Perioperative Opioid Minimization:

A Review of the Literature
Introduction to Perioperative Pain Management

Current State

Evidence from the last few years has confirmed a trend: there is a lack of progress in the management of perioperative pain. A U.S. national survey conducted in 1993 concluded that 77% of adults experience pain after surgery with 80% of these patients reporting moderate to extreme pain (Warfield & Kahn, 1995). In 2003, studies found that approximately 80% of patients said they experienced acute pain after surgery (Apfelbaum, Chen, Mehta, & Gan, 2003). More recently, a paper published by Correll et al. (2014) found that in the last 20 years, national outcomes for pain relief have not improved. New drugs and techniques that have been introduced have not led to better outcomes and patients continue to experience unacceptably high levels of moderate or severe pain.

While the amount of pain Americans continue to experience remains unchanged, the sale of opioids has increased by seven-fold between 1997 and 2010, from 96 milligrams morphine equivalents per person to 710 milligrams (Prevention, 2012; Drug Enforcement Administration, 2011). In addition, the demand for hydrocodone – one of the more commonly prescribed opioids – is significantly higher than what is consumed by the rest of the world: 27.4 million grams per year versus 3,237 grams for Great Britain, Germany, Italy, and France combined (Manchikanti, Boswell, & Hirsch, Lessons Learned in the Abuse of Pain-Relief Medication: A Focus on Health Care Costs: Overuse of Therapeutic Opioids, 2013). Simply put, enough opioids are sold in the U.S. to supply each adult with 5 milligrams of hydrocodone every 6 hours for 45 days (Manchikanti, et al., 2012).

Traditionally, the foundation of perioperative analgesia has been opioid-based. However, increasing evidence indicates that patients are better served through the use of a multimodal approach. Today, perioperative physicians use combinations of acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), selective cyclooxygenase (COX-2) inhibitors, N-methyl-D-aspartate (NMDA) receptor antagonists, regional anesthetics, and local anesthetics in addition to opioids.

Why Optimize Opioid Utilization?

Perioperative pain management is crucial to long term patient quality of life (QoL). Factors such as preoperative pain and postoperative inflammatory processes can cause intensification of acute pain (Vadivelu, et al., 2014). Left untreated, postoperative pain can lead to long term emotional and psychological distress as well as a chronic pain state which becomes extremely difficult to manage. Chronic pain occurs in 10-50% of patients after surgery and greatly affects their QoL (Kehlet, Jensen, & Woolf, 2006).

Opioids remain a mainstay in perioperative pain analgesia, and while opioids are effective, they have many severe disadvantages such as sedation, nausea, constipation, tolerance, dependence, and potential addiction. While side effects of opioid use can be minor, opioids can also cause respiratory depression and death.

Furthermore, greater use of opioids before surgery is associated with slower recovery time, longer hospital length of stay (LOS), and worse outcomes after surgery. There is evidence that indicates that for every 100 morphine equivalents a patient takes preoperatively, their LOS is extended by 1.1 days; this can be extremely burdensome to the patient (Armaghani, et al., 2014).

How Can We Optimize Opioid Consumption?

Evidence indicates that multimodal pain management is the best way to reduce opioid consumption (McKenzie, Goyal, & Hozack, 2013; Young & Buvanendran, 2014). A multimodal pain
regimen incorporates a combination of local anesthetic and systemic drugs and techniques to target multiple pain pathways and sites. These drugs act together to reduce the potential for adverse effects caused by any single agent.

One promising frontier in the landscape of perioperative pain management is the emergence of new drugs that improve the efficacy of local anesthetics. Previously, the use of local anesthetics in perioperative settings was limited by their short duration of action. However, new drugs have been introduced to the market that are an extended-release formulation of bupivacaine and are designed to allow diffusion for up to 72 hours following administration at the end of surgery (Tong, Kaye, & Urman, 2014). Research has shown that these new drugs not only last longer than traditional formulations of bupivacaine, but also decrease the need for opioids postoperatively.

Lastly, maintaining effective communication between the patient and the surgical team is imperative to reducing opioid consumption (Angioli, et al., 2014). An accurate account of patient history, including prior response to pain, analgesia history, current medications, and fears and concerns regarding future pain is important to share with the surgical team to be sure that the best possible care can be provided. Perioperative pain management, physical therapy, and proper disposal of any unused medications should also be discussed.

**Purpose and Methods**

The purpose of this literature review is to examine the most up-to-date research in perioperative analgesia as well as explore promising avenues to improve pain management. In reviewing the literature it became clear that, as eloquently stated in Gritsenko et al. (2014), “...it is not possible or desirable to synthesize these [perioperative analgesia] options into ‘one-size-fits-all’ algorithms”. It is the author’s hope that the information within will serve as an entry point for the Opioid Minimization workgroup to develop educational and informational materials to address the alarmingly high prevalence of perioperative pain and opioid use.
A. Reviews

Armaghani et al (2014):

*Study Design:* Prospective cohort analysis.

*Objective:* To assess the effect of preoperative narcotics on the incidence of 30 and 90-day complications and LOS in spine surgery patients. The secondary aim was to observe other factors that may be associated with complications and increased LOS.

*Methods:* 583 structural lesion patients were evaluated. Self-reported narcotic consumption was converted to morphine equivalents at the initial preoperative appointment.

*Results:* Increased preoperative narcotic use and depression were associated with increased LOS. For every 100 morphine equivalents taken preoperatively, LOS was extended 1.1 days. Narcotic use was not associated with postoperative complications.

*Comments:* Use of a large, diverse patient population was a strength of this study. Limitations included self-reported narcotic use, use of retrospective data, and probable underreporting of complications.

Lee et al (2014):

*Study Design:* Prospective cohort study.

*Objective:* To assess whether greater use of opioids preoperatively yields worse outcomes for patients undergoing spine surgery.

*Methods:* 583 structural lesion patients were evaluated at Vanderbilt. Self-reported preoperative opioid consumption was obtained at the preoperative appointment and was converted to morphine equivalents. Self-reported outcomes measures were obtained postoperatively at 3 and 12 months through the 12-Item Short-Form Health Survey and the EuroQoL-5D. The Oswestry Disability Index and the Neck Disability Index were used when appropriate.

*Results:* Increased preoperative opioid consumption, higher Modified Somatic Perception Questionnaire scores, and higher Zung Depression Scale scores predicted worse outcomes. There may be a benefit to preoperative psychological and opioid screening. Health providers should consider weaning of preoperative opioid use and consider close opioid monitoring postoperatively.

*Comments:* A relatively large sample size, use of prospective analysis, the inclusiveness of all elective spine surgeries, and the treatment of preoperative opioid use as a continuous variable were strengths of this study. However, data regarding preoperative opioid use was self-reported and subsequent analysis did not account for duration of use. Additionally, postoperative opioid use was not tracked; it is possible that postoperative opioid use has a greater impact on patient outcomes than preoperative opioid use.


*Study Design:* Prospective observational study.

*Objective:* To describe perioperative analgesic management, postoperative pain, and opioid consumption as well as its associated adverse events in patients undergoing spine surgery in a single hospital in Denmark.
**Methods:** A cohort of 87 consecutive spine surgery patients was included in this quality assurance study. The scheduled standard perioperative pain treatment plan was as follows:

1. **Preoperative (within 1 hour of surgery):**
   - 2000 milligrams acetaminophen (sustained release)
   - 10 milligrams morphine (sustained release)
   - 600 milligrams gabapentin

2. **At Time of Surgery:**
   - General anesthesia with remifentanil and propofol OR sevoflurane (all dosages at discretion of anesthesiologist)
   - 0.2 milligrams/kilogram morphine delivered 30 minutes before anticipated termination of surgery

3. **Postoperative:**
   - Morphine AND/OR intravenous sufentanil as needed
   - Treat nausea with IV ondansetron
   - In the surgical ward, one of two standardized regimens was used:
     a. **Lumbar discectomy/decompression, non-instrumental fusion, and cervical interbody fusion:**
        - 1 gram acetaminophen every 6 hours
        - 400 milligrams ibuprofen every 8 hours
        - 10 milligrams morphine (sustained release) every 12 hours
        - Supplemental 10 milligrams oral morphine OR 5 milligrams IV morphine as needed
     b. **Instrumented lumbar fusion surgery:**
        - 1 gram acetaminophen every 6 hours
        - 400 milligrams ibuprofen every 8 hours
        - 20 milligrams morphine (sustained release) every 12 hours
        - 300 milligrams gabapentin every 8 hours
        - Supplemental 10 milligrams oral morphine or 5 milligrams IV morphine as needed

**Results:** Most patients experienced acceptable pain levels as assessed by visual analogue scale (VAS) pain scoring. Instrumented lumbar fusions led to moderate-to-severe pain levels and higher opioid consumption. The scheduled standard perioperative pain management protocols were rarely followed, with only 8 of 87 patients receiving the full protocol.

**Comments:** Small sample size and possible observational bias were limitations of this study.

Dold et al (2013):

**Study Design:** Retrospective cohort study.

**Objective:** To evaluate the safety and efficacy of a preoperative femoral nerve block for postoperative pain control in patients undergoing hip arthroscopic surgery at Women’s College Hospital in Toronto, Canada.

**Methods:** Groups were compared with respect to basic demographics (i.e. age, BMI as well as physical status classification); procedure performed; operative time; total intraoperative morphine-equivalent dose; pain scores (0-10 scale) recorded at 0, 15, 30, 45, and 60 minutes postoperatively; total morphine-equivalent dose postoperatively; presence of nausea or vomiting postoperatively; time to discharge;
oxycodeone consumption in the same-day surgery unit (SDCU); and maximal patient-reported pain score in the SDCU.

**Results:** A preoperative femoral nerve block is a relatively safe procedure that may decrease the requirement for intraoperative morphine while providing effective postoperative pain control in patients undergoing hip arthroscopic surgery.

**Interpretation:** Interpretation of these results are limited by the lack of a standardized femoral nerve block protocol, as well as a lack of standardization in the use of intraoperative anesthetic medications, doses, and timing. In addition, this study lacks data beyond postoperative day one.

**McKenzie et al (2013):**

**Objective:** To review the role of patient controlled analgesia (PCA), peripheral nerve blocks (PNBs), local periarticular injections, and extended-release epidural morphine injections that can be used in multimodal analgesia for total hip arthroplasty. The review then informed the development of an internal protocol at the Thomas Jefferson University Rothman Institute of Orthopedics.

**Results:**

1. Use of multimodal analgesia offers significant decreases in overall pain values and leads to an increase in global patient satisfaction. Use of local anesthesia and shorter-acting opioids also significantly decreases incidence of adverse drug effects. Multimodal analgesia is also associated with a decreased LOS with positive economic implications for both patients and hospitals.

2. Review of pain management choices:
   - **PCA:** Limitations of PCA include the short half-life of narcotics, risk of opioid dependence, risk of medication dosing error, and possible synergistic effects between opioids and other drugs. Health providers should consider using PCA pumps for high levels of breakthrough pain in certain situations or as an auxiliary option for postoperative pain.
   - **PNB:** PNBs can significantly decrease postoperative pain VAS scores, promote early mobilization/physical therapy, and shorten LOS. However, PNBs are associated with quadriceps muscle weakening and increased risk for in-hospital falls.
   - **Local periarticular injections:** Multiple randomized controlled trials (RCTs) show that local periarticular injections are effective in decreasing overall VAS pain scores, decreasing adverse effects secondary to opioid consumption, and improving physical therapy (PT) parameters. However, there is a lack of standardization for the injection process, including dosage and injection site. The ability of local periarticular injections to promote postoperative analgesia is relatively unknown.
   - **Extended release epidural morphine injection:** Depofoam technology is an innovative process for prolonging the half-life of drugs. DepoDur is the corresponding drug for total hip arthroplasty epidural injections. Evidence indicates that DepoDur may significantly improve patient satisfaction, decrease VAS pain scores, and decrease opioid consumption. However, patients are also at considerable risk for peripheral side effects. There should be consideration for screening patients who are high-risk, particularly those with respiratory and cardiovascular comorbidities.
   - **Other considerations:**
     - Effective communication between the provider and the patient regarding surgical outcome expectations and rehabilitation is important.
     - Multidisciplinary preoperative classes for patients can help decrease LOS, the amount of therapy needed in the hospital, and reduce anxiety/stress.
Early postoperative mobilization decreases LOS, improves range of motion in PT, and decreases risk for venous thromboembolism (VTE). It may be especially helpful for elderly patients.

- Limiting anti-coagulation postoperatively decreases risk of hematoma and infections.

(3) Rothman Institute pain management protocol with prospective cohort study conducted:

a. Preoperatively within 1 hour of surgery:
   - 975 milligrams acetaminophen
   - 75 milligrams pregabalin
   - 400 milligrams celecoxib

b. Time of Surgery:
   - Spinal anesthesia
   - Intrathecal dose of morphine (duramorph), approx. 0.2-0.5 milligrams

c. Postoperative:
   - 650 milligrams acetaminophen every 6 hours
   - 75 milligrams pregabalin every 12 hours
   - 200 milligrams celecoxib every 12 hours
   - As needed for breakthrough pain: 10-20 milligrams oxycontin
   - As needed for severe pain: PCA pump of dilaudid or fentanyl

d. Other Considerations:

   Pregabalin:
   - Discontinue pregabalin immediately when its common side effects are present.
   - Do not give to elderly patients (>80 years old).
   - Those with low BMI (<25.0 kilogram/meters squared) should receive a half dose, or 37.5 milligrams every 12 hours.

   Celecoxib:
   - For sulfonamide sensitivities substitute 500 milligrams of naproxen once preoperatively and every 12 hours postoperatively.
   - Do not give to patients with elevated preoperative blood urea nitrogen or creatinine levels.

Sivrikoz et al (2014):

Study Design: Double-blinded RCT.

Objective: To evaluate the postoperative pain relief and opioid-sparing effects of dexketoprofen and lornoxicam in patients undergoing elective unilateral hip or knee surgery in Turkey.

Methods: 120 patients were evenly randomized into three groups to receive 2 intravenous injections of 50 milligrams dexketoprofen (GD), 8 milligrams lornoxicam (GL), or saline as placebo (GP). The injections were given as 2 milliliter solutions at the end of surgery and 12 hours later.

   (1) Preoperative:
   - 0.01 milligrams/kilogram intravenous midazolam

   (2) Intraoperative:
• 2 micrograms/kilogram fentanyl
• 2-3 micrograms/kilogram propofol
• Maintenance of anesthesia: 1-2 sevoflurane in 40% O₂ and 60% N₂O
• Either GD, GL, or GP (depending on randomization)

(3) Postoperative:
• 0.05 micrograms/kilogram intravenous morphine, as needed
• PCA (IV morphine 0.01 milligrams/kilogram bolus dose and 10 minute lockout time)

Results: Patients in the GD and GL groups experienced significantly lower VAS pain scores postoperatively compared to the placebo group, with lower scores in the GD group. Patients in the GD and GL groups consumed significantly less morphine postoperative, with less consumption in the GD groups.

Young & Buvanendran (2014):
Objective: To discuss pain management strategies for total hip arthroplasty (THA).

Results:
• General anesthesia advantages include a definitive airway and the patient is asleep; disadvantages include postoperative delirium as well as nausea and vomiting.
• Neuraxial anesthesia (spinal and epidural) appears to be superior to general anesthesia for most measures of acute perioperative measures such as enhanced postoperative anesthesia. However, there may be increased risk for pulmonary complications, falls, and epidural hematoma.
• Multimodal analgesia is suggested to be the best method for perioperative pain management, and the authors discuss the following drugs:
  o Non-steroidal anti-inflammatory drugs (NSAIDs): NSAIDs are the most commonly used analgesic medications due to their ability to reduce pain and inflammation. Non-selective NSAIDs inhibit COX-1 and COX-2.
  o COX-2 inhibitors: Administering a COX-2 inhibitor 2-3 days prior to surgery can be beneficial (through accumulation of the medication in the cerebrospinal fluid). The use of COX-2 inhibitors are shown to decrease postoperative opioid consumption and improve outcomes in joint replacement. Patients should continue to use COX-2 inhibitors for at least 2 weeks after surgery. Contraindications include allergy to aspirin, other NSAIDs, and sulfonamides. The dose should be halved in patients with borderline renal failure and in those aged 70 or older.
  o Acetaminophen: Acetaminophen may be combined with COX-2 inhibitors or NSAIDs as part of a multimodal regimen. Evidence indicates that the combined use of acetaminophen and NSAIDs is superior to either drug alone.
  o Gabapentinoids: Pregabalin has better pharmacokinetic properties, fewer drug interactions, and greater bioavailability than gabapentin. Perioperative use of pregabalin is shown to decrease the incidence of chronic pain after THA.
  o Ketamine: Low doses of ketamine used as an adjunct to opioids, local, and other analgesic agents may reduce postoperative opioid consumption and prolong and improve analgesia. Ketamine may also reduce incidence of chronic pain following THA.
  o Muscle Relaxants: Muscle relaxants are not commonly used as part of multimodal analgesia because of possible side effects such as sedation and cognitive dysfunction.
Also notable are interactions between certain muscle relaxants (e.g. benzodiazepines) and opioids, which can cause respiratory failure.

- **Opioids**: Opioids are commonly used and reliable. Obese patients with a history of sleep apnea may need monitoring with continuous pulse oximetry in intensive care or step-down units. Long-acting formulations are not recommended for older patients because of their decreased gastrointestinal transit time.

- **Other considerations**:
  - Regional anesthesia plus sedation is often preferred for THA
  - Newer opioid medications often contain acetaminophen, and this amount should be taken into consideration in keeping the total daily dose to fewer than 3000 milligrams.

- **The authors have suggested a multimodal regimen for THA patients**:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose/Route</th>
<th>Schedule</th>
<th>Considerations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>1000 milligrams IV or per os</td>
<td>Every 8 hours</td>
<td>Contraindicated in patients with hepatic dysfunction, total daily dose should not exceed 3 grams per day</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>200 milligrams per os</td>
<td>2 tabs before surgery, then 1 tab bis in die</td>
<td>Adjust dose or avoid in patients with renal dysfunction</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>75 milligrams per os</td>
<td>1 tab before surgery, then bis in die</td>
<td>Monitor for side effects such as dizziness or somnolence</td>
</tr>
</tbody>
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**Jakobsen et al (2014)**


*Objective:* To improve the quality of surgical care through the use of procedure-specific standardized fast-track surgical nursing care programs.

*Methods:* Collaborative-based QI framework used to construct, disseminate, and implement evidence-based guidelines for procedure-specific guidelines. Fast-track surgery protocols were disseminated through a “workshop-practice” method and were guided by nurse “implementation agents”.

*Results:* Development of 16 guidelines that were implemented in 51 (of 69 total) hospitals in Denmark. The authors included pain relief recommendations for patients undergoing elective colonic resection:

1. **Preoperative:**
   - Thoracic epidural analgesia for 2 days
   - Acetaminophen and NSIAD/COX2-inhibitors (after epidural removal at 2 days/48 hours)
   - Information about VAS for pain assessment

2. **Day of Surgery:**
   - Thoracic epidural analgesia for 2 days
   - Acetaminophen and NSIAD/COX2-inhibitors (after epidural removal)
   - Pain assessed every 8 hours with VAS
(3) Postoperative (1-3 days):
- Thoracic epidural analgesia for 2 days
- Remove epidural catheter in the morning
- Pain assessed every 8 hours with VASASA

Ahmed et al (2013):

Study Design: Prospective observational study.

Objective: To determine the safety and efficacy of pain management strategies utilized after major abdominal surgery at Aga Khan University in Pakistan.

Methods: 100 patients undergoing elective abdominal surgical procedures with mid-line upper abdominal incisions (i.e. Whipple’s procedure, hemicolecetomy, exploratory laparotomy, extended radical cystectomy and nephrectomy, major de-bulking gynecological surgery, and abdominal aortic aneurysm surgery) were included in the study. Patient demographics, American Society of Anesthesiologists (ASA) physical status classification, and type of surgical procedure were recorded. The postoperative analgesia strategy, co-analgesics used, pain sedation scores, motor block, nausea, and vomiting along with self-reported patient satisfaction were recorded. The acute pain management service (APMS) conducted follow-up and assessed pain, managed inadequate pain relief, and treated any complications.

Results: Multimodal analgesia was employed in 98 of the 100 patients; IV acetaminophen was used in 90, ketorolac in 5, and diclofenac suppositories in 3 patients. The following postoperative pain management was generally adhered to:

1. Epidural analgesia, n=61
   a. 0.1% bupivacaine AND
   b. 2 grams/milliliter fentanyl
   c. For moderate-severe pain, the author states that patients were given 1-2 additional 5 milliliter boluses of the same infusion at half-hour intervals.
   d. If pain relief was still unsatisfactory after the additionally boluses, an IV bolus of 50 milligrams tramadol was administered.

2. Patient-controlled intravenous analgesia, n=25
   a. An undisclosed amount of pethidine
   b. If pain relief was still unsatisfactory, an IV bolus of 50 milligrams tramadol was administered.

3. Intravenous opioid infusion, n=14
   a. 10-15 milligrams/hour pethidine OR
   b. 1-2 milligrams/hour morphine OR
   c. 1-3 milligrams/hour nalbuphine
   d. If pain relief was still unsatisfactory after the additional boluses, an IV bolus of 50 milligrams tramadol was administered.

The authors concluded the following:
- Regular assessments of pain relief and appropriate adjustment of dosage by the APMS and use of multimodal analgesia led to a high level of patient satisfaction.
- The authors recommend that the APMS provide feedback to the primary anesthesiologist to enable practice improvement.
The authors do not explicitly state the time frame for which pain sedation scores, motor block, nausea, and vomiting were recorded. Patient satisfaction with pain relief was assessed by the pain nurse at the time of discharge. The authors also mentioned that the supply of drugs was erratic and the quantity of equipment might not be sufficient for every patient; these issues may be specific to the institution.

Nishimori et al (2014):

Objective: To review the efficacy of postoperative epidural analgesia compared to opioid-based pain relief for patients undergoing abdominal aortic surgery.

Results: This review included 15 RCT and quasi-RCT trials involving 1297 patients. It was found that postoperative epidural analgesia:

- Reduced postoperative duration of tracheal intubation by about one half.
- Provided better pain management (as measure by VAS) for up to 3 days postoperatively regardless of catheter placement and medications used.
- Reduced rates of myocardial infarction, prolonged mechanical ventilation, and renal complications.
- Was comparable to opioid-based pain relief in terms of mortality.

Comments: This review was originally published in 2006 and updated in 2011 (but re-published in 2014). The content is up to date as of November 2010.

Sarakatsianou et al (2013):

Study Design: Double-blinded RCT.

Objective: To evaluate the potential for preoperative administration of pregabalin to reduce postoperative pain and opioid consumption in patients with gallstone disease scheduled for laparoscopic cholecystectomy in Greece.

Methods: Patients with American Society of Anesthesiologists physical status I or II were included in the study and were randomized into pregabalin and placebo groups. Preoperative pain was measured using VAS pain scores. Postoperative pain was assessed using VAS and morphine demands for the following time points: patient arrival to the post-anesthesia case unit (0 hour), 1 hour, 8 hours, 16 hours, and 24 hours after surgery.

Results: Administering 600 milligrams pregabalin significantly reduces postoperative pain as well as opioid consumption at the cost of increased incidence of dizziness.

Comments: This study was limited by the small sample size for data analysis (n=40 patients).

Rodgers et al (2012):

Study Design: Prospective cohort study.

Objective: To assess pain control and quantify the amount of pain medication left over after upper extremity surgery at a Midwestern group of 5 private practice hand surgeons.

Methods: Patients scheduled for surgery were recruited to take part in a phone interview 7 to 14 days after surgery. Information collected included procedure performed, analgesia medication and regimen prescribed, satisfaction with pain control, number of tablets remaining, reasons for not taking medication, other analgesic medications used, user payer classification, and any adverse drug reactions.

Results: 250 patients completed the study.
92% reported adequate pain control. Oxycodone, hydrocodone, and propoxyphene accounted for over 95% of pain medications prescribed. Patients were typically prescribed 30 pills and consumed a mean of 10 pills (which yielded 4,639 leftover pills in total).

Comments: A limitation of this study may be the underreporting of pill use as there is social stigma around opioid consumption.

Prescribing 30 pills may be excessive and unnecessary. The authors recommend prescribing 15 pills with one refill for upper extremity procedures. Additionally, patients frequently save leftover medication for possible future use, and health care providers often do not provide counseling on proper disposal of unused opioids, presenting opportunities for diversion. Although there is no consensus on the “proper” methods, trash disposal, the flushing method, and take-back programs exist as feasible options.

Chronic Pain/Opioid Abuse

Stromer et al (2013):

Objective: To explore and discuss strategies for managing opioid-tolerant and addicted patients.

Results:

(1) Regional Techniques:
- Contraindications include systemic infections, blood clotting disorders, and unstable neurological disorders.
- For epidural analgesia, use an epidural opioid (e.g. 0.5-0.75 microgram/milliliter sufentanil AND 0.5 microgram/milliliter fentanyl) and possibly add an alpha-2 agonist (e.g. 0.5 micrograms/kilogram clonidine single shot OR 0.25 microgram/kilogram/hour infusion).

(2) Postoperative analgesia:
- To reduce stress, do not give substances such as naloxone, flumazenil, or neostigmine.
- Consider continuous infusion or intravenous PCA with background infusion.
- Increase opioid bolus and shorten lockout time.

(3) Co-analgesics:
- Clonidine has opioid-sparing and anti-hyperalgesic properties (e.g. use 0.1-0.2 micrograms/kilogram/hour intravenously OR 75 micrograms 2-3 times a day orally).
- S-(+)-ketamine has opioid-sparing and anti-hyperalgesic properties (e.g. use 0.25-0.5 microgram/kilogram bolus OR as 1-2 microgram/kilogram/minute continuous infusion).
- Tricyclic antidepressants have a sedating effect (e.g. 10-25 milligrams amitriptyline OR 10-25 milligrams doxepin at night).
- Gabapentin and pregabalin may decrease postoperative pain, are opioid-sparing, and prevent chronic persistent pain (e.g. 75 milligrams pregabalin preoperatively then 75 milligrams twice daily for 7 days postoperatively).
- Benzodiazepines should be avoided whenever possible due to their high potential for addiction.
Tumber (2014):

Objective: To explore current perioperative analgesia practices for the management of patients with chronic pain.

Results:

(1) Preoperative (1-2 hours prior to surgery):

- 1,000 milligrams acetaminophen
- Cyclooxygenase-2 selective agent (e.g. 400 milligrams celecoxib) OR anti-inflammatory
- For patients who are at risk for or have neuropathic pain: 600 milligrams gabapentin OR 150 milligrams pregabalin
- For anxiety, lorazepam OR oral clonidine

(2) Intraoperative:

- Intravenous bolus of 0.25-0.5 milligrams/kilogram benzodiazepine after induction followed by 0.25-0.5 milligrams/kilogram/hour
- Consider 40-50 milligrams/kilogram magnesium (shown to reduce postoperative opioid consumption)
- 8 milligrams dexamethasone (can also give preoperatively)
- Consider 30-60 milligrams ketorolac
- Consider 1.5 milligrams/kilogram lidocaine loading dose followed by 1.5 milligrams/kilogram/hour for patients undergoing abdominal procedures without an epidural catheter

(3) Postoperative:

- Referral to acute pain service (APS) management
- Consider using dexmedetomidine and patient-controlled anesthesia techniques
- Possible use of behavioral and cognitive therapy/techniques
**Drug and Technique-Specific**

**Brinkrolf & Hahnenkamp (2014):**

*Objective:* To review the use of lidocaine in the perioperative setting.

*Results:* Evidence indicates that lidocaine may improve bowel mobility in the context of abdominal surgery, but evidence is less conclusive for patients undergoing other surgical procedures. Evidence regarding the impact on LOS as well as postoperative pain is also inconclusive.

*Comments:* All studies conducted to date have a small sample size that is likely not adequately powered.

**Chelly et al (2010):**

*Objective:* To review the use of continuous peripheral nerve (CPN) blocks for treating acute postoperative pain after surgery and/or trauma.

*Results:* CPN blocks are shown to reduce postoperative opioid consumption and related adverse effects, accelerate recovery, and reduce LOS for many patients. Indications for use of CPN blocks include perioperative analgesia, analgesia related to trauma, and chronic pain. They also serve as a safer alternative to epidural analgesia for patients receiving thromboprophylaxis, especially for those on low molecular weight heparin.

**Dolin et al (2002):**

*Objective:* To examine published data around the incidence of moderate-severe and severe pain within 24 hours of major surgery with three analgesic techniques: intramuscular (IM), patient controlled analgesia (PCA), and epidural analgesia.

*Methods:* Pooled data on pain scores from 165 studies represent the experience of nearly 20,000 patients. Pain scores were recorded using one of three measures: visual analogue scale (0-100 mm), numerical rating scale (0-10), and verbal rating scale (mild/moderate/severe).

*Results:* These findings indicate that IM analgesia is associated with the highest percentage of patients experiencing inadequate analgesia support and is the least effective of the three techniques assessed. Also, a lower incidence of moderate-severe and severe pain was associated with epidural analgesia use compared to PCA. However, this epidural analgesia data is confounded by technical failures such as premature epidural catheter displacement.

*Comments:* Interpretation of the results of this review is limited to operations after which moderate-severe and severe postoperative pain could be expected, namely major abdominal gynecological surgery, major orthopedic surgery, and any laparotomy or thoracotomy. Additionally, the review was not confined to RCTs and no attempt was made to grade individual papers according to quality.
Kim et al (2014):

**Objective:** To assess the expression of acute opioid tolerance (AOT) and opioid-induced hyperplasia (OIH) through use of remifentanil.

**Results:**
- Evidence generally supports development of AOT and OIH in specific settings (e.g. acute exposure in human volunteers and postoperative pain cohorts) when remifentanil was infused at ≥0.1 microgram/kilogram/minute either alone or with inhalation anesthetics.
- Physicians suspect OIH when opioid treatment effects seem to decline in the absence of disease progression with unexplained pain reports or allodynia associated with the site of injury.
- Coadministered drugs (e.g. propofol, nitrous oxide, use of the target-controlled infusion model) seem to modulate the development of AOT and OIH.
- No strong evidence exists to support the need to reduce dose of remifentanil or apply strategies for preventing AOT and OIH.

Mariano et al (2014):

**Objective:** To review evidence for the clinical application of ultrasound (US) in regional anesthesia and analgesia.

**Results:** There is evidence to support the use of US for regional anesthesia and analgesia based on short-term outcomes studies. However, further research is needed regarding optimal methods of use, best techniques, the impact on long-term outcomes, and considerations for special populations.

**Comments:** The authors state, “The art of regional anesthesia lies in the anesthesiologists’ ability to accurately and precisely deliver a desired dose of local anesthetic in close proximity to a target nerve and selectively anesthetize a specific part of the body” (Mariano, Marshall, Urman, & Kaye, 2014). Due to a lack of training around US-guided regional anesthesia, physicians in practice mostly teach themselves this skill.

Merritt et al (2014):

**Objective:** To review the utilization of peripheral nerve catheters (PNC) and local anesthetic infiltration (LIA) in perioperative analgesia.

**Results:**
1. PNC has been shown to be beneficial in providing surgical anesthesia and in prolonging postoperative analgesia:
   - PNC is especially effective for those with moderate to severe pain, pre-existing chronic pain, or opioid tolerance.
   - US should be considered as part of a comprehensive multimodal analgesia strategy.
   - The use of US offers a potential for faster, safer, and more efficacious placement of PNC.

2. LAI efficacy varies, depending on the procedure and anatomical location:
   - The recent advent of ultra-long-lasting liposomal bupivacaine has potential to increase the utility of single injection LAI’s.
Smith et al (2011):

Objective: To examine the use of intravenous acetaminophen (IV APAP) in the postoperative setting.

Results: IV APAP is a safe, well-tolerated, and effective pain analgesic:

- IV APAP yields more consistent and quicker results than oral or rectal analgesia.
- IV APAP has a postoperative opioid-sparing effect.
- No clinically significant adverse effects were present for IV APAP. IV APAP may serve as a preferable alternative to NSAIDs for rapid analgesia and is associated with fewer adverse events.
- IV APAP was not associated with adverse GI events that occur with nonselective NSAIDs or the adverse cardiovascular events associated with selective COX-2 inhibitors.

Comments: CIV APAP should be considered for use in mild-to-moderate pain, especially when surgical bleeding is a concern.

Tong et al (2014):

Objective: To review the clinical literature around liposomal bupivacaine and its evolving role in perioperative analgesia.

Results:

- Liposomal bupivacaine is shown to be significantly improved in terms of opioid-sparing effects, prolonged analgesia, patient satisfaction, shorter LOS, and lower hospital cost when used in wound infiltration compared to bupivacaine hydrochloride.
- The data does not support liposomal bupivacaine use in regional anesthesia; to date, data shows an unreliable dose-to-response relationship in femoral nerve blocks and limited improvement in duration in the epidural space.
- More multicenter trials are needed to evaluate the efficacy and safety of liposomal bupivacaine:
  - From the limited number of studies that have been done, liposomal bupivacaine seems to be safe and does not seem to cause more adverse effects compared to plain bupivacaine.
  - However, liposomal bupivacaine has not been evaluated for:
    - Pregnant women
    - Patients with significant comorbidities
    - When other methods of administration are used (e.g. nerve block or spinal)
    - Special patient populations (e.g. chronic opioid therapy or use of other concomitant medications)

Comments: Although the authors primarily addressed products developed by Pacira Pharmaceuticals in this article, they had no conflicts of interest to disclose.

Yao, Chen, & Zhong (2014):

Objective: To perform a meta-analysis of clinical trials of pregabalin for analgesia efficacy after gynecologic surgery.
Methods: Pooled data for 452 patients collected in 6 clinical trials between 2007-2010 from Greece, India, Denmark, and Australia were included in the analysis. The primary outcomes of interest were pain outcomes and postoperative opioid consumption.

Results: Given preoperatively, pregabalin yielded beneficial results:

- Patients consumed significantly fewer opioids postoperatively in the first 24 hours.
- Pain at rest and on movement or coughing was significantly lower for the first 24 hours postoperatively.
- No differences were found between the pregabalin and control groups in terms of adverse events.
Pain Management at Large

Garimella & Cellini (2013):

**Objective:** To summarize the current evidence for various approaches to managing postoperative pain.

**Results:**

- **Assessment:** A thorough patient evaluation is crucial and recommended components include a directed pain history, a directed physical exam, and a pain control plan. Preparation may include adjusting any medications the patient might be taking to avoid withdrawal, treatment of preoperative anxiety or pain, and preoperative initiation as part of a multimodal pain management regimen.

- **Pre-emptive Analgesia:** Few robust studies have demonstrated pre-emptive analgesia to be efficacious. Overall, this approach may offer some short-term benefits, especially in the ambulatory surgery setting.

- **Opioid Analgesia:** All opioids have the potential to cause significant side effects, including respiratory depression that can lead to hypoxia and respiratory arrest, so it is important to monitor respiration and oxygen saturation. Long-term use of opioids can lead to dependence and addiction. Opioids can be administered using intravenous PCA. PCA requires proper equipment and training but is shown to be preferred by the patient because they are able to better control pain without an increased risk for side effects.

- **Epidural and Spinal Analgesia:**
  - A Cochrane database review of 9 RCTs comparing IV PCA and continuous epidural analgesia (CEA) demonstrated that CEA achieved better pain control in the first 72 hours after abdominal surgery, with no difference in LOS and incidence of adverse events.
  - A recent observational study demonstrated that single-dose Intrathecal opioid followed by IV PCA resulted in better pain control than CEA in patients undergoing colorectal procedures.

- **Non-opioid Analgesia:**
  - There is risk for bleeding with NSAIDs, so their use is dependent on the patient’s risk factors. Nonselective agents have an increased side effect profile (e.g. bleeding, antiplatelet effects); however, there is general consensus in the literature that COX-1 inhibitors are preferred over selective COX-2 inhibitors, given the evidence around the cardiovascular risks associated with COX-2 inhibitors.
  - Ketorolac can be used as a pre-emptive analgesia and as an adjunct to other agents. It has been shown to reduce narcotic consumption by 25-45% and is a common adjunct in colorectal surgery postoperative protocols. The usual dose is 30 milligrams given intravenously.
  - Acetaminophen is widely used and is a common ingredient in oral pain medications; at the same time, it is important to make sure a patient does not exceed the 4000 milligram daily maximum dose due to risk of hepatotoxicity. The IV form has advantages over NSAIDs due to its lack of interference with platelet function and safe administration in patients with a history of peptic ulcers or asthma. A systematic review of 21 studies has found that acetaminophen in combination with other NSAIDs increases efficacy compared to either agent alone.
- **Peripheral Nerve Block**: The transversus abdominis plane (TAP) block can be done blind, laparoscopically, or ultrasound-guided. It is thought to have a lower risk of complications and greater acceptability to patients than epidural analgesia. However, it is subject to operator variability and skill. Further assessment comparing TAP to other standard methods of postoperative analgesia are needed.

- **Local Infiltration**: Utilization of local infiltration as part of a multimodal approach appears to have great potential. However, reported experiences with newly released drugs like Exparel have been limited to date.

**Gritsenko et al (2014):**

*Objective*: To review perioperative multimodal analgesic options for surgical procedures, specifically general surgery, orthopedic surgery, gynecology/urology, and cardiothoracic procedures. The authors also reviewed descriptions of analgesic modalities and provided notes on considerations for usage.

Figure 1. Basic components of multimodal analgesia regimens.

### Results

Appendix 1 provides a summary of select analgesic options by surgical procedure, and Appendix 2 provides a summary for the description of analgesic modalities.

**Comments**: This is a comprehensive review of perioperative multimodal analgesia for a variety of surgical procedures.

**Kaye, Ali, & Urman (2014):**

*Objective*: To give an overview of the current landscape of perioperative analgesia.

**Results**:

- **Acetaminophen**: Acetaminophen is a safe and effective for treatment of mild-to-moderate pain. When combined with opioids, it can reduce pain, provide sedation, and reduce postoperative nausea and vomiting. Acetaminophen may be superior to ketamine for patients undergoing abdominal hysterectomy. IV acetaminophen paired with transverse abdominal block has been shown to reduce LOS in patients undergoing laparoscopic colon resection.
• **IV Ibuprofen**: Ibuprofen can be used to treat mild-to-moderate pain and can be used in combination with IV morphine. It is contraindicated in renal insufficiency and immediate postcoronary artery bypass graft patients due to risk of bleeding. Early IV ibuprofen use may significantly reduce opioid consumption and LOS in rib fracture patients.

• **Capsaicin**: The topical form of capsaicin is used for arthritic and neuropathic pain. Injectable capsaicin is used in treatment of postoperative orthopedic and abdominal pain. Capsaicin is advised for patients with elevated liver enzymes and concurrent use of angiotensin-converting enzyme inhibitors.

• **Gabapentin/pregabalin**: Gabapentin and pregabalin are used for treatment of neuropathic pain, perioperative analgesia, and to block hyperalgesia. Newer preparations such as Gralise have increased tolerability, improved pharmacokinetics, and fewer side effects.

• **Dexmedetomidine**: Dexmedetomidine is used for sedation and analgesia and has opioid-sparing properties. Side effects include hypotension, bradycardia, and sedation.

• **Ketamine**: Perioperative use of ketamine is associated with opioid-sparing and improved hyperalgesia and tolerance.
  - For fast pain control postoperatively, ketamine can be administered as a small IV bolus of 5-20 milligrams.
  - As part of a multimodal regimen, ketamine can be given as a 0.1-0.4 milligrams/kilogram/hour infusion.
  - As part of PCA, ketamine can be administered by demand doses of 0.01-0.02 milligrams/kilogram with a 5-10 minute lockout interval.
  - Ketamine may be especially useful for opioid-tolerant patients or those on opioid agonists/antagonists/partial agonists, typically at rates of 60-120 micrograms/kilogram/hour for approximately 4 hours.

• **Opioids**: Opioids are important for management of moderate-to-severe pain and are a cornerstone of perioperative analgesics. PCA result in improved patient pain control and satisfaction and while they are associated with high doses, they are not associated with increased risk of serious side effects. Common PCA agents include morphine, hydromorphone, and fentanyl with usage of 1 milligram, 0.2 milligrams, and 12.5 micrograms every 6-10 minutes, respectively.

**Vadivelu et al (2014):**

*Objective:* To review techniques around preventative analgesia for postoperative pain control.

*Results:*

1. **Preoperative Strategies:**
   - Consider taking a thorough account of patient history, including prior response to pain, analgesia history, current medications, and fears and concerns regarding future pain.
   - Consider discussing perioperative pain management and physical therapy.

2. **Preventative Analgesia of Postoperative Pain:**
• Multimodal analgesia and the use of nerve-sparing techniques are beneficial in preventing chronic postoperative pain, reduce side effects, and facilitate more rapid recovery and discharge.
• NMDA receptor antagonists (e.g. dextromethorphan, ketamine) are known to decrease acute and chronic pain.
• Preoperative systemic lidocaine may decrease opioid consumption postoperatively.

Comments: Studies on efficacy of pre-emptive analgesia yielded contradictory results. The authors argue that preventative analgesia is the more appropriate term for describing perioperative pain control.
Other Considerations

Abe et al (2014):

Objective: To describe the effects of dietary supplements on perioperative analgesia.

Results:

- Use of dietary supplements in patients who require anesthesia should be approached with caution as they can cause sedation, have drug-drug interactions, and are linked to adverse effects, including bleeding. It should be noted that over 90 supplements are associated with bleeding which can be a problem during surgery or if regional analgesia is to be used postoperatively.
- It is considered appropriate to discontinue use of supplements prior to admission to the hospital if it is known that anesthetics are to be used. If supplement are to be discontinued, the American Society of Anesthesiologists recommends cessation at least 2 weeks prior to the procedure.

Comments: It is important to take an assessment of all dietary supplements from the patient preoperatively and properly address possible cessation. However, obtaining an accurate account of supplements used can be difficult. The authors suggest the use of specific terminology – such as “fortified foods”, “herbal supplements”, and “natural extracts” – and encouraging patients to bring in all containers of supplements they may be taking.

Angioli et al (2014):

Study Design: Prospective RCT.

Objective: To assess the efficacy of verbal and written preoperative information in patients undergoing surgery for gynecologic malignancies.

Methods: 190 patients were randomized into two groups (verbal versus written information).

Results: Patients who received written information had statistically significant improved information satisfaction, better mean VAS scores, lower LOS, and used fewer pain medications (daily).

Comments: Providing written materials may improve information assimilation and retention, reduce anxiety, help facilitate communication around pain management, and increase patient participation in their care. Giving patient preoperative written information may better prepare patients for surgery, yield faster recovery, lessen the amount of pain medications needed, and yield a better QoL.

Linares & Linares (2011):

Objective: To implement a pharmacokinetics-based mathematical model technique (termed computational opioid prescribing, or COP) to assist with opioid dosing. The primary aim is to use COP to predict plasma opioid concentrations within a safe and effective range.

Methods: Population pharmacokinetic parameter values for 12 commonly prescribed opioids were estimated from various sources using bootstrap resampling.

Results: COP is feasible in assisting with point-of-care opioid dosing regimen design, evaluation, and modification. Potential benefits include opioid dosing optimization and minimization of adverse opioid drug effects.
While providers may be skeptical of such an approach, it is clear that the empirical method of opioid dosing involves a long and inefficient period of trial and error. Along these lines, COP may be considered as a clinical-decision support tool that provides some guidance for individualized opioid dosing at the point-of-care.

**Pham et al (2014):**

*Study Design:* Retrospective cohort.

*Objective:* To estimate the effect of modifiable comorbidities on postoperative outcome and to identify potential targets for preoperative management.

*Methods:* Retrospective data was collected regarding 9 modifiable comorbidities, LOS, postoperative complications, and in-hospital mortality from hospitals in Southern Australia. The 9 modifiable comorbidities included ischemic heart disease, congestive heart failure, stroke, DM, renal impairment, anemia, dementia/Alzheimer’s, asthma/COPD, and primary hypertension.

*Results:* Data on 46,925 surgical patients were included in the analysis. Compared to patients with no identified modifiable comorbidities, patients with one comorbidity have a significantly increased LOS, postoperative complications, and in-hospital mortality. These values were increased exponentially for patients with more than one comorbidity.

All comorbidities were associated with significantly increased LOS and, with the exception of renal impairment, the minimum difference in LOS between patients with and without each comorbidity was over 4 days. All comorbidities, with the exception of stroke, were significantly associated with increased postoperative complications and in-hospital mortality.

*Comments:* The authors compiled a table of preoperative interventions for each comorbidity. (Appendix 3).

**Walker (2007):**

*Objective:* To examine the relationship between giving patients written information prior to surgery and postoperative recovery. Among other outcome variables, the author discusses postoperative pain and patient satisfaction.

*Results:*

- Research findings are contradictory in regards to the efficacy of providing written information before surgery on outcomes such as postoperative pain and patient satisfaction. However, written information that is provided to the patient is often inappropriate; it may be too technical, complicated, or presented ineffectively.
- Providing clear, multidisciplinary information that is appropriate and effective to the patient has great benefits when given preoperatively. It enables patients to be more informed about their treatment and care, provides a memory aid, and serves as a point of discussion preoperatively; these factors facilitate informed decision-making and improve patient satisfaction.

*Comments:* Much of the research that was cited by the author is limited by small sample size, publication bias, and measurement subjectivity. The scope of the literature review encompasses research conducted prior to 2005.
### Appendix 1: Summary of perioperative analgesic modalities by surgical type

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Preoperative</th>
<th>Intraoperative</th>
<th>Postoperative</th>
</tr>
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<tbody>
<tr>
<td>Colorectal surgery</td>
<td></td>
<td>Thoracic epidural&lt;br&gt;Intrathecal morphine (if epidural not placed)&lt;br&gt;Dexamethasone&lt;br&gt;Lidocaine infusion (if epidural not placed)&lt;br&gt;TAP block beginning of case (if epidural not placed)&lt;br&gt;Ketamine&lt;br&gt;Magnesium&lt;br&gt;Acetaminophen&lt;br&gt;NSAIDs/COX2 selective</td>
<td>Epidural&lt;br&gt;Acetaminophen&lt;br&gt;NSAIDs&lt;br&gt;IVPCA</td>
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<td>Liver resection</td>
<td>Gabapentinoids</td>
<td>Thoracic epidural&lt;br&gt;Intrathecal morphine (if epidural not placed)&lt;br&gt;Subcostal TAP blocks (if epidural not placed)&lt;br&gt;Acetaminophen&lt;br&gt;NSAIDs/COX2 selective</td>
<td>Epidural&lt;br&gt;Acetaminophen&lt;br&gt;Gabapentinoids&lt;br&gt;NSAIDs/COX2 selective&lt;br&gt;IVPCA</td>
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<td>Hernia surgery</td>
<td>Gabapentinoids</td>
<td>Wound infiltration&lt;br&gt;Acetaminophen&lt;br&gt;NSAIDs/COX2 selective&lt;br&gt;PVB</td>
<td>Acetaminophen&lt;br&gt;NSAIDs/COX2 selective&lt;br&gt;IVPCA or per os opioid</td>
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<tr>
<td>Cholecystectomy</td>
<td>Gabapentinoids</td>
<td>Wound infiltration&lt;br&gt;Dexamethasone&lt;br&gt;Acetaminophen&lt;br&gt;NSAIDs/COX2 selective&lt;br&gt;TAP block</td>
<td>Acetaminophen&lt;br&gt;NSAIDs/COX2 selective&lt;br&gt;IVPCA or per os opioid</td>
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<td>Non-cosmetic breast surgery</td>
<td>Gabapentinoids</td>
<td>Acetaminophen&lt;br&gt;NSAIDs/COX2 selective&lt;br&gt;Dexamethasone IV</td>
<td>Acetaminophen&lt;br&gt;NSAIDs/COX2 selective&lt;br&gt;IVPCA or per os opioid</td>
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<td>Procedure</td>
<td>Gabapentinoids</td>
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<td>Acetaminophen</td>
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<td>Total hip arthroplasty</td>
<td>Gabapentinoids</td>
<td>Epidural Lumbar plexus block</td>
<td>Acetaminophen</td>
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<td>Fascia iliaca block</td>
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<td>Intrathecal morphine (if epidural not placed)</td>
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<td>Ketamine</td>
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<td>NSAIDs/COX2 selective</td>
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<td>Total knee arthroplasty</td>
<td>Gabapentinoids</td>
<td>Epidural Femoral nerve block</td>
<td>Acetaminophen</td>
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<td>(if epidural not placed)</td>
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<td>Intrathecal morphine (if epidural not placed)</td>
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<td>NSAIDs/COX2 selective</td>
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<td>Spine surgery</td>
<td>Gabapentinoids</td>
<td>Epidural Intrathecal morphine</td>
<td>Acetaminophen</td>
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<td>Ketamine</td>
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<td>Lidocaine infusion</td>
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<td>Acetaminophen</td>
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<td>NSAIDs/COX2 selective</td>
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<tr>
<td>Cesarean section</td>
<td>Gabapentinoids</td>
<td>Epidural Intrathecal morphine</td>
<td>Acetaminophen</td>
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<td>TAP block</td>
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<td>NSAIDs/COX2 selective</td>
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<tr>
<td>Total abdominal hysterectomy</td>
<td>Gabapentinoids</td>
<td>Epidural Intrathecal morphine</td>
<td>Acetaminophen</td>
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<td>TAP block</td>
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<td>Incisional infiltration/infusion</td>
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<td>NSAIDs/COX2 selective</td>
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<td>Surgery</td>
<td>Gabapentinoids</td>
<td>Adjuncts</td>
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<tr>
<td>Radical prostatectomy</td>
<td>Gabapentinoids</td>
<td>Epidural</td>
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<td>Intrathecal morphine (if epidural not placed)</td>
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<td>PVB</td>
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<td>Incisional infiltration/infusion</td>
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<td>NSAIDs/COX2 selective</td>
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<td>Cardiothoracic surgery</td>
<td>Gabapentinoids</td>
<td>Epidural</td>
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<td>Intrathecal morphine (if epidural not placed)</td>
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<td>Incisional infiltration/infusion</td>
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<td>Acetaminophen</td>
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<td>NSAIDs/COX2 selective</td>
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<tr>
<td>Consider for all surgeries</td>
<td>Gabapentinoids</td>
<td>Epidural</td>
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<td>NSAIDs/COX2 selective</td>
<td>Acetaminophen</td>
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<td>Gabapentinoids</td>
<td>NSAIDs/COX2 selective</td>
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<td>IVPCA or PO opioid</td>
<td>Gabapentinoids</td>
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<td>Gabapentinoids</td>
<td>Incisional infiltration</td>
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<td>NSAIDs/COX2 selective</td>
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## Appendix 2: Description of analgesic modalities

<table>
<thead>
<tr>
<th>Modality</th>
<th>Dosing</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidural infusion</td>
<td>- Multiple regimens</td>
<td>- Consider in major cardiothoracic, abdominal, and orthopedic procedures</td>
</tr>
<tr>
<td>Intrathecal morphine</td>
<td>- 100–300 micrograms</td>
<td>- Consider in major cardiothoracic, abdominal, and orthopedic procedures</td>
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<tr>
<td></td>
<td></td>
<td>- Requires postoperative respiratory monitoring due to risk of delayed respiratory depression</td>
</tr>
<tr>
<td>Transversus Abdominis Plane</td>
<td>- 15–20 milliliters per side</td>
<td>- Consider in abdominal surgical procedures in absence of epidural (liver resection, cholecystectomy, C-section, TAH)</td>
</tr>
<tr>
<td>Block (TAP)</td>
<td></td>
<td>- Usually performed under ultrasound guidance</td>
</tr>
<tr>
<td>Wound infiltration</td>
<td>- Any long-acting local anesthetic (i.e. bupivacaine 0.25–0.5%, ropivacaine 0.5–0.75%, etc)</td>
<td>- Consider for all procedures</td>
</tr>
<tr>
<td></td>
<td>- Liposomal bupivacaine</td>
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<tr>
<td></td>
<td>- Purified capsaic</td>
<td></td>
</tr>
<tr>
<td>Paravertebral Block (PVB)</td>
<td>- Any long-acting local anesthetic (i.e. bupivacaine 0.25–0.5%, ropivacaine 0.5–0.75%, etc)</td>
<td>- Consider for hernia, breast, thoracic, prostate</td>
</tr>
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<td></td>
<td>- 3–5 milliliters/level</td>
<td>- May decrease the incidence of chronic postoperative pain (breast, thoracic)</td>
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<td></td>
<td>- Considered a deep block by ASRA (same anticoagulation precautions as for neuraxial anesthetics)</td>
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<tr>
<td></td>
<td>- 15–20 milliliter single shot</td>
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</tr>
<tr>
<td>Peripheral nerve blocks (single shot or continuous infusion)</td>
<td>- Any long-acting local anesthetic (i.e. bupivacaine 0.25–0.5%, ropivacaine 0.5–0.75%, etc)</td>
<td>- Consider for orthopedic and other extremity procedures</td>
</tr>
<tr>
<td></td>
<td>- Volumes vary with site</td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>- 15 milligrams/kilogram in adults 650–1000 milligrams q6h</td>
<td>- Consider for all surgical procedures intraoperative and postoperative on a standing basis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- May be used in conjunction with NSAIDs</td>
</tr>
</tbody>
</table>
| NSAIDS/COX2 Selective Inhibitors | - Multiple agents/dosing regimens exist | - Consider for all surgical procedures intraoperative and postoperative on a standing basis  
- Discuss with surgeon prior to administration (some want to avoid, i.e., very high risk of bleeding, spinal fusion, etc)  
- May be used in conjunction with acetaminophen |
<table>
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</thead>
<tbody>
<tr>
<td>Tramadol</td>
<td>- 50–100 milligrams per os every 6 hours</td>
<td>- Consider as addition to acetaminophen/NSAIDs for moderate postoperative pain instead of opioids</td>
</tr>
</tbody>
</table>
| Gabapentinoids                  | **Gabapentin**  
- 600 milligrams per os preoperatively  
- 100–600 milligrams every 8 hours postoperatively  
**Pregabalin**  
- 150–300 milligrams per os preoperatively  
- 50–100 milligrams every 12 hours postoperatively | - Consider for all major surgical procedures  
- Optimal duration of postoperative administration unknown |
| Methadone                       | - Bolus: 0.1–0.2 milligrams/kilogram intraoperatively | - Minimize other opioids if giving methadone at dose of 0.2 milligrams/kilogram to opioid naïve patients  
- Consider pain specialist consultation for use in postoperative regimen |
| Alpha-2 Agonists                | **Clonidine**  
Bolus:  
- 2–5 micrograms/kilogram per os/IV before  
- 150 micrograms per os 60–90 minutes before  
**Dexmedetomidine**  
- Bolus: 0.2–1 micrograms/kilogram/hour over 10 minutes at induction  
- Infusion: 0.2–0.5 micrograms/kilogram/hour | - Consider as adjuvants for all surgical procedures  
- Consider as additives to neuraxial and peripheral regional anesthetics  
- Best dose and timing unclear  
- Choice between clonidine and dexmedetomidine unclear  
- May continue postoperatively |
| Ketamine                        | **Intraoperative**  
- Bolus: 0.25–0.5 milligrams/kilogram | - Consider sub-anesthetic adjuvant infusion for all major surgical procedures  
- Consider as single bolus to mitigate hyperalgesia (especially after remifentanil) |
<table>
<thead>
<tr>
<th>Medication</th>
<th>Bolus Dose</th>
<th>Infusion Dose</th>
<th>Additional Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion:</td>
<td>0.2–0.3 milligrams/kilogram/hour OR 2.5–10 micrograms kilogram/minute</td>
<td>- Consider postoperatively for patients with difficult to control pain (i.e., opioid tolerant patients, etc.) as infusion or additive to IVPCA</td>
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<tr>
<td>Postoperative:</td>
<td></td>
<td>- Consider benzodiazepine and antiallagogue administration</td>
<td></td>
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<tr>
<td>Magnesium</td>
<td>- Bolus: 30–50 milligrams/kilogram</td>
<td>- Infusion: 8–15 milligrams/kilogram/hour</td>
<td>- Consider for all major surgical procedures</td>
</tr>
<tr>
<td></td>
<td>- Infusion: 8–15 milligrams/kilogram/hour</td>
<td>- Infusion may be continued postoperatively</td>
<td></td>
</tr>
<tr>
<td>Lidocaine</td>
<td>- Bolus: 1–1.5 milligrams/kilogram over 10 minutes</td>
<td>- Consider lidocaine IV in abdominal and spine surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Infusion: 1–3 milligrams/kilogram/hour OR 30–40 micrograms/kilogram</td>
<td>- Consider peri-incisional lidocaine patches</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>- Infusion may be continued postoperatively</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>- 0.1 milligrams/kilogram</td>
<td>- Consider for all surgical procedures</td>
<td></td>
</tr>
</tbody>
</table>
### Appendix 3: Preoperative interventions for the nine potentially modifiable comorbidities

<table>
<thead>
<tr>
<th>Co-morbidity</th>
<th>Preoperative medical intervention</th>
</tr>
</thead>
</table>
| Anaemia                          | Diagnose if previously undetected  
Investigate cause of anaemia  
Arrange appropriate iron/B12 or folate supplementation as required  
Consider for erythropoetin in associated renal failure |
| Diabetes mellitus                | [Patient Blood Management Guidelines](#)  
Diagnose severity of diabetes  
Screen for suboptimal diabetic control  
Suggest post-operative inpatient guideline management  
Optimize medication prior to surgery  
Arrange lifestyle intervention |
| Congestive heart failure         | Diagnose severity of symptoms and investigate if appropriate  
Plan appropriate post-operative fluid management  
Optimize medication for long-term outcome |
| Stroke                           | [Guidelines for the Prevention, Detection and Management of Chronic Heart Failure in Australia](#)  
Optimize antiplatelet therapy  
Optimize use of guideline therapy, e.g. ACE inhibition |
| Renal impairment                 | Consider lifestyle intervention if required  
[Clinical Guidelines for Stroke Management](#)  
Diagnose if previously undetected  
Plan management of perioperative medication  
Consider treatment of associated anaemia  
Plan dialysis requirements if dialysis dependent |
| Ischaemic heart disease          | Diagnose severity of any ischaemic symptoms and investigate if appropriate  
Optimize medication for prevention of perioperative ischaemia  
[Reducing Risk in Heart Disease](#) |
| Dementia incl. Alzheimer’s       | Determine the presence or extent of any cognitive impairment  
Plan nursing requirements for post-operative delirium  
Implement guidelines for delirium management  
[Delirium in Older People](#) |
| Asthma/chronic obstructive pulmonary disease | Diagnose if previously undetected  
Investigate severity of disease and associated respiratory failure  
Optimize inhaled and oral therapy for prevention and treatment  
Recommend post-op management plans  
[COPD-X Guidelines](#) |
| Primary hypertension             | Diagnose if previously undetected  
Optimize medication prior to surgery  
[Guide to Management of Hypertension](#) |


