



U·P·O·J

# Multimodal Analgesia for Total Joint Arthroplasty

<sup>1</sup>Rosemary MG Hogg, MBChB

<sup>2</sup>Jiabin Liu, MD, PhD

<sup>3</sup>Eric Hume, MD

<sup>4</sup>Nabil M. Elkassabany, MD, MSCE

<sup>1</sup>Department of Anesthesiology and Critical Care, University of Pennsylvania, Philadelphia, PA

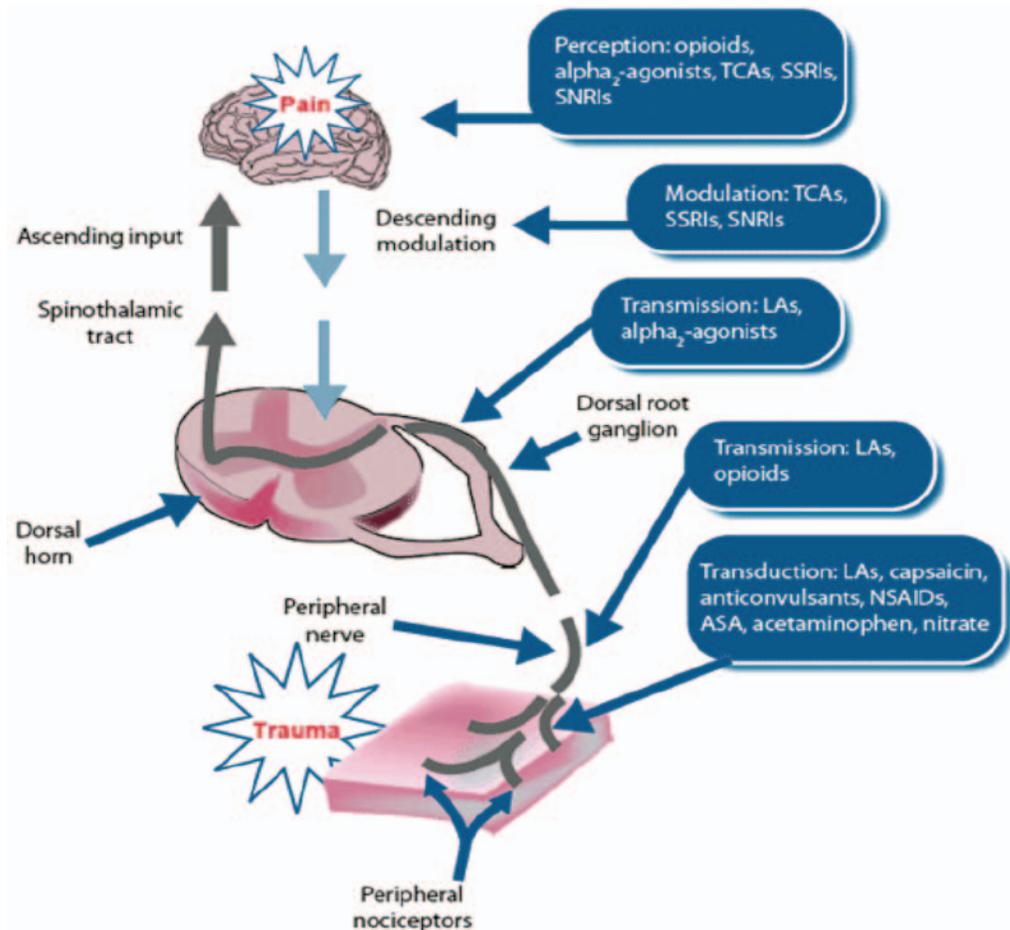
<sup>2</sup>Department of Orthopedic Surgery, University of Pennsylvania, Philadelphia, PA

## Introduction

Despite the advances in surgical techniques and the improved safety of anesthetic practice, a large percentage of patients continue to experience inadequate postoperative pain relief.<sup>1</sup> Several recent surveys have found that more than 60% of patients report moderate to severe pain after surgery.<sup>2,3</sup> Most treatment regimens for managing postoperative pain include significant doses of systemic opioids. Opioid-related side effects, including sedation, nausea, vomiting, pruritus, ileus, and respiratory depression, continue to be a major source of patient discomfort, dissatisfaction, and morbidity in the postoperative period.<sup>4</sup> The demographics of patients scheduled for total joint arthroplasty is changing. Patients are getting older and have higher body mass index, which makes opioid-related side effects more challenging.<sup>5</sup>

Multimodal analgesia (MMA) is defined as the combination of different analgesics and techniques that act by different mechanisms, resulting in additive or synergistic analgesia with lowered adverse effects (Figure 1), compared to sole administration of an individual pharmacological agent.<sup>6</sup> Initially described by Kehlet *et al* over 20 years ago,<sup>6</sup> many different regimes have been described in the literature with some consensus found in large international working groups.<sup>5,7</sup> The American Society of Anesthesiologists task force on acute postoperative pain management recommends using multimodal analgesia whenever possible.<sup>8</sup>

Through close collaboration between the Departments of Orthopedic Surgery and Anesthesiology at Penn Presbyterian Medical Center (PPMC), an evidence-based MMA protocol has been designed and implemented to facilitate



**Figure 1.** Site of action of different agents involved in multimodal analgesia and the receptors involved in the pain pathway. Adapted from Kehlet *et al*.<sup>6</sup>

**Corresponding author:**  
Nabil M. Elkassabany, MD, MSCE  
Department of Anesthesiology and Critical Care  
University of Pennsylvania  
3400 Spruce St.  
Philadelphia, PA 19104  
Nabil.Elkassabany@uphs.upenn.edu

**Table 1. MP3 multimodal analgesia regimes for use after primary total joint arthroplasty at PPMC. +2hrs before procedure. \*Avoid or reduced dose in patients >70yrs; the duration of therapy is extended to two weeks in opioid-tolerant patients. #Avoid in patients with GFR<60, Creatinine >1.4, sulfa or NSAID allergy.**

Total Knee Arthroplasty (TKA)	Total Hip Arthroplasty (THA)
Preoperative+	Preoperative+
Gabapentin 300mg PO + Celecoxib 200mg PO + Acetaminophen 1g PO	Gabapentin 300mg PO + Celecoxib 200mg PO + Acetaminophen 1g PO
Intraoperative	Intraoperative
Spinal anesthesia preferred using 10-15mg bupivacaine Femoral nerve or adductor canal block with 20- 30mls 0.2% ropivacaine with insertion of an indwelling catheter	Spinal anesthesia preferred using 10-15mg bupivacaine
Consider ketamine/sciatic nerve blockade for patients with chronic pain, high opioid usage or intolerance to opioids.	Single shot Lumbar plexus or Fascia iliaca block or ketamine 0.5mg/kg to be considered for patients with chronic pain, high opioid usage or intolerance to opioids.
Postoperative	Postoperative
Continuous Femoral nerve or adductor canal block infusion – 0.2% Ropivacaine @ 8-10mls/hr	Oxycodone 10mg Q4-6hrs
Oxycodone 10mg Q4-6hrs	Oxycontin 10-20mg Q12hrs
Oxycontin 10-20mg Q12hrs	Gabapentin 300mg PO Q8 for 7 Days*
Gabapentin 300mg PO Q8 for 7 Days*	Celecoxib 200mg PO for 72 hrs#
Celecoxib 200mg PO for 72 hrs#	Acetaminophen 1g PO for 72 hrs
Acetaminophen 1g PO for 72 hrs	IV opioid for breakthrough pain
IV opioid for breakthrough pain	

both improved analgesia and expedient rehabilitation in patients undergoing total joint arthroplasty. This protocol has been branded as the Multimodal Perioperative Pain Protocol (MP3). It consists of specific guidelines to be implemented throughout the perioperative period and allows for adaptation depending on specific patient requirements (Table 1).

### Preoperative Regime

The use of preemptive analgesia is commonplace in most surgical settings and aims to prevent the establishment of central sensitization secondary to the surgical insult. In recent years, it has developed into an integral part of pain management, particularly in those institutions which employ “fast-track” surgical protocols.<sup>9</sup>

Pain control after surgery starts with patient education before surgery. A preoperative discussion with the patient should include the patient’s previous experiences with pain management and give the patient information about pain management therapies that are available as well as the rationale behind their use. During this discussion, the importance of a factual report of pain and avoiding stoicism or exaggeration should be emphasized. Setting the patient’s expectations right, especially when it comes to pain relief versus “pain-free status,” can positively impact the patient’s overall experience and improve satisfaction.<sup>10</sup> In our institution, we are working on making patient education material available through the internet and in the surgeons’ offices.

Gabapentin has been shown to interact with central voltage-sensitive sodium and calcium channels, increase the concentration of GABA in neuronal synapses, and

decrease monoamine oxidase expression.<sup>11</sup> Its role in acute postoperative pain management originated from its use in management of chronic pain conditions, such as fibromyalgia, in which it is thought to limit the development and propagation of dysfunctional neurons. Earlier clinical trials with gabapentin for early postsurgical pain have shown improved analgesia with opioid-sparing effect. In addition to its role in acute postoperative pain, gabapentin has been shown to improve movement and reduce chronic postoperative pain in TKA at both 3 and 6 months.<sup>12</sup> Side effects, such as sedation or delirium, can be observed in elderly patients, and dose adjustments may be required

The use of COX-2 inhibitors is considered somewhat controversial for perioperative pain management due to the increased risk of cardiovascular events in patients on long-term treatment.<sup>13</sup> Celecoxib, however, has been shown to reduce opioid requirements by up to 40% with significantly improved visual assessment scale (VAS) scores and higher active range of motion over 72 hours in patients undergoing TKA and is not associated with the same cardiovascular risk.<sup>14</sup> Concerns regarding the use of NSAIDs in orthopedic surgery center mainly around the potential for decreased bone healing in fracture patients. However, it has been shown that the short term use of celecoxib has no effect on bone healing in total joint arthroplasty.<sup>15</sup>

Acetaminophen is thought to act primarily by inhibiting central prostaglandin synthesis without the side effects of NSAIDs. Despite recent FDA warnings concerning patient use of multiple medications containing acetaminophen, it has repeatedly been shown to reduce morphine consumption by up to 40% with minimal complications, particularly when used

as an intravenous preparation due to increased cerebrospinal concentrations.<sup>16,17</sup> At PPMC, the use of acetaminophen is within the daily dosing limits set by the FDA.

### Intraoperative Regime

The use of regional anesthesia (RA) in orthopedic surgery in general and specifically in total joint replacement has been demonstrated in numerous studies to improve patient outcomes, including decreased mortality and length of stay in the hospital. RA is also associated with lower incidence of significant morbidity indices, including pulmonary complication, venous thromboembolism, acute renal impairment, and postoperative infectious complications.<sup>18-20</sup> Spinal anesthesia is more cost-effective than general anesthesia for orthopedic surgery and is associated with similar or higher overall patient satisfaction with the anesthetic technique.<sup>21</sup> Monitored sedation is commonly used in addition during the procedure to improve patient comfort and reduce anxiety.

The use of single shot or continuous nerve blockade for postoperative analgesia after total joint replacement has been an integral part of postoperative analgesia protocols for a number of decades. The choice of which block is largely driven by the culture of the institution and the emphasis on postoperative mobility and rehabilitation protocols. Traditionally, a combined femoral and sciatic nerve block was advocated for TKA to eliminate discomfort arising from the complex innervation of the knee joint. This technique has decreased in popularity due to the increased likelihood of motor weakness with the potential for subsequent delayed mobilization, fall risks, and the need for prompt assessment of sciatic nerve functionality in the postoperative period.<sup>22</sup> At PPMC, sciatic nerve blocks are only reserved for patients who are having major difficulty in pain control with our conventional protocol or patients in whom opioid use may be detrimental.

Continuous femoral nerve block (FNB) provides effective analgesia in the postoperative period, significantly reducing opioid requirements, particularly when a continuous catheter technique is employed.<sup>23</sup> It does, however, have the potential to cause quadriceps weakness at higher concentrations of local anesthesia. Recently, the use of continuous adductor canal blockade (ACB), which aims to avoid motor weakness by solely targeting the saphenous nerve, has been shown to provide equivalent analgesia to FNB but with significantly greater preservation of quadriceps strength (52% vs. 18%).<sup>24</sup> A recent study by Memtsoudis *et al* has shown that peripheral nerve blockade is not correlated with the incidence of postoperative falls in patients undergoing joint replacement surgery.<sup>25</sup> The acute pain and regional anesthesia service in our institution works closely with the physical therapy and rehabilitation team in designing protocols to minimize the risk of falling. With development of protocols for fast-track recovery after TKA, the ACB may have a role in these protocols as they continue to evolve.

Local wound infiltration with low dose, high volume local anesthesia has been increasing in popularity in recent years with optimum results demonstrated when used with

femoral nerve blockade in TKA.<sup>26,27</sup> It is, however, pertinent to note that significant volumes of local anesthesia must be injected (up to 100mls of 0.1% ropivacaine), particularly in the posterior compartment, to produce these analgesic effects in TKA. Peripheral nerve block for total hip replacement may be facilitated in the form of lumbar plexus or fascia iliaca nerve block or local infiltration. However, it is commonly agreed that these may be reserved for patients with complex pain issues or those at increased risk of complications from opioid medications.

Ketamine is used as an adjunct in patients with preexisting chronic pain due to antagonism of the N-methyl-D-aspartate (NMDA) receptor and potentiation of opioid analgesia. It has been shown to reduce morphine usage by up to 32% when given alone and by 51% when used in combination with gabapentin after THA.<sup>28</sup> It is rarely used as a sole analgesic agent due to its potential to produce psychotomimetic side effects, although these are rarely seen when lower doses are used as part of a multimodal regime.

### Postoperative Regime

The continuation of the multimodal regime into the postoperative period allows for a reduction in opioid usage and, in particular, aims to reduce the need for PCA or intravenous bolus-dose opioids and their concomitant side effects. The continuous nerve block infusion may be commenced in the immediate postoperative period to allow a smooth transition after the resolution of the spinal and initial femoral nerve blockade.

Oral slow release preparations, such as oxycodone, can significantly reduce the need for intravenous opioids in patients undergoing joint replacement.<sup>29</sup> This method of preemptive analgesia management has the potential to facilitate physical therapy, improve sleep, and decrease the incidence of chronic postoperative pain.<sup>30</sup> While these medications are potentially associated with significant side effects, patient

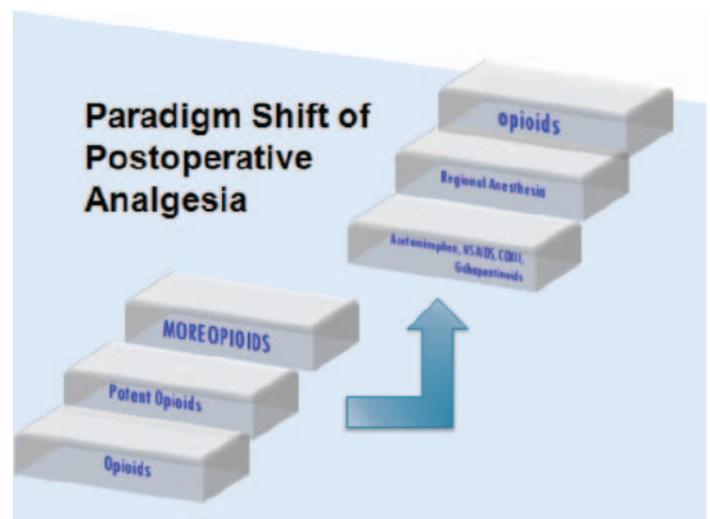


Figure 2. Paradigm shift in postoperative analgesia.

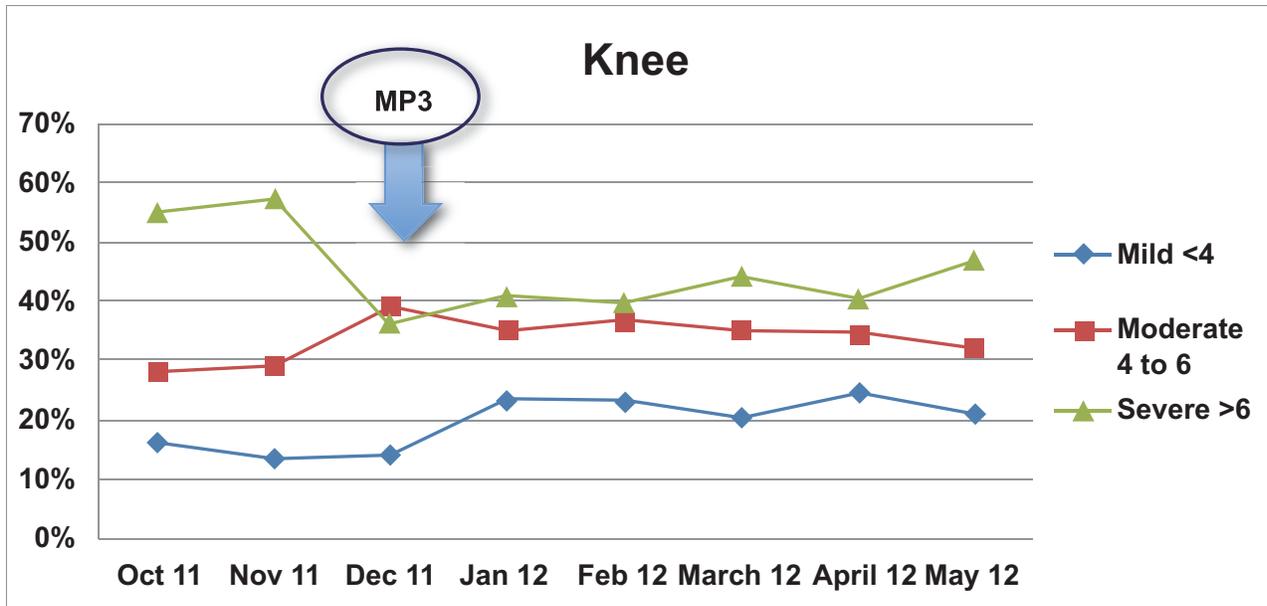


Figure 3. Percentage of patients with severe pain, as assessed by VAS, decreased after implementation of the MP3 protocol starting January, 2012.

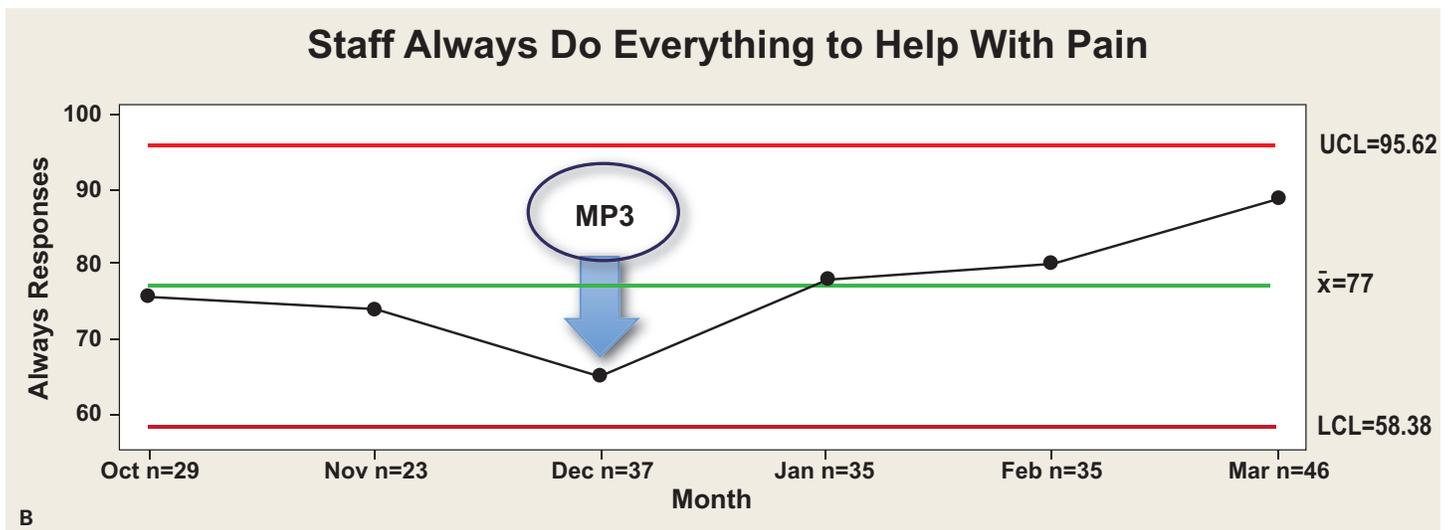
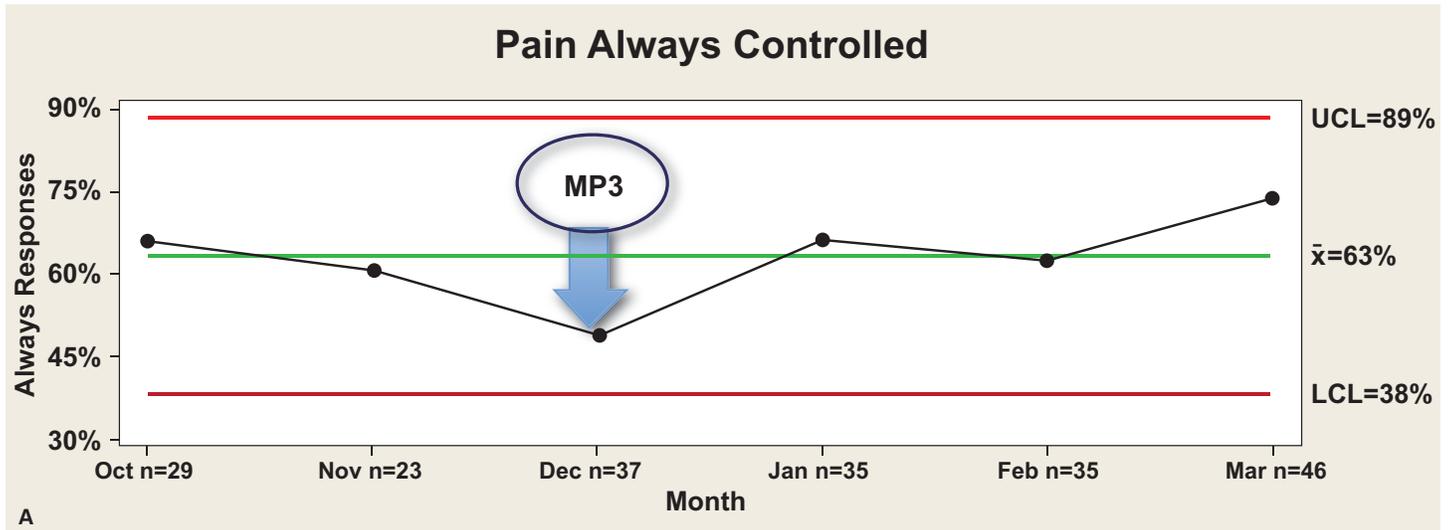


Figure 4. (A) The number of patients answering the question (How often your pain was always controlled?) increased after January, 2012. (B) The number of patients answering the question (Did you feel the staff always did everything to help with your pain?) also increased after January, 2012.

and healthcare staff education may allow responsible use of these medications while avoiding potential complications and prolonged dependence. Patients with complex chronic pain issues should be assessed on a case-by-case basis and a perioperative pain management program instigated with the assistance of orthopaedic surgeons, anesthesiologists, and chronic pain physicians.

## Implementation of the MP3 Protocol at PPMC

Implementation of the MP3 protocol at PPMC was a true collaborative effort between the Departments of Anesthesiology, Orthopedic Surgery, Internal Medicine, Pharmacy, Nursing, Physical Therapy, and Physical Medicine and Rehabilitation. The protocol was implemented in January of 2012, and since then, it has been a huge success and resulted in a large paradigm shift (Figure 2). After putting the protocol together, we relied on a core group of individual super users, representing their respective disciplines within the institution, to be the liaisons to their departments and to do the necessary education for all those who are involved with implementation of the protocol. We were able to eliminate relying predominately on intravenous narcotics and have seen a decrease in patient pain scores after total joint arthroplasty. In the first few months after implementation of the MP3 protocol, the number of patients with severe pain after TKA decreased (Figure 3). The HCAHPS survey has a pain domain to assess the percentage of patients answering that their pain was always controlled and who affirm that everything was done, from the patient perspective, to control their pain. The number of patients whose pain was always controlled increased in the first three months after implementation of the MP3 protocol as well as the percentage of patients stating that the staff did everything to help them with their pain (Figure 4A-B).

In summary, the concept of multimodal analgesia will continue to spread as it is not exclusive for total joint arthroplasty. Other service lines within the Department of Orthopaedic Surgery are starting to apply the concept to both inpatient and outpatient procedures.

## References

- Dahl JL, Gordon D, Ward S, et al. Institutionalizing pain management: the Post-Operative Pain Management Quality Improvement Project. *J Pain* 2003 Sep;4(7):361-71.
- Apfelbaum JL, Chen C, Mehta SS, et al. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. *Anesth Analg* 2003 Aug;97(2):534-40, table of contents.
- Huang N, Cunningham F, Laurito CE, et al. Can we do better with postoperative pain management? *Am J Surg* 2001 Nov;182(5):440-8.
- Dahl JL. The myths and realities of pain control with opioids. *WMJ* 2003;102(5):19.
- Hebl JR, Dilger JA, Byer DE, et al. A pre-emptive multimodal pathway featuring peripheral nerve block improves perioperative outcomes after major orthopedic surgery. *Reg Anesth Pain Med* 2008 Nov-Dec;33(6):510-7.
- Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. *Anesth Analg* 1993 Nov;77(5):1048-56.
- Hebl JR, Kopp SL, Ali MH, et al. A comprehensive anesthesia protocol that emphasizes peripheral nerve blockade for total knee and total hip arthroplasty. *J Bone Joint Surg Am* 2005;87 Suppl 2:63-70.
- American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology* 2012 Feb;116(2):248-73.
- Husted H, Lunn TH, Troelsen A, et al. Why still in hospital after fast-track hip and knee arthroplasty? *Acta Orthop* 2011 Dec;82(6):679-84.
- Soever LJ, Mackay C, Saryeddine T, et al. Educational needs of patients undergoing total joint arthroplasty. *Physiother Can* 2010 Summer;62(3):206-14.
- Sills GJ. The mechanisms of action of gabapentin and pregabalin. *Curr Opin Pharmacol* 2006 Feb;6(1):108-13.
- Buvanendran A, Kroin JS, Della Valle CJ, et al. Perioperative oral pregabalin reduces chronic pain after total knee arthroplasty: a prospective, randomized, controlled trial. *Anesth Analg* 2010 Jan 1;110(1):199-207.
- McGettigan P, Henry D. Cardiovascular risk and inhibition of cyclooxygenase: a systematic review of the observational studies of selective and nonselective inhibitors of cyclooxygenase 2. *JAMA* 2006 Oct 4;296(13):1633-44.
- Schroer WC, Diesfeld PJ, LeMarr AR, et al. Benefits of prolonged postoperative cyclooxygenase-2 inhibitor administration on total knee arthroplasty recovery: a double-blind, placebo-controlled study. *J Arthroplasty* 2011 Sep;26(6 Suppl):2-7.
- Remy C, Marret E, Bonnet F. Effects of acetaminophen on morphine side-effects and consumption after major surgery: meta-analysis of randomized controlled trials. *Br J Anaesth* 2005 Apr;94(4):505-13.
- Meunier A, Aspenberg P, Good L. Celecoxib does not appear to affect prosthesis fixation in total knee replacement: A randomized study using radiostereometry in 50 patients. *Acta Orthop* 2009 Feb;80(1):46-50.
- Delbos A, Boccard E. The morphine-sparing effect of propacetamol in orthopedic postoperative pain. *J Pain Symptom Manage* 1995 May;10(4):279-86.
- Memtsoudis SG, Sun X, Chiu YL, et al. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients. *Anesthesiology* 2013 May;118(5):1046-58.
- Neuman MD, Silber JH, Elkassabany NM, et al. Comparative effectiveness of regional versus general anesthesia for hip fracture surgery in adults. *Anesthesiology* 2012 Jul;117(1):72-92.
- Liu J, Ma C, Elkassabany N, et al. Neuraxial anesthesia decreases postoperative systemic infection risk compared with general anesthesia in knee arthroplasty. *Anesth Analg* 2013 Oct;117(4):1010-6.
- Gonano C, Leitgeb U, Sitzwohl C, et al. Spinal versus general anesthesia for orthopedic surgery: anesthesia drug and supply costs. *Anesth Analg* 2006 Feb;102(2):524-9.
- Ilfeld BM, Madison SJ. The sciatic nerve and knee arthroplasty: to block, or not to block—that is the question. *Reg Anesth Pain Med* 2011 Sep-Oct;36(5):421-3.
- Paul JE, Arya A, Hurlburt L, et al. Femoral nerve block improves analgesia outcomes after total knee arthroplasty: a meta-analysis of randomized controlled trials. *Anesthesiology* 2010 Nov;113(5):1144-62.
- Jaeger P, Zaric D, Fomsgaard JS, et al. Adductor canal block versus femoral nerve block for analgesia after total knee arthroplasty: a randomized, double-blind study. *Reg Anesth Pain Med* 2013 Nov-Dec;38(6):526-32.
- Memtsoudis SG, Danninger T, Rasul R, et al. Inpatient falls after total knee arthroplasty: the role of anesthesia type and peripheral nerve blocks. *Anesthesiology* 2014 Mar;120(3):551-63.
- Gibbs DM, Green TP, Esler CN. The local infiltration of analgesia following total knee replacement: a review of current literature. *J Bone Joint Surg Br* 2012 Sep;94(9):1154-9.
- Toftdahl K, Nikolajsen L, Haraldsted V, et al. Comparison of peri- and intraarticular analgesia with femoral nerve block after total knee arthroplasty: a randomized clinical trial. *Acta Orthop* 2007 Apr;78(2):172-9.
- Martinez V, Cymerman A, Ben Ammar S, et al. The analgesic efficiency of combined pregabalin and ketamine for total hip arthroplasty: a randomised, double-blind, controlled study. *Anaesthesia* 2014 Jan;69(1):46-52.
- Rothwell MP, Pearson D, Hunter JD, et al. Oral oxycodone offers equivalent analgesia to intravenous patient-controlled analgesia after total hip replacement: a randomized, single-centre, non-blinded, non-inferiority study. *Br J Anaesth* 2011 Jun;106(6):865-72.
- Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. *Am J Surg* 2002 Jun;183(6):630-41.