid prescription regimens are presented in Table 4.5. Fourteen general surgical, 6 obstetrics-gynecological and 6 urological procedures were solicited from the providers on the panel. No vascular surgery procedure was proposed.

4.5 Proposed Procedures For the Development of Opioid Prescription Regimens at Discharge

General Surgery	Obstetrics-Gynecology	Urology
Laparoscopic cholecystectomy	Minimally invasive hysterectomy-bilateral salpingo-oophorectomy	Ureteroscopy and laser
Laparoscopic hernia repair	Abdominal hysterectomy	Transurethral resection of the prostate
Laparoscopic gastric bypass	Cytoreductive surgery (multivisceral organ resections)	Laparoscopic nephrectomy
Laparoscopic appendectomy	Vaginal hysterectomy	Robotic prostatectomy
Laparoscopic sleeve gastrectomy	Tubal ligation	Transurethral resection of bladder tumor
Laparoscopic rectopexy	Diagnostic laparoscopy	Lithotripsy
Laparoscopic lysis of adhesions		
Diagnostic laparoscopy		
Laparoscopic washout		
Laparoscopic splenectomy		
Laparoscopic colorectal resection		
Open oncologic procedures		
Laparoscopic or open hepatectomy		
Retroperitoneal adrenalectomy		

Prescribing After Inpatient Surgery

More than half (65%) of the respondents indicated that the prescription of opioids at discharge after inpatient surgery should be informed on the amount of opioid consumed in the 24 hours prior to discharge.

Opioid-Free Pain Management

Most (96%) of the respondents indicated that the guideline should recommend opioid-free pain management strategies at discharge after certain abdominal-pelvic surgical procedures.

Opioid Disposal

Most (90%) of the respondents indicated the panel should recommend specific methods of opioid disposal.

Referral to Pain Specialists

Most (90%) of the respondents indicated that the panel should develop a recommendation regarding when, how and for whom referral to pain specialists should be made.

DISCUSSION

To summarize, I have initiated the development of practice recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery in Canada. In order to achieve this objective, I plan to use an agreement-building methodology to develop recommendations. I have completed the assembly of a multidisciplinary 50-member guideline panel consisting of providers involved in the care of patients treated with opioids following an abdominal-pelvic

surgical procedure, as well as patients experienced with the use opioids in the post-operative setting. Following the assembly of this panel, I have disseminated the results of my two systematic reviews to the panel using summary documents and 1.5-hour webinars where I initiated discussion regarding current practices as well as ideas for the development of recommendations. A survey was developed to define the scope of my guidance document. Based on the results of my first survey, my guidance document should target opioid-naïve patients undergoing abdominal-pelvic surgery. Topics for which my guideline panel should develop recommendations include patient education, the prescription of non-opioid therapies, the need to screen for risk factors of chronic post-operative opioid use, the use of PDMPs, the management of patients management at the time of prescription refill, the avoidance of specific practices, the appropriate communication between providers, the best practices for prescribing opioids, the specific opioid regimens after outpatient surgery, the prescription of opioids after inpatient surgery, the management of patients that involve an opioid-free strategy, the appropriate disposal of opioids as well as the details of referring to pain specialists.

Our decision to develop recommendations using agreement methods, rather than formal guideline development frameworks such as the GRADE approach,[177] was driven by the results of my systematic reviews. As I have previously demonstrated in Chapter 2, the evidence basis for existing recommendations on the prescription of opioids after abdominal-pelvic surgery is poor. Given that the GRADE approach mainly relies on the availability of high-level evidence (e.g., multiple randomized controlled trials and/or meta-analyses) to generate meaningful assessment of recommendation strength and level of evidence,[178] the current relevant body of evidence is insufficient to meaningfully use this approach. Consequently, I chose the modified Delphi method, an agreement-building technique, to develop the recommendations of interest.

I have designed my study to reflect best practices in guideline development.[68] I have informed my guideline with the data gathered from two recently performed systematic reviews. I have assembled a 50-member guideline panel group that include stakeholders with a diversity of healthcare disciplines and geographical backgrounds. Importantly, I included patient representatives with first-hand experience in using opioids for post-surgical pain. I have familiarized my panel with the evidence gathered to-date and initiated discussions on potential recommendations. Finally, I have started to define the scope of my recommendations with all provider members of my guideline panel in an explicit and transparent process by achieving agreement using web-based surveys.

Our work to-date has several limitations. First, despite my attempt to recruit experts from different geographical backgrounds across Canada onto my guideline panel, most of the participants originated from Ontario. While this is not surprising given that I used a snowball sampling strategy, a maximum variation sampling technique, where researchers purposefully pick a wide range of variation on dimensions of interest,[176] may have improved the geographical diversity of my guideline panel. However, I do not expect the lack of geographical diversity to substantially bias my recommendations as the over-prescription of opioids at discharge after surgery is likely an equally relevant issue across Canada, and the recommendations would be applicable to a diversity of clinical settings. Second, while I invited all providers to participate in my webinars and survey, the participation rates were 76% for the webinars and 69% for the survey, which demonstrates the difficulties of coordinating a large group of busy experts for this research. Third, due to the large number of recommendations for the prescription of opioids identified in my systematic review, I only presented the five most common interventions during the webinar, which may have biased the discussions and priorities for the development of my recommendations.

Nonetheless, participants were sent a document summarizing the full results of the systematic reviews before and after the webinar. Finally, despite the fact that I presented the existing recommendations on the prescription of opioids at discharge following abdominal-pelvic surgery, I did not specifically review individual studies that support these recommendations, which may have provided further clarification to guide the recommendation development process.

FUTURE STEPS

Future work to develop recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery will involve further defining the scope of guidance document using web-based surveys. As I have identified a large number of recommendation topics through my systematic review and solicited the preliminary opinion of my guideline panel on their inclusion in the guidance document, I plan to more precisely define the topics on which recommendations will be made through ranking exercises. Indeed, I have observed in the results of my survey that the guideline panel agreed to include the majority of proposed topics for recommendations in my document. However, in order to develop accessible, actionable and feasible guidance for the prescription of opioids at discharge targeted towards Canadian abdominal-pelvic surgeons, further work in concisely defining the scope of my recommendations is needed.

Next, as I have done with provider members of the guideline panel, I plan to familiarize patient members of the panel with the literature reviews I conducted as well as the progress I have made so far in the development of recommendations. I plan to do so using summary documents and a 1.5-hour webinar in a similar fashion as described previously. Following this, I plan to use web-based surveys to elicit patient values and preferences on the use of opioids for the treatment of pain after abdominal-pelvic surgery, as the confidence of the guideline panel in the variability

of these elements among patients is an important determinant of the strength of recommendations.[161]

Finally, based on a clearly defined scope of my guidance document as well as values and preferences of patients regarding the use of opioids after abdominal-pelvic surgery, I plan to develop a set of preliminary recommendations for agreement building using a modified Delphi method. An a priori threshold of 85% will be used to indicate agreement or disagreement with the recommendation. In the first round of the modified Delphi, I will solicit the level of agreement of the guideline panel with each of these preliminary recommendations using a 7-point Likert scale (1=entirely disagree, 2=disagree, 3=somewhat disagree, 4=unsure, 5=somewhat agree, 6=agree, 7=entirely agree) in a web-based survey. A rating of 1 or 2 would indicate disagreement, and a rating of 6 or 7 would indicate agreement. Following this, an in-person meeting will be organized with 25 individuals selected from the original 50-member panel, ensuring multidisciplinary and geographically diverse representations. During the in-person meeting, each member will be provided with their own results from the first round as well as the group result. I will use a nominal group technique to facilitate discussion on issues of disagreements regarding the preliminary set of recommendations. After the in-person meeting, the preliminary recommendations will be modified according to the feedback obtained during the in-person meeting, and a second round of modified Delphi will be conducted, where the entire guideline panel will again vote on their level of agreement with the revised recommendations using a 7-point Likert scale. Following this final step, the final set of recommendations to be included in my guidance document will be generated, and the document finalized.

Chapter 5

Summary and Synthesis

Summary of Findings

As North America struggles to cope with the devastating consequences of an epidemic of deaths related to opioid overdoses, there has been increasing scrutiny on the appropriateness of opioid prescriptions by medical professionals. Although the majority of deaths are from acute intoxication with fentanyl and fentanyl-analogues,[11,179] the use of opioids in clinical settings likely remains a significant contributor to the current crisis. Indeed, prescription opioids such as methadone, oxycodone and hydrocodone can be involved in more than 35% of deaths due to opioid overdose.[180] Additionally, the medical use of opioids can lead to the development of misuse, where these drugs are used in a way other than prescribed for non-medicinal purposes. Opioid misuse can subsequently increase the risk for physical dependence and the development of an opioid use disorder.[17]

Recent studies investigating the prescription of opioids at discharge following surgical procedures have demonstrated that existing practices are often suboptimal. Using patient-reported data to compare the amount of opioids consumed after discharge versus the amount prescribed by surgeons, several studies have demonstrated that the prescription of opioids at discharge can be highly variable after the same surgical procedure and is often much in excess of the amount actually required by patients.[31,33-36,42,78,181] Moreover, studies have also demonstrated that, after an initial exposure to opioids in the immediate post-operative period, a significant proportion of opioid naïve patients will continue to use prescription opioids long-term after their surgical procedure.[48,49,51-53,57,58] Given the known risks associated with the chronic use of opioids,[16] the prevention of this event early in the perioperative period is likely a worthwhile endeavour.

The Knowledge-to-Action process is a widely used framework to guide the implementation of medical knowledge into practice to improve health care.[67] In this thesis, I

applied this framework with the goal of improving opioids prescription practices at discharge following abdominal-pelvic surgery. According to this framework, the creation of tools or products that synthesize the medical knowledge on a given topic into user-friendly format is a necessary first step in preparation for their eventual application into clinical practice. CPGs, a set of statements that contain recommendations intended to optimize patient care that are informed by a systematic assessment of evidence, are examples of such tools.[71] As the lack of guidance for surgeons has been hypothesized to be a major reason driving the suboptimal nature of current practices for the prescription of opioids in the post-operative setting,[29,31,35,42] I sought to identify and summarize existing recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery as a first step in the implementation of this guidance to improve clinical practice.

Existing Recommendations for the Prescription of Opioids at Discharge After Abdominal-Pelvic Surgery

In Chapter 2 of this thesis, I conducted a systematic review of recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery. Using an extensive search of MEDLINE, PsycINFO, Healthstar, EMBASE as well as various grey literature sources such as websites of surgical, anesthesia and pain societies, theses, grey literature databases and Google, I identified 41 contemporary English-language documents published by professional societies or health care institutions that contain recommendations relevant to the prescription of opioids at discharge after abdominal-pelvic surgery. Of these documents, 15 clinical practice guidelines (CPGs) were identified, however the quality of these guidelines varied significantly when assessed using the AGREE II tool.[85] From the included documents, 98 recommended interventions were

identified for prescribing opioids at discharge after abdominal-pelvic surgery, 8 for the disposal of excess opioids and 8 for preventing the development of chronic post-surgical opioid use. However, of all these interventions, only 13/114 were supported by an assessment of strength or level of evidence (11.4%), and the amount of opioid recommended following specific abdominal-pelvic surgical procedures varied widely between guidance documents, even for the same procedure.

Our results suggest that existing CPGs for the prescription of opioids at discharge after abdominal-pelvic surgery are limited in their intrinsic quality as well as in their external applicability to abdominal-pelvic surgeons. The majority of CPGs scored poorly on the AGREE II domains. However, even the CPGs that scored moderate or high on the AGREE II domain scores either did not contain recommendations specific to the management of pain after abdominal-pelvic surgical procedures (APS-ASRA-ASA[60], ASA[59], CDC[16], ACOEM[90]) or contained recommendations that were not accompanied by an explicit assessment of strength and/or level of evidence (AMDG-Bree Collaborative[91]). Specifically, many recommendations were developed to provide guidance on the management of "post-operative pain" or "acute pain", which lack the specificity to be directly actionable in the care of patients undergoing abdominal-pelvic surgery. For example, the degree and duration of acute pain experienced after a laparoscopic procedure is different than that experienced after a thoracotomy or a fracture, and this is not reflected in many non-procedure specific recommendations. Given that existing CPGs on the prescription of opioids at discharge after abdominal-pelvic surgery are not sufficient to guide practice, it is not surprising that opioid prescribing has been found to be suboptimal in the recent literature.[31,33-36,42,78,181]

A main area of guidance that may be sought by abdominal-pelvic surgeons is the amount of opioid to prescribe to patients in discharge prescriptions. Only one guideline provided recommendations for the amount of opioid to be prescribed at discharge after specific abdominal-

pelvic surgical procedures.[91] However, this guideline was not developed using a systematic assessment of the evidence with an explicit appraisal of recommendation strength or level of evidence. Indeed, the majority of recommendations identified through my systematic review were formulated using institutional data on patient-reported opioid consumption[43,63,65] or by a consensus-building process,[62,66] likely as a result of an urgent need for recommendations on this topic that is driven by the ongoing opioid epidemic coupled with a lack of rigorous supporting scientific evidence to guide decision-making.

As previously discussed in Chapter 2 of this thesis, several limitations may have affected the validity of my systematic review of existing recommendations, such as the heterogeneity in the focus of the guidance documents included, the lack of using the PRESS guidelines in the peer-review process of my search strategy and the discontinuation of the National Guideline Clearinghouse during the course of my study. However, I am confident that the majority of existing guidance documents on the topic were captured using the methods I outlined. The several deficiencies I identified in the body of existing recommendations imply that future work on this topic should strive to develop high-quality evidence to determine optimal practices for the prescription of opioids at discharge after abdominal-pelvic surgery.

In light of these deficiencies, however, the direct adaptation and implementation of this knowledge product into the Action Cycle of the KTA process would likely be inappropriate. The paucity of high-quality, specific, actionable and evidence-based recommendations on this topic may be driven in part by a lack of high-quality scientific data supporting the recommended interventions and a lack of structured and explicit guidance development process in existing documents. However, given the increasing scrutiny on the appropriateness of post-operative opioid prescribing that is driven by the ongoing opioid epidemic, guidance is needed on this topic targeted

towards Canadian surgeons. As such, I initiated the development of agreement-based recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery in Canada in Chapter 4 of this thesis.

Developing Recommendations for the Prescription of Opioids at Discharge After Abdominal-Pelvic Surgery

In accordance to the definition of CPGs set out by the Institute of Medicine, I have used the results of my systematic review of recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery to inform my guideline development process. In Chapter 4 of this thesis, I created a 50-member guideline panel involving stakeholders from different disciplines across Canada as well as the work I have done in familiarizing these panel members with the result of my reviews. Specifically, I prepared documents summarizing the interventions identified through my systematic reviews and presented my findings through a series of webinars, during which I initiated discussions on the recommendation development process. Following the webinars, I used a web-based survey to elicit the opinion of panelists regarding the preliminary scope of my recommendations. I have also detailed the plan for future steps in the development of these recommendations, including the use of a modified Delphi method to build agreement on the proposed statements.

Our decision to use a systematic review of recommendations to inform my guideline development process is driven by the assumption that the existing guidance would be supported by the best available evidence. Therefore, by systematically identifying existing recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery, I have also identified the best available evidence supporting the interventions addressed in those recommendations in

the references section of those documents. In this thesis, I did not systematically summarize the supporting studies themselves. While I acknowledge that this may represent a limitation of my guideline development process, only 11.4% of identified interventions were supported by an explicit assessment of the level of evidence, which would be not expected to contribute in a meaningful manner in generating useful recommendations targeted at Canadian abdominal-pelvic surgeons.

An alternative approach to using a systematic review of recommendations to form the evidence basis to my guideline development process would be to clearly define specific questions that need to be addressed in my guidance document and to conduct systematic reviews of the literature on each of these questions. However, this is a time-consuming process and, given the small body of evidence I have already identified, this approach is unlikely to contribute new information to direct the development of my guidelines.

In contrast to formal frameworks for guideline development such as the GRADE approach,[161] I plan to develop my recommendations by building agreement around the proposed statements. As described in detail in the introductory section of Chapter 4, GRADE provides a structured, step-by-step, method of developing clinical practice guidelines, involving 1) framing the health care questions, 2) selecting and rating the importance of outcomes, 3) summarizing the evidence, 4) rating the quality of evidence and 5) going from evidence to recommendations.[161] However, the proper application of the GRADE approach requires the availability of high-quality evidence, such as randomized controlled trials and meta-analyses, without which the resultant recommendations would likely be all considered weak and supported by a very low quality of evidence. As previously discussed, few existing recommendations for the prescription of opioids at discharge after abdominal-pelvic surgery are supported by a formal assessment of evidence. The

application of GRADE in this setting would be unlikely to yield recommendations with useful and meaningful classifications of grade or level of evidence, as all the resultant guidance would be supported by a very low quality of evidence. Therefore, I plan to develop guidance for the prescription of opioids at discharge after abdominal-pelvic surgery by building agreement among my 50-member guideline panel on the proposed recommendations using a modified Delphi method.

Based on the results of my web-based surveys used in defining the scope of my intended recommendations, I came to appreciate a need to more clearly define the scope of my recommendations in future work. Indeed, for most of the categories of interventions proposed in my survey, I observed a high-level of agreement among the respondents for inclusion into my guideline. However, this may potentially lead to an exhaustive and over-whelming set of recommendations, which will likely undermine the usefulness of the document to busy surgical providers who are likely in need of concise, specific and actionable guidance on opioid prescribing at patient discharge. In this sense, future work using web-based surveys to elicit the views of the guideline panel on the guideline scope should attempt to clearly define a concise subset of goals that the recommendations can address without being overwhelming and exhaustive. Strategies that could be used to achieve this goal could include the use of ranking exercises to prioritize the most important interventions for inclusion and/or imposing a limit on the number of recommendations to direct the guideline development process.

Several limitations may have undermined the quality of this study. As discussed in Chapter 4 of this thesis, these limitations include an over-representation of individuals from Ontario on the guideline panel, a moderate rate of participation on the webinars and the survey, the difficulties presenting all of the review findings during the webinar as well as my inability to review individual

studies that supported the existing recommendations. Given the preliminary stage of this work, I am unable to draw any implications for practice at this point.

Behavioral Interventions to Decrease Opioid Prescribing at Discharge After Surgery

In Chapter 3 of this thesis, I created a second knowledge tool in my systematic review of behavioral interventions to decrease post-operative opioid prescribing at patient discharge. Given the increased scrutiny on post-surgical opioid prescribing that is driven by the ongoing opioid epidemic, many health care institutions across North America have reported strategies used to change the behavior of surgeons in reducing the amount of opioid in discharge prescriptions. A systematic summary of these strategies may be useful in preparation for their dissemination and implementation into clinical practice. Using the classification of behavioral strategies provided by the Cochrane Effective Practice and Organisation of Care (EPOC) group,[130] I searched MEDLINE, EMBASE, CINAHL and PsycINFO to identify studies of interventions designed to decreased opioid prescribing at discharge after any surgery. Out of 24 studies included in my review, I identified six types of behavioral interventions: local consensus-based processes (18 studies), patient-mediated interventions (2 studies), clinical practice guidelines (1 study), educational meetings (1 study), inter-professional education (1 study) and clinician reminders (1 study). Almost all studies reported a statistically significant decrease in the amount of opioid prescribed at discharge after surgery without no associated increased in the intensity of pain experienced by patients. However, primarily due to study design, all studies were found to have a medium-to-high risk of bias based on criteria suggested by the Cochrane EPOC group[132] as well as the Newcastle-Ottawa Quality Assessment Scale.[137]

The consistency in the direction of effect of these interventions suggests that, across all specialties, surgeons are willing to change their behavior and reduce the amount of opioid provided to their patients at discharge. More importantly, in the majority of studies, this can be done without affecting the degree of pain experienced by patients post-discharge. Although a number of different types of interventions have been identified, the majority of the studies used a local consensus-based process to develop institution-based opioid prescribing recommendations in order to change the behavior of surgeons. This finding provides further evidence to support the hypothesis that current opioid prescribing practices are in part driven by a lack of useful guidelines designed for surgeons. This is also consistent with my finding in Chapter 2 that most existing recommendations have not been developed based on a systematic review but rather a local consensus process. Furthermore, this provides support to my decision to use agreement-building methods to develop recommendations in Chapter 4 of this thesis.

Limitations of my systematic review include the lack of pilot-testing and calibration of the screening, data extraction and risk of bias assessment processes. Also, the application of the Cochrane EPOC taxonomy to classify behavioral interventions was at times imperfect, and strategies to influence practitioner behavior at the policy level were excluded. Despite these issues, my systematic review of behavioral interventions is an important first step in translating the existing knowledge into action to improve the practices of surgeons on the prescription of opioids at patient discharge. The synthesis of effective strategies to change the behavior of surgeons provides a starting point for health care institutions across North America seeking to decrease the over-prescription of opioids by their local surgeons. Institutions can use my study to review the best available evidence on this topic, select the type(s) of intervention they would like to implement and adapt these interventions to their local context. Although these interventions will need to be

tailored to the circumstances of the local health care system, I have demonstrated that a potential major barrier to the implementation of these strategies, the concern for a suboptimal control of post-surgical pain among patients, can be mitigated successfully. Following the implementation of these interventions, institutions can, in accordance to the KTA process, monitor the use of their interventions among surgical providers, evaluate important outcomes (i.e. the amount of opioid prescribed after surgery) and ensure that the use of this knowledge is sustained in the long-term. The iterative nature of the KTA process allows that further problems may be identified throughout the action cycle, which may require the creation of further knowledge products and implementation into action. Ultimately, the goal of this exercise is to ensure that surgical practices for the prescription of opioids at discharge are optimized in that they are evidence-based and developed with the consideration of balancing the appropriate control of post-surgical pain and the risks associated with the excessive prescription of opioids.

Importance

The work conducted in this thesis is important in the effort to improve the prescription of opioids at patient discharge after surgery. Systematic reviews are powerful tools to rigorously and explicitly synthesize the existing knowledge on a topic, identify strengths and deficiencies as well as guide future research. Given the devastating effect of the ongoing opioid epidemic in North America and the resultant intense scrutiny on the appropriateness of post-surgical opioid prescribing, my current work, grounded in the KTA process, is timely. My conduct of two systematic reviews on the topic provides an updated view of the current state of the literature as well as areas of priorities future research should focus. In addition, I have initiated the development of recommendations targeted towards Canadian abdominal-pelvic surgeons, which is much needed.

Although decreasing opioid prescriptions after surgery may have little immediate impact on the epidemic of opioid-related mortality and morbidity, the appropriate prescribing of opioids by surgeons is a worthwhile goal to strive for in order to minimize the potential harms associated with narcotics.

Implications for Policy

Given the potential harms associated with the excessive prescription of opioids after surgery, future policy should target this area as a priority to improve the quality of health care provided to Canadians. My research findings highlighted a lack of useful guidance for the prescription of opioids at discharge after surgery. While I initiated the development of recommendations targeted towards Canadian abdominal-pelvic surgeons, future policies could encourage similar initiatives in other surgical specialties. As I have shown in Chapter 3 of this thesis, the development of guidelines targeted at surgeons can be an effective method of reducing the amount of opioid prescribed after surgery without affecting the patient experience with their post-operative recovery.

Our systematic review of recommendations also identified a number of co-interventions that can be used when prescribing opioids at discharge after surgery. For example, the use of prescription drug monitoring programs (PDMP) is common in the United States and the mandatory use of this program in certain settings has been shown to be associated with decreased opioid prescriptions.[159] Although a similar system is available in most of the provinces in Canada, few surgeon guideline panel members in my research were aware of or routinely used these systems. Future policy should address whether further education about the use of such systems should be

considered and potentially if the systems should be considered mandatory when prescribing opioids in Canada.

Future Research

Based on the results of my systematic reviews, future research should focus on conducting scientifically rigorous studies to create high-level evidence upon which to develop guidelines targeted at surgeons. In this sense, the use of randomized controlled trials to compare two regimens of prescription opioids at patient discharge after surgery may be worthwhile, as this may be a low-resource and easy way of demonstrating the safety and effectiveness of prescriptions that contain lower dosages of opioids using a rigorous study design.

Patient characteristics are likely strong determinants of individual requirements for opioids for the control of pain after surgery as well as for the development of chronic opioid use. In a recent descriptive study of 3412 patients undergoing elective surgery at an academic health center, Thiels *et al.* identified several risk factors associated with higher post-discharge opioid consumption including pre-operative opioid use, young age, anxiety and high discharge pain scores.[61] Regarding the risk of chronic post-surgical opioid use, recent studies have shown that younger age, lower household income, pre-operative use of benzodiazepines or antidepressants, presence of substance use disorders, mood disorders or pain disorders are associated with an increased risk of using opioids long-term.[48-53] Future research should focus on the development of easy-to-use tools specifically designed to allow surgeons to accurately identify patients at risk of increased opioid requirements in the immediate post-operative setting as well as those who are at increased risk of developing a chronic opioid use disorder. The development of such tools would allow the early identification of at-risk patients and could alter management starting in the

immediate perioperative period, for example by targeting opioid-minimization protocols only to those who are at high risk. Currently, few studies assess the effectiveness of perioperative strategies to prevent the development of long-term opioid related complications, such as the development of an opioid use disorder, and this is a needed focus of future research work.

Additional research is also needed on the role of non-opioid medications in the management of acute surgical pain and whether opioid-free strategies can be a feasible alternative to existing pain management strategies that involve opioids. In Chapter 3 of this thesis, I have identified a number of procedures for which opioids may not be required for a significant proportion of patients after surgery: caesarean section, breast lumpectomy and aesthetic surgery. Future work is warranted to look at the degree of pain experienced after these procedures, and whether an opioid-free strategy involving non-opioid medications can be successfully implemented. As opioids are associated with significant short-term and long-term adverse effects, a complete replacement of these medications with other pharmacological agents to control of post-surgical pain would be an effective way to prevent opioid-related complications.

Conducting the work presented in this thesis has allowed me to acquire an important skill set to initiate my career as a clinician-researcher. Indeed, I came to appreciate the invaluable knowledge and content expertise that the rigorous and explicit step-by-step processes of a systematic review confers. By conducting a systematic review, researchers are able to critically appraise the current state of research in a given field and identify important gaps in research upon which to focus their future endeavours. Moreover, I gained experience in the early steps of consensus-building studies as well from the processes of manuscript writing and publication. I believe that these skills will serve me tremendously in my future research endeavours on improving the quality of care in post-operative pain control.

Conclusion

The ongoing epidemic of opioid-related mortality has shed light on suboptimal practices by surgeons when prescribing opioids at discharge in their patients. Given the risks associated with excessive prescription of opioids, the appropriate use of these medications after surgery is important. In this thesis, I used the knowledge translation framework provided by the KTA process to develop knowledge tools on the prescription of opioids at discharge after surgery for implementation into clinical practice. Specifically, I have conducted a systematic review of existing recommendations after abdominal-pelvic surgery as well as a systematic review of behavioral strategies to change opioid prescribing practices after any type of surgery. My results demonstrated that, while surgeons are generally receptive to strategies to improve their practice, useful guidance in this area is lacking. Based on this finding, I have initiated the develop of opioid prescribing recommendations targeted at Canadian abdominal-pelvic surgeons. The work conducted in this thesis has meaningfully contributed to the current literature and will service as an impetus for future work to improve post-surgical opioid prescribing.

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APPENDIX

Appendix 2.1 PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	34
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	35
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	36
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	35-36
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	37
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	37
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	38
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	38-44
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	45
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	45
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	45
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	45
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Not applicable

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	46
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Not applicable
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	46-47
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	47-51
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	52-54
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	55-72
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Not Applicable
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Not applicable
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not applicable
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	73-76
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	76
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	77
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	4

Appendix 2. 2 Grey Literature Websites Searched To Identify Recommendations for the Prescription of Opioids at Discharge After Abdominal-Pelvic Surgery

Title	Link
09.16.15 696 Minutes of the Town of Riverhead Board meeting held …	09.16.15 696 Minutes of the Town of Riverhead Board meeting held ...
2014 HYDE County Community Health Assessment	2014 HYDE County Community Health Assessment
2015 community health needs assessment - University Hospitals	2015 community health needs assessment - University Hospitals
2015 Employee Benefits Booklet - City of Casper	2015 Employee Benefits Booklet - City of Casper
2015 NZNC Chair report to AGM	http://www.anzca.edu.au/documents/4-1-nznc-chair-2015-agm-final
2016 community health needs assessment - University Hospitals	2016 community health needs assessment - University Hospitals
2016 Press Releases	· 2016 Press Releases
2016 state legislative year in review and a look ahead | The ...	· 2016 state legislative year in review and a look ahead | The ...
2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain	2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain
2017 state legislative year in review and a look toward 2018 ...	· 2017 state legislative year in review and a look toward 2018 ...
2018 Program and Abstracts	http://meeting.americansurgical.org/abstracts/2018-Program.cgi
39662_Anzca-Bulletin-June-14	http://www.anzca.edu.au/documents/39662_anzca-bulletin-june-14
9 Million Prescriptions – What we know about the growing use of …	9 Million Prescriptions – What we know about the growing use of ...
A Guideline for the Clinical Management of Opioid ... - Government of BC	A Guideline for the Clinical Management of Opioid ... - Government of BC
A primary care approach to sodium and potassium imbalance - best …	https://bpac.org.nz/BT/2011/September/imbalance.aspx
A Structured Approach to Opioid Prescribing	https://www.rcoa.ac.uk/node/21173
ACMT and AACT Position Statement: Preventing Occupational …	ACMT and AACT Position Statement: Preventing Occupational ...
ACS achieves notable legislative victories in 2016 | The ...	· ACS achieves notable legislative victories in 2016 | The ...
ACS Chapter Grant Program supports opportunities to lobby …	· ACS Chapter Grant Program supports opportunities to lobby ...
ACS Chapter Lobby Days Program: Surgeons work the halls ...	· ACS Chapter Lobby Days Program: Surgeons work the halls ...
ACS in the News	· ACS in the News
ACS in the news | The Bulletin	· ACS in the news | The Bulletin
ACS Launches Education Program on Opioids and Surgery ...	· ACS Launches Education Program on Opioids and Surgery ...
Acute coronary syndromes open consultation report - Scottish …	http://www.sign.ac.uk/assets/sign155_consultation_report.pdf
Acute heart failure: diagnosing and managing acute heart failure in adults.	Acute heart failure: diagnosing and managing acute heart failure in adults.
Acute Pain Management in the Perioperative Setting	http://anesthesiology.pubs.asahq.org/article.aspx?articleid=1933589

Adapting your practice: treatment and recommendations for unstably housed patients with HIV/AIDS.	https://www.guideline.gov/summaries/summary/47766/adapting-your-practice-treatment-and-recommendations-for-unstably-housed-patients-with-hivaids?q=guideline+OR+recommendation+OR+consensus+OR+position+OR+best+practice+OR+statement+AND+opioid+OR+opiate+OR+narcotic+AND+Prescrib+or+Prescription+AND+postoperat+OR+operat+OR+surg
Alcohol misuse: how to help patients in primary care - BPJ 75 May …	https://bpac.org.nz/BPJ/2016/May/alcohol.aspx
AMDG 2017 Dental Guideline on Prescribing Opioids for Acute Pain …	AMDG 2017 Dental Guideline on Prescribing Opioids for Acute Pain ...
American Academy of Orthopaedic Surgeons appropriate use criteria for non-arthroplasty treatment of osteoarthritis of the knee.	American Academy of Orthopaedic Surgeons appropriate use criteria for non-arthroplasty treatment of osteoarthritis of the knee.
American Academy of Orthopaedic Surgeons clinical practice guidelineon the treatment of osteoarthritis of the knee, 2nd edition.	American Academy of Orthopaedic Surgeons clinical practice guidelineon the treatment of osteoarthritis of the knee, 2nd edition.
American Geriatrics Society abstracted clinical practice guideline for postoperative delirium in older adults.	https://www.guideline.gov/summaries/summary/49932/american-geriatrics-society-abstracted-clinical-practice-guideline-for-postoperative-delirium-in-older-adults?q=guideline+OR+recommendation+OR+consensus+OR+position+OR+best+practice+OR+statement+AND+opioid+OR+opiate+OR+narcotic+AND+Prescrib+or+Prescription+AND+postoperat+OR+operat+OR+surg
Amputation	http://www.anzsvs.org.au/patient-information/amputation/?sstat=1274
An Evidence-Based Approach to the Prescription Opioid Epidemic in …	An Evidence-Based Approach to the Prescription Opioid Epidemic in ...
An Update on Analgesics for the Management of Acute Postoperative …	An Update on Analgesics for the Management of Acute Postoperative ...
An update on antithrombotic medicines - BPJ Issue 67	https://bpac.org.nz/bpj/2015/april/antithrombotic.aspx
anaesthesia-training-program-curriculum	http://www.anzca.edu.au/documents/anaesthesia-training-program-curriculum
Anesthesia & Analgesia Focuses on Postoperative Cognitive Dysfunction (POCD)	http://www.iars.org/anesthesia__analgesia_focuses_on_postoperative_cognitive_dysfunction_pocd/
Annual Meeting Live Stream	http://www.iars.org/education/annual_meeting/live_stream/
annual-report-2009	http://www.anzca.edu.au/documents/annual-report-2009
ANTICOAGULATION AFTER PANCREAS RESECTION AND AUTOLOGOUS ISLET TRANSPLANTATION: WHAT IS A SAFE PROTOCOL?	https://www.esot.org/events-education/education-channel/anticoagulation-after-pancreas-resection-and-autologous-islet
ANZCA-annual-report-2012-FINAL	http://www.anzca.edu.au/documents/anzca-annual-report-2012-final
ANZCA-Blue-Book-2011-P9	http://www.anzca.edu.au/documents/anzca-blue-book-2011-p9
anzca-bulletin-2007-jul	http://www.anzca.edu.au/documents/anzca-bulletin-2007-jul
anzca-bulletin-2008-dec	http://www.anzca.edu.au/documents/anzca-bulletin-2008-dec
anzca-bulletin-2008-jul	http://www.anzca.edu.au/documents/anzca-bulletin-2008-jul
anzca-bulletin-2009-dec	http://www.anzca.edu.au/documents/anzca-bulletin-2009-dec
anzca-bulletin-2009-jul	http://www.anzca.edu.au/documents/anzca-bulletin-2009-jul
anzca-bulletin-2009-mar	http://www.anzca.edu.au/documents/anzca-bulletin-2009-mar
anzca-bulletin-2009-oct	http://www.anzca.edu.au/documents/anzca-bulletin-2009-oct

anzca-bulletin-2010-mar	http://www.anzca.edu.au/documents/anzca-bulletin-2010-mar
ANZCA-Bulletin-2012-March	http://www.anzca.edu.au/documents/anzca-bulletin-2012-march
ANZCA-Bulletin-December-2011	http://www.anzca.edu.au/documents/anzca-bulletin-december-2011
ANZCA-Bulletin-March-2018-web-version	http://www.anzca.edu.au/documents/anzca-bulletin-march-2018-web-version
ANZCA-Prescription-strong-(Schedule-8)-opioid-use-and-misuse-in-Australia-submission-FINAL	http://www.anzca.edu.au/documents/anzca-prescription-strong-(schedule-8)-opioid-use
April - June 2013 JSLS - JOURNAL OF THE ... - Laparoscopy Today	http://laparoscopy.blogs.com/jslsjournal/JSLSPDFs/JSLSVol17No2.pdf
Arizona Opioid Prescribing Guidelines - Arizona Department of Health …	Arizona Opioid Prescribing Guidelines - Arizona Department of Health ...
ASC Physician Focus Volume 1, Number 4	https://www.ascaconnect.org/HigherLogic/System/DownloadDocumentFile.ashx?DocumentFileKey=2a8bc359-681b-777f-d979-b51edfd5b2f6&forceDialog=0
AST Washington Round-Up (March 2018)	https://www.myast.org/public-policy/ast-washington-round-march-2018
ATC Schedule	https://www.myast.org/atc-schedule
Audit Recipe Book: Section 11, Pain medicine	https://www.rcoa.ac.uk/system/files/CSQ-ARB2012-SEC11.pdf
Audit Recipe Book: Section 3, Post-operative care	https://www.rcoa.ac.uk/system/files/CSQ-ARB2012-SEC3.pdf
Australasian-Anaesthesia-2009	http://www.anzca.edu.au/documents/australasian-anaesthesia-2009
Australasian-Anaesthesia-2013	http://www.anzca.edu.au/documents/australasian-anaesthesia-2013
Baldini, Gabriele. Intravenous lidocaine as sole analgesic technique for laparoscopic cholecystectomy [electronic resource]. -- Montréal : McGill University, 2011	http://digitool.library.mcgill.ca/thesisfile97154.pdf
Bariatric Surgical Patients at Risk for Newly Persistent Opioid ...	· Bariatric Surgical Patients at Risk for Newly Persistent Opioid ...
BEGIN PRIVACY-ENHANCED MESSAGE----- Proc-Type: 2001,MIC …	BEGIN PRIVACY-ENHANCED MESSAGE----- Proc-Type: 2001,MIC ...
Best Practice Journal Issue 61	https://bpac.org.nz/bpj/2014/june/contents.aspx
Biliary colic and complications from gallstones - BPJ 61 June 2014	https://bpac.org.nz/bpj/2014/june/gallstones.aspx
Bladder cancer: diagnosis and management	https://www.nice.org.uk/guidance/ng2
Blunt Thoracic Trauma (BTT), Pain Management in - Practice …	http://www.east.org/education/practice-management-guidelines/blunt-thoracic-trauma-btt-pain-management-in
BPJ 44: Update on oxycodone	https://bpac.org.nz/bpj/2012/may/oxycodone.aspx
BPJ 47: Managing medicines in older people	https://bpac.org.nz/BPJ/2012/october/elderlyMedicines.aspx
BPJ 48: When and how to use a syringe driver in palliative care	https://bpac.org.nz/bpj/2012/november/syringedrivers.aspx
BPJ 49: Strong opioids for pain management in adults in palliative …	https://bpac.org.nz/bpj/2012/december/opioids.aspx
BTS guideline for oxygen use in adults in healthcare and emergency settings.	BTS guideline for oxygen use in adults in healthcare and emergency settings.
Bulletin December 17 FINAL spreads	http://www.anzca.edu.au/documents/bulletin-december-17-final-spreads

Bulletin-Dec-2013-FINAL	http://www.anzca.edu.au/documents/bulletin-dec-2013-final
Buprenorphine/Naloxone for Opioid Dependence: Clinical Practice …	Buprenorphine/Naloxone for Opioid Dependence: Clinical Practice ...
Caesarean section.	Caesarean section.
Canadian Cardiovascular Society/Canadian Anesthesiologists' Society/Canadian Heart Rhythm Society joint position statement on the perioperative management of patients with implanted pacemakers, defibrillators, and neurostimulating devices	http://www.cas.ca/English/Page/Files/97_Joint_Statement_CAS CHRS_Cardiology 2012.pdf
Canadian Guideline for Safe and Effective Use of Opioids - Michael G …	Canadian Guideline for Safe and Effective Use of Opioids - Michael G ...
Care of the patient with myasthenia gravis.	Care of the patient with myasthenia gravis.
CDC Guideline for Prescribing Opioids for Chronic Pain — United …	CDC Guideline for Prescribing Opioids for Chronic Pain — United ...
CHI Allergy Recommendation - NCVHS - HHS.gov	CHI Allergy Recommendation - NCVHS - HHS.gov
Choosing Wisely	http://www.auanet.org/practice-resources/2017-quality-reporting-program/choosing-wisely
Chronic Non-Cancer Pain Management and Opioid Resources | CPD …	Chronic Non-Cancer Pain Management and Opioid Resources | CPD ...
Chronic obstructive pulmonary disease in over 16s: diagnosis and management	https://www.nice.org.uk/guidance/cg101
Chronic Pain Management	http://anesthesiology.pubs.asahq.org/article.aspx?articleid=1932775
Chronic pelvic pain in women - BPJ70	https://bpac.org.nz/bpj/2015/september/pelvic.aspx
CIHR Assessment of the Canadian Guideline for Opioids for Chronic …	CIHR Assessment of the Canadian Guideline for Opioids for Chronic ...
Clarke, Hance. The Effects of Gabapentin on Pre-operative Anxiety, Morphine Consumption and Pain after Surgery [electronic resource]. -- Toronto : University of Toronto, 2013	https://tspace.library.utoronto.ca/bitstream/1807/35795/1/Clarke_Hance_A_201306_PhD_thesis.pdf
Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain (2009)	http://www.jpain.org/article/S1526-5900(08)00831-6/abstract
Clinical Practice Guideline for Ambulatory Anorectal Surgery	Clinical Practice Guideline for Ambulatory Anorectal Surgery
Clinical Practice Guideline for the Evaluation and Management of Constipation	Clinical Practice Guideline for the Evaluation and Management of Constipation
Clinical practice guideline for the management of patients with Parkinson's disease.	Clinical practice guideline for the management of patients with Parkinson's disease.
Clinical Practice Guideline for the Treatment of Fecal Incontinence	Clinical Practice Guideline for the Treatment of Fecal Incontinence
Clinical Practice Guidelines	https://vascular.org/research-quality/clinical-practice-documents/clinical-practice-guidelines
Clinical Practice Guidelines for Enhanced Recovery	Clinical Practice Guidelines for Enhanced Recovery
Clinical Practice Guidelines for the Management of Hemorrhoids	Clinical Practice Guidelines for the Management of Hemorrhoids
Colinic Diverticular Disease Commissioning Guide	https://www.rcseng.ac.uk/-/media/files/rcs/library-and-publications/non-journal-publications/colinic-diverticular-disease-commissioning-guide.pdf
collective bargaining agreement - City of Rockford	collective bargaining agreement - City of Rockford

Commentary to Society position statement	http://www.cas.ca/English/Page/Files/97_Commentary.pdf
Consensus guidelines for enhanced recovery after gastrectomy	https://onlinelibrary.wiley.com/doi/full/10.1002/bjs.9582
Consensus Review of Optimal Perioperative Care in Breast Reconstruction: Enhanced Recovery after Surgery (ERAS) Society Recommendations	https://journals.lww.com/plasreconsurg/Abstract/2017/05000/Consensus_Review_of_Optimal_Perioperative_Care_in.9.aspx
Control of pain in adults with cancer. (SIGN Guideline No 106)	http://www.sign.ac.uk/assets/sign106.pdf
Core Standards for Pain Management Services in the UK	https://www.rcoa.ac.uk/system/files/FPM-CSPMS-UK2015.pdf
Core Topics Exeter	https://www.aagbi.org/education/event/2059
Correspondence - BPJ 75 May 2016	https://bpac.org.nz/BPJ/2016/May/correspondence.aspx
CPD-PACU-pain-clinical-audit-guide-v2-2018	http://www.anzca.edu.au/documents/pacu-pain-clinical-audit-guide-v1-2017
CPSA: Home	CPSA: Home
Cumulative trauma conditions medical treatment guidelines.	Cumulative trauma conditions medical treatment guidelines.
CVS tightens restrictions on opioid prescriptions in bid to stanch - Stat	CVS tightens restrictions on opioid prescriptions in bid to stanch - Stat
Day Case Breast Surgery Pathway	Day Case Breast Surgery Pathway
December 2005 - The 1st Edition: Prevention & Management:	http://laparoscopy.blogs.com/prevention_management/2005/12/index.html
Decreased Risk of Delirium with Use of Regional Anesthesia in Geriatric Trauma Patients with Multiple Rib Fractures	http://americansurgical.org/meeting/abstracts/2018/15.cgi
Dental Sedation Report	https://www.rcseng.ac.uk/-/media/files/rcs/library-and-publications/non-journal-publications/dental-sedation-report.pdf
Dentistry and the Opioid Epidemic - Medscape	Dentistry and the Opioid Epidemic - Medscape
Diagnosis and management of epilepsy in adults. A national clinical guideline.	Diagnosis and management of epilepsy in adults. A national clinical guideline.
Diagnosis and treatment of interstitial cystitis/bladder pain syndrome	http://www.cua.org/themes/web/assets/files/3786v3.pdf
Diagnosis and Treatment of Low Back Pain: A Joint Clinical Practice Guideline from the American College of Physicians and the American Pain Society (2007)	http://www.annals.org/cgi/content/full/147/7/478
Discharge prescription patterns of opioid and nonopioid analgesics …	Discharge prescription patterns of opioid and nonopioid analgesics ...
Early Use Of Low Residue Diet Is Superior To Clear Liquid Diet After Elective Colorectal Surgery	http://meeting.americansurgical.org/abstracts/2014/25.cgi
Eastern Association for the Surgery of Trauma	www.east.org/content/documents/2015_apsworkshop_handout_rev_12_23_2014.pdf
editorial scientific papers - Laparoscopy Today	http://laparoscopy.blogs.com/files/jsls18_2.pdf
Effect of Alvimopan on Gastrointestinal (GI) Recovery Following Small Bowel Resection (SBR) in Patients With and Without Crohn's Disease (CD): Results of a Pooled Analysis of 3 Randomized, Placebo-Controlled Trials	http://meetings.ssat.com/abstracts/06ddw/SSAT_DDW06_237.cgi
Endometriosis: diagnosis and management.	Endometriosis: diagnosis and management.

Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 1: pathophysiological considerations	https://onlinelibrary.wiley.com/doi/full/10.1111/aas.12601
Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice	https://onlinelibrary.wiley.com/doi/full/10.1111/aas.12651
Enhanced Recovery after Surgery: ERAS for All	http://bestpracticeinsurgery.ca/wp-content/uploads/2017/11/ERAS_BPS_FINAL_Nov2017.pdf
Essential Pain Management	https://www.rcoa.ac.uk/faculty-of-pain-medicine/essential-pain-management-global
Etoricoxib Is Effective for Postoperative Pain	http://www.iars.org/etoricoxib_is_effective_for_postoperative_pain/
European Journal of Surgical Oncology (EJSO), Volume 41, Issue 1, Pages 1-174, S1-S16 (January 2015)	European Journal of Surgical Oncology (EJSO), Volume 41, Issue 1, Pages 1-174, S1-S16 (January 2015)
Extent of HIV and hepatitis C co-infections revealed | FIGO	https://www.figo.org/news/extent-hiv-and-hepatitis-c-co-infections-revealed-0015215
Factors Predicting Outcomes After Total Pancreatectomy And Islet Auto Transplant - Lessons Learned From Over 500 Cases	http://meeting.americansurgical.org/abstracts/2015/19.cgi
FA-PERI-SIG-Carol-Douglas-Considerations-at-end-of-life_20161109	http://www.anzca.edu.au/documents/fa-peri-sig-carol-douglas-considerations-at-end-of
Final report on the AFMC Response to the Canadian Opioid Crisis	Final report on the AFMC Response to the Canadian Opioid Crisis
Getting Started with Medication-assisted Treatment - William White …	Getting Started with Medication-assisted Treatment - William White ...
Global Competency-Based Fistula Surgery Training Manual	https://www.figo.org/sites/default/files/uploads/wg-publications/fistula/FIGO_Global_Competency-Based_Fistula_Surgery_Training_Manual_0.pdf
Gold Preferred Plan - Otay Water District	Gold Preferred Plan - Otay Water District
Guideline for care of the patient receiving moderate sedation/analgesia.	Guideline for care of the patient receiving moderate sedation/analgesia.
Guideline for Discharge Opioid Prescriptions after Inpatient General …	Guideline for Discharge Opioid Prescriptions after Inpatient General ...
Guideline for opioid therapy and chronic noncancer pain	Guideline for opioid therapy and chronic noncancer pain
Guideline for prescribing opioids to treat pain in injured workers.	Guideline for prescribing opioids to treat pain in injured workers.
Guideline for the Management of Acute and Chronic Pain in Sickle-Cell Disease (1999)	http://americanpainsociety.org/education/guidelines/sickle-cell-guideline
Guidelines for perioperative care after radical cystectomy for bladder cancer: Enhanced Recovery After Surgery (ERAS®) society recommendations	https://www.clinicalnutritionjournal.com/article/S0261-5614(13)00254-9/fulltext
Guidelines for Perioperative Care for Liver Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations	https://link.springer.com/article/10.1007/s00268-016-3700-1
Guidelines for Perioperative Care for Pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS®) Society Recommendations	https://link.springer.com/article/10.1007/s00268-012-1771-1
Guidelines for Perioperative Care in Bariatric Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations	https://link.springer.com/article/10.1007/s00268-016-3492-3

Guidelines for Perioperative Care in Elective Colonic Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations	https://link.springer.com/article/10.1007/s00268-012-1772-0
Guidelines for Perioperative Care in Elective Rectal/Pelvic Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations	https://link.springer.com/article/10.1007/s00268-012-1787-6
Guidelines for postoperative care in gynecologic/oncology surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations — Part II	https://www.gynecologiconcology-online.net/article/S0090-8258(15)30222-5/abstract
Guidelines to the Practice of Anesthesia	http://www.cas.ca/English/Page/Files/97_Guidelines-2018.pdf
Head injury. Triage, assessment, investigation and early management of head injury in children, young people and adults.	Head injury. Triage, assessment, investigation and early management of head injury in children, young people and adults.
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Appendix 3. 1 PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	78
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	79
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	80
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	80
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	81
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	81-83
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	83-90
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	83-90
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	90
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	90
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	90
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	91-92
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	92
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	92

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Not applicable
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	92-93
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	94-99
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	100-103
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	104-114
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Not Applicable
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Not applicable
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not applicable
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	115-118
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	118-119
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	119
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	5

Appendix 4. 1 Templates Used To Recruit Providers and Patients

Provider	Subject Line: Invitation to Participate in a Guideline Panel to Develop Opioid Prescribing Recommendations after Abdominal Surgery Dear (name), The current opioid epidemic has shed light on poor opioid prescribing practices after abdominal surgery in Canada. Part of this problem is driven by the lack of opioid prescribing guidelines for Canadian surgeons. Our research team is in the process of developing best practice recommendations for the prescription of opioids after abdominal surgery funded by the Canadian Institutes of Health Research. To date, our team has completed a systematic review of existing recommendations of opioid prescription after abdominal and pelvic surgery. We have also identified a "toolbox" of implementation strategies for changing post-discharge opioid prescribing practice. Given your expertise, we would like to invite you to participate in our guideline panel. Our objective is to develop recommendations addressing three main areas: 1) Opioid prescribing at discharge after abdominal-pelvic surgery 2) Appropriate use and disposal of unused opioids 3) Management of opioid-naive patients at high risk of chronic opioid use. We plan to use the framework proposed by the GRADE working group, a scientifically rigorous and internationally-validated method to develop recommendations. Your involvement in this project will mainly consist of participating in online surveys as well as attending an in-person meeting in Toronto. Travel-related expenses will be reimbursed. (Name) recommended you for participation on the panel, and your input would be highly valued by our team. • If you wish to participate, please contact us by emailing (name) (email), program manager, by (date). ○ Please find the terms of reference attached to this email. • If you do not wish to participate, please reply back with a no thank you as it will help us identify others. • If you are aware of anybody who might be potentially interested in participating in this panel, please email us back with the recommendation. We look forward to your participation in this important work. Thanks in advance, (name) (signature)
Patient	Subject Line: Please help us recruit patients for the opioid prescribing guideline panel Dear (name), Our final study with the CIHR Opioid Knowledge Synthesis grant consists in the development of opioid prescribing guidelines after abdominal-pelvic surgery. We are currently in the process of finalizing our

guideline panel, and we need your assistance to identify potentially interested patients. We would like to recruit a total of 5 patients. Specifically, we are looking for:

- Patients who underwent a previous abdominal surgery
- Patients with chronic post-surgical pain
- Patients with a previous history of opioid dependence undergoing surgery

If you are aware of any individual who would be willing to participate in this guideline panel, please help us by contacting them. My research team will then contact the patient directly to obtain formal consent.

Should you need it, we have prepared the following email template for contacting potentially interested patients:

Subject Line: Invitation to participate in developing opioid prescribing guidelines after abdominal surgery

Dear Mr./Ms. (name),

The current opioid epidemic has shed light on poor opioid prescribing practices after abdominal surgery in Canada. Part of this problem is driven by the lack of opioid prescribing guidelines for Canadian surgeons.

My colleague Dr. (name), a surgeon at St Michael's hospital in Toronto, is in the process of developing clinical guidelines for the prescription of opioids after abdominal surgery. This work is funded by the Canadian Institutes of Health Research.

Given your experience, I would like to invite you participate in the guideline panel. Your input would be highly valuable to develop guidance for Canadian abdominal surgeons on prescribing opioids for their patients.

The required time commitment will consist of participation in webinars and online surveys (approximately 5 hours/month) in addition to attendance to an in-person meeting in Toronto in spring of 2019 (date to be determined).

Please let me know if you would like to participate in this project. If you choose to participate, I will forward your contact information to Dr. Baxter's research team, and you will be sent the official invitation.

(Signature)

Please let (name), my research manager, know of any interested individual by contacting her at (email).

Thanks in advance,

(name)

(signature)

Appendix 4. 2 First Survey Used To Define The Scope of the Recommendations

Changing Opioid Prescribing Practices After Abdominal and Pelvic Surgery
Canadian Guideline Development
Survey #1

BACKGROUND

With the goal of improving current practices after abdominal and pelvic surgery for 1) the prescription of opioid at discharge, 2) the appropriate disposal of excess opioids and 3) the prevention of chronic post-surgical opioid use, we have synthesized contemporary recommendations targeting these issues by systematically reviewing the literature. Additionally, we have identified effective behavioral strategies to improve opioid over-prescribing practices after surgery to facilitate dissemination.

Based on the findings of these systematic reviews, we seek to create a guidance document for the prescription of opioids at discharge following abdominal and pelvic surgery in Canada. This document will be targeted towards health care professionals who are involved in the prescription of opioids at discharge and in the management of patients using opioids for acute pain following discharge from abdominal and pelvic surgery.
In this survey, the aim is to define the scope of our guideline for opioid prescribing at discharge after abdominal surgery.
Your expertise and opinion are important to this work and we thank you in advance for your involvement.

INSTRUCTIONS

1. Please review the documents attached to this survey. We have included summaries of our systematic reviews, guidelines and original studies that may be relevant for you.
2. Please complete the questionnaire in one setting as you will not be able to save your results for completion at a later date. The questionnaire should take approximately 15 minutes to complete.
3. We would appreciate your responses within 2 weeks of receiving the survey. A reminder email will be sent one week following the initial mail out of the survey link.
4. No direct quotes from your responses will be published or used in reports of the results.
5. The decision to participate or not, and the survey responses, will have no impact on you professionally or else.
6. As this survey is anonymous, you cannot withdraw from the study once the survey has been submitted.
7. If you have any questions regarding your rights as a research participant, you may contact the Research Ethics Board Office at 416-864-6060 ext. 2557 during business hours (9:00am to 5:00pm).
8.

This is a research study conducted by Dr. Nancy Baxter at St Michael's hospital in Toronto, Ontario, Canada. Your consent to participate is implied by completing and submitting this survey.
If you require clarification at any point throughout the survey, please contact us at daviddq.zhang@mail.utoronto.ca.
Thank you for dedicating your time to participate in this study, your input is critical to the success of our guideline.

Our guidelines are being developed to guide prescribing practices at the time of discharge after abdominal and pelvic surgery. With this in mind

1. What patient population(s) should this guideline be applicable to? (check as many as apply)
    - Opioid naïve patients
    - Patients currently taking opioids
    - Patients at risk of development of chronic post-surgical opioid use
    - Patients with chronic pain
    - Patients on opioid agonist therapy

    Please comment on your selection: (free text)

2. If you selected more than one group in the previous question, should there be a separate section of recommendations for each group? (Please select "Not applicable" if you only selected one group in the previous question)
    - Yes
    - No
    - Not applicable

3. Should the guideline panel make recommendations regarding patient education?
    - Yes
        i. What key component(s) of patient education should this guideline address?
            1. Please specify: _____
    - No

4. Should the guideline panel include patient education materials in the recommendations?
    - Yes
    - No

5. Should the guideline panel make recommendations regarding the prescription of non-opioid therapies?
    - Yes
    - No

6. Should the guideline panel make recommendations regarding screening for risk factors for the development of chronic post-surgical opioid use?
    - Yes
        i. What key component(s) of this should this guideline address? (check as many as apply)
            1. Who should be doing the screening
            2. When to do the screening
            3. What to screen for
            4. Other, please specify: _____
    - No

7. Should the guideline panel make recommendations regarding the use of prescription drug monitoring programs when prescribing at discharge for all patients?
    - Yes
    - No

8. Should the guideline panel make recommendations for the management of patients presenting for opioid refill?
    - Yes
        i. What key component(s) of this should this guideline address?
            1. Please specify: _____
    - No

9. Should the guideline panel make recommendations regarding certain practices to avoid (e.g. to not prepare the discharge prescription prior to surgery)?
    - Yes
        i. What key component(s) of this should this guideline address? (check as many as apply)
            1. Concurrent prescribing of sedating medications
            2. Prescribing long-acting opioids
            3. Pre-operative preparation of prescription
            4. Other, please specify: _____
    - No

10. Should the guideline panel make recommendations regarding communication between surgeons and other providers (e.g. GP)?

- Yes
- No

11. Should the guideline panel make recommendations regarding how to best write a prescription for opioids (e.g. specified maximum length, limiting the initial dispensing with the ability for patients to get more)?
    - Yes
    - No

12. There was agreement on the webinar that recommendations are needed for specific opioid regimens at discharge after same-day surgical procedures and those involving an inpatient stay of less than < 24 hours in duration. According to your expertise, what specific procedures should be included in our guidelines?
    - _____

13. For procedures that involve an inpatient stay of greater than 24 hours, should the guideline recommend opioid regimens based on the amount used by the patient in the 24 hours prior to discharge?
    - Yes
    - No

14. Should the guideline panel make recommendations regarding opioid-free pain management strategies after discharge from abdominal-pelvic surgery?
    - Yes
    - No

15. Should the guideline panel make recommendations regarding specific methods of opioid disposal?
    - Yes
    - No

16. Should the guideline panel make recommendations regarding when, how and for whom referral to pain specialists should be made?
    - Yes
    - No