**Reviews** 

## Opioid Use Consequences, Governmental Strategies, and Alternative Pain Control Techniques Following Total Hip Arthroplasties

Kevin Berardino<sup>1</sup> <sup>*a*</sup>, Austin H. Carroll<sup>1</sup> <sup>*a*</sup>, Daniel Popovsky<sup>1</sup> <sup>*a*</sup>, Robert Ricotti<sup>2</sup>, Matthew D. Civilette<sup>1</sup>, William F. Sherman<sup>3</sup> <sup>*a*</sup>, Alan D. Kaye<sup>4</sup> <sup>*a*</sup>

<sup>1</sup> Georgetown University School of Medicine, <sup>2</sup> George Washington University Hospital, <sup>3</sup> Department of Orthopedic Surgery, Tulane University, <sup>4</sup> Department of Anesthesiology, Louisiana State University Shreveport

Keywords: total hip arthroplasty, opioids, pain control, postoperative, addiction, dependence, recovery

https://doi.org/10.52965/001c.35318

### **Orthopedic Reviews**

Vol. 14, Issue 3, 2022

Over the last several decades, rates of opioid use and associated problems have dramatically increased in the United States leading to laws limiting prescription duration for acute pain management. As a result, orthopedic surgeons who perform total hip arthroplasty (THA), a procedure that often leads to significant postoperative pain, have been faced with substantial challenges to adequately mitigate patient pain while also reducing opioid intake. Current strategies include identifying and correcting modifiable risk factors associated with postoperative opioid use such as preoperative opioid use, alcohol and tobacco abuse, and untreated psychiatric illness. Additionally, recent evidence has emerged in the form of Enhanced Recovery After Surgery (ERAS) protocols suggesting that a multidisciplinary focus on patient factors perioperatively can lead to reduced postoperative opioid administration and decreased hospital stays. A cornerstone of ERAS protocols includes multimodal pain regimens with opioid rescue only as needed, which often includes multiple systemic pain therapies such as acetaminophen, gabapentin, non-steroidal anti-inflammatory drugs, as well as targeted pain therapies that include epidural catheters and ultrasound-guided nerve blocks. Many hospital systems and states have also implemented opioid prescribing limitations with mixed success. As the opioid epidemic continues in the United States, while contributing to poor outcomes following elective surgeries, further research is warranted to identify multidisciplinary strategies that mitigate opioid use while also allowing for adequate pain control and rehabilitation.

#### INTRODUCTION

#### OPIOID EPIDEMIC AND SEQUELAE

Rates of opioid misuse in the United States have rapidly progressed over the past two decades as the opioid epidemic continues to burgeon. Reported statistics of opioidrelated harm demonstrate the ongoing acceleration of the epidemic and its expanding impact on a number of populations. One study suggests that annual opioid overdose deaths are projected to reach nearly 82,000 by 2025, which is a 147% increase from 2015.<sup>1</sup> Furthermore, the Centers for Disease Control and Prevention (CDC) reported that there were over 81,000 opioid overdose deaths in 2020. These numbers are expected to increase during the ongoing coronavirus disease 2019 (COVID-19) pandemic, triggering responses on individual, community, and policy levels to mitigate the effects that the opioid epidemic has on our society.<sup>2,3</sup>

Outside of overdose deaths, opioid misuse can result in several negative health outcomes. Sequelae of opioid misuse include, but are not limited to, increased risk of the acute coronary syndrome (ACS), infective endocarditis secondary to injection drug use (IDU), periprosthetic joint infection, analgesic tolerance with chronic use, chronic constipation, acute respiratory depression, and many others.<sup>4–7</sup> Additionally, chronic opioid users experience

 a Corresponding author: Kevin Berardino, BS
 Georgetown University School of Medicine
 Washington DC
 email: kmb364@georgetown.edu more negative postoperative outcomes than opioid-naïve individuals, including worse functional outcomes, delayed return to work, increased pain, and higher rates of revision.<sup>7–10</sup>

#### OPIOID PRESCRIPTIONS AND SURGERY

Many of the millions of Americans who suffer from opioid use disorder were first introduced to opioids through a healthcare prescription.<sup>11,12</sup> The large majority of these prescriptions are given following surgery or trauma.<sup>12</sup> In fact, surgery has been identified as a common risk factor for chronic opioid abuse.<sup>13</sup> Studies reveal that 60-92% of patients have unused opioids following surgery, and about 70% of these patients keep them rather than dispose of them properly.<sup>14–16</sup> Those particularly at risk for developing chronic opioid dependence include opioid-naïve individuals.17 Patients are considered to be opioid naïve if they have used a continuous dose of opioids for less than 7 days or have previously used opioids intermittently.<sup>18</sup> Orthopaedic procedures account for approximately 8.8% of surgical cases in the opioid-naïve population, creating an opportunity for orthopaedic surgeons to consider alternatives for pain management.<sup>17,19</sup> Unfortunately, opioid medications are considered the standard of care for postoperative pain management, and there is insufficient evidence to conclude that complementary and alternative medicines alone are sufficient in controlling postoperative pain from orthopaedic procedures.<sup>20</sup>

## OPIOID PRESCRIPTIONS AND TOTAL HIP ARTHROPLASTY

Total hip arthroplasty (THA) is one of the most common surgeries performed, and its primary goal is to alleviate pain and disability caused by trauma or osteoarthritis (OA). While THA is regarded as highly successful at alleviating pain in the long term, it can cause significant pain in the acute postoperative period.<sup>21</sup> Opioids remain the foundation of pain control in the acute postoperative period following several orthopaedic procedures including THA.<sup>21</sup> In the United States, 98% of patients are prescribed opioid medications after orthopaedic procedures.<sup>22</sup> The strongest predictor of persistent opioid use at 6 months follow-up after THA is preoperative opioid use.<sup>23</sup> One study of 574 total knee arthroplasty (TKA) and THA patients found that 4.3% of opioid-naïve patients who underwent THA were still using opioids at 6 months, while 34.7% of chronic opioid users reported taking opioids at 6-month follow-up.<sup>23</sup> The specifics regarding opioid prescription and usage following THA vary widely between individual patients and providers, prompting some institutions to work towards reducing narcotic usage following THA with some success.<sup>24</sup>

THA is inherently invasive and postoperative opioid regimens are routinely warranted for patients undergoing THA. Several studies have reviewed opioid use following THA, however there is limited published data comparing opioid usage between different approaches to THA.<sup>8,21–23</sup> The three most common approaches to THA include the anterior approach (AA), antero-lateral approach (AL), and posterior approach (PA). Two recent studies suggest that the AA correlates with the lowest early postoperative opioid consumption, largely thought to be related to decreased soft tissue damage and inflammation associated with this approach.<sup>25,26</sup> While surgical approach is influenced by patient needs or surgeon preference, it is important to consider how certain approaches to THA may impact postoperative pain management.

Despite concerns regarding excessive prescription of opioids in the perioperative setting of THA, they remain the cornerstone of pain management in the ongoing opioid epidemic. It is important to monitor the impact that opioids have on patient outcomes and tailor prescriptions based on individual patient needs. Multimodal treatment regimens have shown some promise in improving functional outcomes and reducing postoperative opioid use following THA.<sup>27,28</sup> However, more research is indicated to determine if alternative treatments are sufficient in controlling pain on their own.

#### IMPACT ON OUTCOMES

Excessive opioid use has a well-documented impact on patient outcomes after THA. There is a growing amount of interest in research regarding opioid use prior to THA because of its potential to predict postoperative outcomes.<sup>29–32</sup> When compared to opioid-naïve individuals, patients receiving chronic opioid therapy (COT) are subject to worse outcomes following THA including poorer functional outcomes, increased pain scores, 33,34 higher revision and readmission rates, and longer length of stay (LOS).<sup>9,10,32,34–37</sup> While clinical outcomes are well-studied in literature, there is a growing interest in the use of patient-reported outcome measures (PROMs) to assess pain management following THA.<sup>29,34,38</sup> PROMs are important to consider along with clinical outcomes because they may provide additional insight into the efficacy of alternative pain management at the individual level.

#### REVISIONS

Revision rates following THA vary based on surgical approach and individual patient characteristics.<sup>39</sup> Recent studies suggest that revision rates following THA range from 0.88% at 2 years follow-up to 4.2% at 5 years followup.<sup>9,37</sup> Current literature regarding the effects of opioid misuse on revision rates is limited, but two recent studies have investigated how revision rates are impacted by COT and postoperative opioid use. Bedard et al. analyzed revision rates in a cohort of 17,695 patients undergoing primary THA and found that 36.7% of patients were preoperative opioid users.<sup>9</sup> Univariate analysis suggested that patients receiving COT were significantly more likely to undergo early THA revision than opioid-naïve patients (1.2% vs. 0.7%).<sup>9</sup> Another study of 9943 patients undergoing THA found that patients receiving medium to high doses of opioids following surgery were more likely to undergo revision procedures at one and five year follow-up.<sup>37</sup> There is an increasing amount of literature regarding revision rates following other orthopaedic procedures, and more studies are needed to better understand the correlation between opioid use and THA revision rates.

#### COMPLICATIONS

THA is associated with a relatively low complication rate overall.<sup>40</sup> Some of the more common complications include dislocation, periprosthetic fracture, nerve injury, and infection.<sup>40,41</sup> Rozell et al. conducted a study of 802 patients undergoing TKA or THA, all of which were managed with a multimodal pain regimen.<sup>42</sup> Of 802 patients, 266 (33%) required rescue with intravenous opioids for additional pain relief. The strongest predictor of increased postoperative opioid requirement was preoperative opioid use, and those patients who required narcotic rescue were significantly more likely to experience inpatient complications following THA. Sing et al. demonstrated similar results in a cohort of 174 patients receiving TKA or THA; preoperative longacting opioid use was the strongest predictor of postoperative opioid requirement, and these patients experienced the highest number of complications when compared to nonopioid users and short-acting opioid users.<sup>30</sup> In particular there were more periprosthetic fractures in the short and long-acting opioid groups compared to the opioid naïve group, and almost all of the medical complications including urinary tract infections, delirium, hypotension, and acute kidney injury were experienced in the opioid groups.

However, there remains conflicting evidence regarding the association between postoperative opioid use and increased complications. One recent study of 5304 patients undergoing primary THA found that preoperative opioid use was predictive of increased postoperative opioid use and increased minor complications, however there was no significant difference in major complications between opioid users and opioid-naïve patients.<sup>7</sup> Stratification of complication severity in future studies could be beneficial to better understand the correlation between opioid use and complication rates following THA.

#### LENGTH OF STAY

Length of stay is directly associated with increased costs, complication rates, and functional outcomes following THA. Multimodal pain protocols combined with early mobilization efforts have reduced the average LOS following THA from 4-12 days to 1-3 days, <sup>43</sup> however, not all patients are responsive to multimodal pain management and may require additional opioid supplementation.<sup>42</sup> Postoperative opioid use has been shown to significantly increase LOS following THA in a number of studies.<sup>7,30,42</sup> Rozell et al. found that the average LOS for patients undergoing THA was 3.15 days (standard deviation [SD], 1.92) regardless of opioid use, and LOS in patients receiving COT was 3.36 days (SD, 2.46).<sup>42</sup> Bell et al. found similar results, LOS in nonopioid users was 3.09 days (SD, 0.92) and 3.27 days (SD, 1.96) in opioid users.<sup>7</sup> Sing et al. suggested that different types of opioid medications may impact LOS. In patients undergoing TKA or THA, nonopioid users had an average LOS of 2.4 days (SD, 0.6), short-acting opioid users had an average

LOS of 2.8 days (SD, 0.9), and long-acting opioid users had the highest average LOS of 4 days (SD, 4.5).<sup>30</sup> These findings implicate that opioid use does increase LOS, but the extent to which LOS is lengthened may be dependent upon specific types of opioid medications.

#### **RISK FACTORS**

#### PRESCRIPTION FACTORS

There are many opioid prescription characteristics that are associated with higher levels of postoperative opioid use. Several characteristics that have found to be associated with long-term opioid use include first-prescriptions with long-acting opioids, prescription duration over 7 days, and daily MMEs (morphine milliequivalents) over 50.44 In addition, the number of prescription refills is correlated with long-term opioid use, with 10.6% of patients with two refills becoming long-term opioid users and 26.1% of those with over four refills becoming long-term users.<sup>45</sup> Delaney et al. also studied how prescription MME quantity affects post-operative utilization and showed that patients with a total post-operative prescription of 335 MMEs during 30 days post-op had lower persistent rates of opioid use compared to the groups receiving 512 MMEs and 654 MMEs.<sup>46</sup> Factors that a physician can alter to decrease post-operative opioid usage are therefore limiting refills and prescribing lower-dose prescriptions.

#### PRE-OPERATIVE OPIOID USE

Pre-operative opioid use has been found to be associated with greater pain, lower functional status, and higher complications following total joint arthroplasty (TJA).<sup>29,30,42,47</sup> Specifically related to THA, preoperative opioid use is associated with longer hospital stays, greater likelihood of discharge to rehabilitation facilities, and decreased patient-reported outcomes.<sup>38</sup> In a study across 29,767 patients who underwent THA, 33.3% of those who used opioids preoperatively continued to chronic use after surgery.48 Further, opioid users are significantly more likely to use opioids at the three-month postoperative point (OR=5.4) if having used pre-operatively.<sup>49</sup> Another study showed that pre-operative users were 1.7, 5.0, and 8.0 times more likely to be filling an opioid prescription at 1, 2, and 3 months following THA, respectively.<sup>8</sup> Compared to opioid naïve patients, THA patients with preoperative opioid use were 4 times more likely to fill a second prescription and at 12 times more likely to have ongoing chronic opioid use.<sup>50</sup> Opioid users who successfully discontinued opioid use prior to TJA demonstrated similar metrics of health outcomes as those who were opioid naïve prior to surgery; therefore, attempts to discontinue preoperative prescriptions should be made if possible.33

#### REVISION

There are differences in opioid consumption between patients undergoing primary versus revision surgery for THA. Compared to patients undergoing primary THA, those undergoing revision THA were found to utilize 1.7 times more opioids in a 48-hour period following surgery.<sup>51</sup> A study on 17,695 patients who underwent THA also showed that preoperative opioid use within 3 months of surgery is associated with early revision, once again indicating the pre-operative opioid use negatively affects outcomes within THA.<sup>9</sup> Inacio et al. came to a similar conclusion, showing that opioid use 91-180 days post-surgery is associated with a higher risk of revision surgery and can be used as one indicator of surgical failure.<sup>37</sup>

#### DEMOGRAPHIC FACTORS

Certain demographic factors have been associated with increased post-operative opioid use. Female sex and African American race have both been found to be associated with an increased number of post-operative prescriptions.<sup>52–54</sup> In addition, younger and unemployed individuals were found to be more likely to need greater opioid quantities in the post-operative period compared to older individuals or those with employment.<sup>55</sup> Additionally, Medicare patients were found to be more likely to demonstrate chronic opioid use in contrast to their non-Medicare counterparts.<sup>56</sup>

#### OTHER

Many medical comorbidities afflicting patients undergoing THA are associated with increased post-operative opioid utilization. Certain comorbidities that have been linked with increased opioid use after THA include mental health disorders, diabetes, hypertension, chronic pulmonary disease, chronic kidney disease, acquired immunodeficiency syndrome (AIDS), peripheral vascular disease, chronic nonspecific pain, and substance abuse.<sup>51,52,54,55</sup> History of prior hospital complications is also associated with increased post-operative opioid use.<sup>50</sup> In addition, patients who have inferior health statuses pre-operatively, denoted by an ASA score over 2, have been found to have inferior outcomes with regards to chronic opioid use.<sup>56</sup> Further, the use of other medications preoperatively such as stimulants and sedatives, particularly benzodiazepines, are associated with increased post-operative opioid use.<sup>50,57</sup> Tobacco use has also been found to be associated with a 90% greater MME consumption postoperatively, while alcohol abuse has been shown to be an independent predictor of prolonged postoperative opioid use.<sup>54,57</sup>

# INTERVENTIONS TO REDUCE OPIOID USAGE AND THEIR OUTCOMES

#### ERAS PROTOCOL

Enhanced Recovery After Surgery (ERAS) is an umbrella acronym encompassing diverse protocols used by various surgical specialties, so as to optimize patient care in a way that improves post-surgical outcomes.<sup>58</sup> This multidisciplinary, team-centric approach endeavors to minimize the deleterious effect of the physiologic stress response that transpires following surgical procedures, in order to restore organ function to preoperative levels as well as to mitigate

the financial burden on the patient from a prolonged hospital stay. Pioneered by Henrik Kehlet in 1995 initially for use in gastrointestinal surgery, ERAS protocols have proven effective for a variety of procedures.<sup>41</sup> In particular, ERAS has recently gained traction as a method to reduce patient morbidity and foster expedited recovery following orthopaedic surgery.<sup>59</sup> Sharrock et al. laid the groundwork for ERAS procedures in patients undergoing elective hip and knee arthroplasty by making changes to traditional treatment modalities and documented a decrease in mortality rates from .44 to .07% in patients undergoing knee arthroplasty.<sup>60</sup> While a standardized ERAS model for hip arthroplasty has yet to be fully articulated, ERAS components are commonly incorporated into the broader patient care setting of THA procedures. These, in turn, have been shown to significantly decrease length of stay at hospitals, diminish perioperative costs, increase patient satisfaction, and reduce dependence on opioid use.<sup>61</sup> Specific recommendations in this regard are issued by the ERAS society, a group which utilizes evidence-based research on how best to implement ERAS protocols in varied surgical disciplines.<sup>62</sup> By analyzing the plethora of relevant studies and forming a multidisciplinary consensus, the ERAS society has recently been able to form guidelines on how ERAS protocols could be implemented in THA. These guidelines focus on three distinct phases of patient care: preoperative, intraoperative, and postoperative care.

In the context of preoperative care components, ERAS society guidelines place particular emphasis upon patient education and optimization of patient conditions. Currently, there is no direct evidence to demonstrate that providing information to the patient improves outcomes, rather its effectiveness likely resides in its potential to decrease patient anxiety. The information supplied to a patient preoperatively can be broad, and thus there exists little in the way of specific data, or a professional consensus surrounding what precise guidelines should be provided. Moreover, owing to the great variety of patients undergoing THA, it is challenging in general to create uniform standards on what would constitute proper education across diverse patient cohorts. Nevertheless, preoperative education has been shown to improve patient perspective about the procedure, and since there is no harm in providing such information; as such, most ERAS protocols all include a component of preoperative patient education.<sup>28</sup> The concept of optimization prior to surgery refers to fostering a physiologic state in a patient to decrease postoperative complications. Recommendations for preoperative optimization of patients undergoing THA procedures focus on several risk factors. In particular, smoking cessation for greater than 4 weeks prior to surgery is associated with significantly improved outcomes, especially those relating to wound healing.<sup>61</sup> Conversely, heavy alcohol use before surgery is associated with elevated complication rates, and referral to alcohol cessation programs is recommended for heavy drinkers prior to THA.63 Identifying and treating anemia in preoperative patients has been shown to decrease the need for transfusions and thereby minimize complications. Therefore, it is strongly recommended that anemia be corrected, and hematocrit optimized prior to undergoing THA. An additional integral preoperative factor for THA, and a major focus of the ERAS society more broadly, is nutrition. Both preoperative fasting–2 hours NPO prior to surgery for clear liquids, and 6 hours prior for solid foods–as well as preoperative carbohydrate loading have been shown to decrease perioperative complications and enhance recovery.<sup>61</sup> Preoperative sedation and use of anxiolytic medications, however, are not recommended as there is little evidence to suggest that these improve rates of discharge or other postop outcome metrics.<sup>62</sup>

Intraoperative management following ERAS protocols focuses on maintaining normothermia, averting intraoperative blood loss, proper use of intra urinary catheters to ensure effective monitoring of fluid levels, providing sufficient antibiotic prophylaxis and skin preparation, and proper anesthetic management, either through spinal or general anesthesia. A study by Basques et al. analyzed a database (N= 20,936) of patients who had received either spinal (epidural or nerve block) or general anesthesia intraoperatively for elective THA.<sup>64</sup> The data indicated that general anesthesia use resulted in a higher rate of adverse effects-including extended operative time, prolonged ventilation, unplanned intubation, and need for blood transfusion-as compared to patients that were treated with spinal anesthesia. Additionally, use of spinal anesthetic methods in THA has been shown to diminish opioid usage postoperatively.62

Postoperative management per ERAS guidelines focuses on minimizing nausea and vomiting, using a combined multimodal pain regimen, boosting early mobility, and providing nutritional support.<sup>62</sup> It is important to recognize that ERAS protocols are highly flexible and dynamic, changing based on new and emerging clinical evidence. Furthermore, due to the lack of evidence surrounding many ERAS pathways, it is important to audit and be mindful of current clinical guidelines so that future research can be optimized to produce the best outcomes. The remainder of this discussion will center on the post-op course, with a particular interest in post-operative analgesia and the variety of methods available to optimize pain control following THA procedures.

# MULTIMODAL PAIN REGIMENS AND PRESCRIPTION MEDICATIONS

Prescription of opioids for postoperative pain has been a subject of intense discussion and debate owing to the many potential adverse effects of this drug class, with a highly direct impact on patients. A study of opioid prescribing practices showed that from 2014 to 2017, the proportion of patients receiving opioid prescriptions within 60 days of discharge from an elective THA procedure had increased markedly, from 82% to 89.7%.<sup>65</sup> Opioids do have certain indications for acute pain management as well as palliative care and tackling chronic pain. However, their marked addiction potential and significant side effects including but not limited to dizziness, constipation, nausea, respiratory depression, and dependence, have also made them potentially dangerous to large patient cohorts, as evidenced by

the significant increase in opioid-related mortality and the devastating American opioid epidemic of the last decade. The use of multimodal analgesia for THA is therefore quickly becoming the standard of care across medical institutions due to its capacity not only to provide effective pain relief, but also to materially reduce dependence on opioids.<sup>66</sup> Current multimodal pain regimens for the treatment of pain after THA procedures encompass a broad range of analgesic agents with diverse pharmacodynamic actions: acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), gabapentinoids, and opioids as needed.<sup>62</sup>

Acetaminophen is an anti-inflammatory drug that, among other mechanisms of action, is believed to selectively inhibit cyclooxygenase-2 (COX-2), an enzyme involved in the breakdown of arachidonic acid and formation of inflammatory intermediates including prostaglandins. Through this inhibition, for example, acetaminophen decreases levels of Prostaglandin E2 (PGE2), which has both anti-inflammatory and antipyretic effects. Intravenous infusion of 1g of acetaminophen was found to provide significant pain relief in patients who had recently undergone major orthopaedic surgery.<sup>67</sup> NSAIDs, another important component of this multimodal pain regimen, work by inhibiting cyclooxygenase-1 and cyclooxygenase-2, which likewise diminishes production of both pyretic and inflammatory mediators. NSAIDs have in turn been shown to both reduce pain and decrease opioid use following hip and knee replacement.<sup>68</sup> Gabapentoid medications, such as gabapentin and pregabalin, function by decreasing neuronal excitability through targeting of the alpha-2-delta-1 subunit of voltage gated calcium channels located on neurons present throughout many tissues. It is thought that decreased release of excitatory neurotransmitters decreases production of inflammatory mediators involved in neuropathic pain.<sup>69</sup> Gabapentin has been shown to decrease levels of neuropathic pain following THA, resulting in a concomitant decrease of narcotic analgesic consumption.<sup>70</sup>

An increase in practitioners are implementing multimodal pain regimens due to their ability to target various pain mechanisms while also reducing overall consumption of and dependence upon opioids.<sup>71</sup> Multimodal regimens decrease the periods of sedation brought upon by opioids as well as decrease the other associated side effects such as nausea, vomiting, and respiratory depression.<sup>72</sup> In a large database study (N = 1,318,165) of patients that were treated with a multimodal pain regimen or opioids only following hip or knee arthroplasty, Memtsoudis et al. found that patients who were status-post THA and being treated with multimodal regimens, consisting of 2 or more pain medications, experienced 26% fewer gastrointestinal complications, 19% fewer respiratory complications, a 12.1% decrease in length of stay, and an 18.5% decrease in opioid prescription as compared to patients who were treated with opioids alone.73 It was noted that NSAIDs and acetaminophen were the most effective in providing analgesia and minimizing complications.73 A systematic review by Zhao and Davis, analyzing literature pertaining to multimodal pain management in patients with THA, found that while each drug of a multimodal regimen does contribute

a unique benefit, there has not been one specific regimen that has proven to be more effective than another. Nevertheless, one common thread among the varying regimens analyzed by Zhao and Davis is that the majority of the studies showed a clear decrease in opioid consumption following utilization of any of the major multimodal regimens.<sup>27</sup> While the benefits of using multimodal regimens are apparent, further research is needed in order to optimize combinations.

#### EPIDURAL CATHETERS AND PERIPHERAL NERVE BLOCKS

Epidural catheters and peripheral nerve blocks are methods of postoperative local pain control that are oftentimes components of multimodal pain regimens, supplementing more systemic agents. Epidurals involve placement of a catheter into the epidural space; it is through this delivery system that medication can be injected to provide a sensory blockade and relieve pain. A variety of drugs can be supplied through an epidural catheter including, but not limited to, anesthetics, opioids, and steroids. As such, the analgesic effect of epidurals naturally depends on the substance being injected. Typically these medications are administered using either a patient-controlled medication pump or via single-dose injections of anesthetics or narcotics. A metaanalysis by Choi looked to see the effectiveness of pain relief post-operatively when using epidurals following THA. While epidurals do provide adequate analgesia, their effectiveness can be limited to the immediate postoperative period, or 4-6 hours, with anesthetics such as bupivacaine, and up to 48 hours using long-acting narcotics such as morphine.<sup>74,75</sup> Additionally, it was noted that a local anesthetic-narcotic mixture, such as bupivacaine and fentanyl, provided more effective relief than a narcotic alone.<sup>74</sup> Not all patients are candidates for epidural use and they may pose several troublesome side effects, including urinary retention, pruritus, motor blockade, and epidural hematoma.<sup>62</sup> There is currently no evidence to suggest that epidural usage alone following THA leads to a decrease in opioid consumption post-operatively.

Peripheral nerve blocks have also been utilized in combination with standard pain regimens to decrease postoperative pain. A variety of nerve blocks are used for THA including lumbar plexus block, parasacral sciatic block, femoral nerve block, three-in-one block, and a quadratus lumborum block.<sup>76</sup> A study performed by Nishio et al. has indicated that combination sciatic and femoral nerve block offers adequate analgesia, on the basis of reported pain scores at 6- and 12-hour time points in patients undergoing THA.<sup>77</sup> Recent evidence has suggested that nerve block analgesia for patients after THA should be avoided in favor of systemic analgesia, owing to onset of low extremity weakness.<sup>76</sup> Specifically, in up to 90% of cases following femoral nerve block or quadratus lumborum block, there is onset of significant quadriceps weakness, in which case the adverse consequences of falling may significantly outweigh the benefit of analgesia.<sup>78</sup> A study by Becker et al. of elective THA patients undergoing either epidural or psoas nerve block showed that, on average, postoperative consumption of morphine was greater with the psoas nerve block (12.6mg) as compared to epidural (5.8mg).<sup>79</sup>

#### PRESCRIBING LIMITATIONS

As noted previously, over the last two decades, there has been a significant increase in opioid-related mortality across the United States, precipitating an ongoing public health emergency linked to widespread dependency on the drugs. Poor prescribing practices and ease of access to prescription opioids have resulted in so severe a healthcare crisis that life expectancy in the US decreased significantly from 2016-2019, even before the sharp declines of the COVID-19 pandemic.<sup>47</sup> The Center for Disease Control released recommendations in 2016 that encouraged doctors to prescribe only circumscribed 7-day regimens of opioids for acute pain, however, this is difficult for post-operative patients. Since 2016, 36 states have enacted further legislation that sets regulations on the morphine milligram equivalents (MME) of narcotics an adult patient can be prescribed by physicians.<sup>80</sup> This regulatory change is significant since opioids have long been used as a tool for pain relief in surgical procedures, in particular invasive procedures with long recovery times, such as THAs. It is thus important to consider the implications that prescribing limitations have on the treatment of postoperative pain and patient outcomes. A study by Pannu et al. analyzed prescribing rates of opioids and complications in patients who underwent joint arthroplasty prior to passage of legislation limiting opioid prescriptions and after passage.<sup>81</sup> They found that while there was a marked decline in the MMEs prescribed to patients, there was no corresponding increase in rates of patient clinic visits, or readmissions. Many major hospital institutions have followed suit and modified their own guidelines and practices to better address the opioid crisis. A study by Chalmers et al. analyzed a group of 20,000 patients at a major hospital that received either a THA or TKA between 2016 and 2019.82 In this time period, the institution implemented opioid-prescribing restrictions which physicians were expected to adhere. Despite the policy changes, it was shown that rates of re-prescribing of opioid medications remained the same following the prescription limitations for patients who underwent THA. However, because such limitations in the US have been implemented so recently, further research is needed to determine the impact this will have on postoperative pain management of patients undergoing surgical procedures. It remains of utmost importance to maintain patient comfort and not undertreat pain in the post-op context, which can lead to complications and interfere with proper convalescence. Patients also can be problematic when not receiving what they perceive as adequate pain control in the post-operative setting, which further complicates the ability of a surgeon to decrease opiate usage after arthroplasty.

#### CONCLUSION

As the US population continues to increasingly age, there will likely be a corresponding increase in the number of to-

tal hip arthroplasties performed each year. Due to the invasive nature of this procedure that typically warrants a large incision, significant disruption of underlying musculature, and post-operative movement restrictions, the clinician faces a substantial challenge in adequately controlling patient pain while simultaneously reducing patient opioid consumption and opioid related side effects. This challenge is further compounded by the ongoing opioid epidemic in the United States that has drawn national and political attention. In order to circumvent these issues, the focus has largely been on patient selection, prescribing limitations, the elimination of specific modifiable risk factors, and multimodal pain regimens that remain the cornerstone of the ERAS protocol. Moving forward, additional prospective research is needed to further identify ways to reduce opioid usage while adequately controlling patient pain and promoting recovery after THA.

.....

DISCLOSURES

No relevant disclosures

FUNDING

No funding

Submitted: September 14, 2021 EDT, Accepted: January 10, 2022 EDT

## REFERENCES

1. Chen Q, Larochelle MR, Weaver DT, et al. Prevention of Prescription Opioid Misuse and Projected Overdose Deaths in the United States. *JAMA Netw Open*. 2019;2(2):e187621. doi:10.1001/ja manetworkopen.2018.7621

2. Rollston R. Our Medical and Social Responsibility in Addressing the Opioid Epidemic. *Med Care*. 2020;58(7):582-585. <u>doi:10.1097/MLR.00000000000</u> <u>1349</u>

3. Haley DF, Saitz R. The Opioid Epidemic during the COVID-19 Pandemic. *J Am Med Assoc*. 2020;324(16):1615-1617. <u>doi:10.1001/jama.2020.1854</u> <u>3</u>

4. Kovacs RJ, Gilbert JH, Oetgen WJ. Call to Action: Opioid Crisis Impacting More Than Just Patients. *J Am Coll Cardiol*. 2020;75(3):341-343. <u>doi:10.1016/jac</u> <u>c.2019.12.010</u>

5. Mercadante S, Arcuri E, Santoni A. Opioid-Induced Tolerance and Hyperalgesia. *CNS Drugs*. 2019;33(10):943-955. <u>doi:10.1007/s40263-019-0066</u> <u>0-0</u>

6. Imam MZ, Kuo A, Ghassabian S, Smith MT. Progress in understanding mechanisms of opioidinduced gastrointestinal adverse effects and respiratory depression. *Neuropharmacology*. 2018;131:238-255. doi:10.1016/j.neuropharm.2017.1 2.032

7. Bell KL, Shohat N, Goswami K, Tan TL, Kalbian I, Parvizi J. Preoperative Opioids Increase the Risk of Periprosthetic Joint Infection After Total Joint Arthroplasty. *J Arthroplasty*. 2018;33(10):3246-3251.e1. <u>doi:10.1016/j.arth.2018.0</u> 5.027

8. Bedard NA, Pugely AJ, Dowdle SB, Duchman KR, Glass NA, Callaghan JJ. Opioid Use Following Total Hip Arthroplasty: Trends and Risk Factors for Prolonged Use. *J Arthroplasty*. 2017;32(12):3675-3679. doi:10.1016/j.arth.2017.08.01

2017;32(12):3675-3679. <u>doi:10.1016/j.arth.2017.08.01</u> <u>0</u>

9. Bedard NA, DeMik DE, Dowdle SB, Owens JM, Liu SS, Callaghan JJ. Does Preoperative Opioid Use Increase the Risk of Early Revision Total Hip Arthroplasty? *J Arthroplasty*. 2018;33(7):S154-S156. <u>d</u> <u>oi:10.1016/j.arth.2018.01.018</u> 10. Weick J, Bawa H, Dirschl DR, Luu HH. Preoperative opioid use is associated with higher readmission and revision rates in total knee and total hip arthroplasty. *J Bone Jt Surg - Am Vol.* 2018;100(14):1171-1176. doi:10.2106/JBJS.17.01414

11. Hoffman KA, Ponce Terashima J, McCarty D. Opioid use disorder and treatment: challenges and opportunities. *BMC Health Serv Res.* 2019;19(1). doi:1 0.1186/s12913-019-4751-4

12. Brummett CM, Waljee JF, Goesling J, et al. New persistent opioid use after minor and major surgical procedures in us adults. *JAMA Surg.* 2017;152(6). do i:10.1001/jamasurg.2017.0504

13. Fearon NJ, Benfante N, Assel M, et al.
Standardizing Opioid Prescriptions to Patients After Ambulatory Oncologic Surgery Reduces
Overprescription. *Jt Comm J Qual Patient Saf.*2020;46(7):410-416. doi:10.1016/j.jcjq.2020.04.004

14. Bartels K, Mayes LM, Dingmann C, Bullard KJ, Hopfer CJ, Binswanger IA. Opioid use and storage patterns by patients after hospital discharge following surgery. *PLoS ONE*. 2016;11(1). doi:10.137 1/journal.pone.0147972

15. Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription opioid analgesics commonly unused after surgery: a systematic review. *JAMA Surg.* 2017;152(11):1066-1071. <u>doi:10.1001/jamasurg.201</u> 7.0831

17. Trasolini NA, McKnight BM, Dorr LD. The Opioid Crisis and the Orthopedic Surgeon. *J Arthroplasty*. 2018;33(11):3379-3382.e1. doi:10.1016/j.arth.2018.0 7.002

 Nafziger AN, Barkin RL. Opioid Therapy in Acute and Chronic Pain. *J Clin Pharmacol*.
 2018;58(9):1111-1122. doi:10.1002/jcph.1276

19. Schoenfeld AJ, Jiang W, Chaudhary MA, Scully RE, Koehlmoos T, Haider AH. Sustained prescription opioid use among previously opioid-naive patients insured through TRICARE (2006-2014). *JAMA Surg.* 2017;152(12):1175-1176. doi:10.1001/jamasurg.2017.2628

20. Bakker CJ, Wise KL, Williams BR, Swiontkowski MF. Complementary and Alternative Medicine for Postoperative Pain: A Systematic Review. *J Bone Joint Surg Am*. 2020;102(Suppl 1):36-46. <u>doi:10.2106/JBJS.1</u> 9.01439

21. Gaffney CJ, Pelt CE, Gililland JM, Peters CL.
Perioperative Pain Management in Hip and Knee
Arthroplasty. *Orthop Clin North Am*.
2017;48(4):407-419. doi:10.1016/j.ocl.2017.05.001

22. Grace TR, Choo KJ, Patterson JT, Khanna K, Feeley BT, Zhang AL. A Review of Inpatient Opioid Consumption and Discharge Prescription Patterns After Orthopaedic Procedures. *J Am Acad Orthop Surg.* 2020;28(7):279-286. <u>doi:10.5435/JAAOS-D-19-0</u> 0279

23. Goesling J, Moser SE, Zaidi B, et al. Trends and predictors of opioid use after total knee and total hip arthroplasty. *Pain*. 2016;157(6):1259-1265. doi:10.109 7/j.pain.00000000000516

24. Wyles CC, Hevesi M, Trousdale ER, et al. The 2018 Chitranjan S. Ranawat, MD Award: Developing and Implementing a Novel Institutional Guideline Strategy Reduced Postoperative Opioid Prescribing after TKA and THA. *Clin Orthop Relat Res*. 2019;477(1):104-113. doi:10.1007/s11999.00000000 0000292

25. Miller LE, Gondusky JS, Bhattacharyya S, Kamath AF, Boettner F, Wright J. Does Surgical Approach Affect Outcomes in Total Hip Arthroplasty Through 90 Days of Follow-Up? A Systematic Review With Meta-Analysis. *J Arthroplasty*. 2018;33(4):1296-1302. doi:10.1016/j.arth.2017.11.011

26. Seah S, Quinn M, Tirosh O, Tran P. Postoperative Opioid Consumption After Total Hip Arthroplasty: A Comparison of Three Surgical Approaches. *J Arthroplasty*. 2019;34(11):2676-2680. doi:10.1016/j.ar th.2019.05.057

27. Zhao J, Davis SP. An integrative review of multimodal pain management on patient recovery after total hip and knee arthroplasty. *Int J Nurs Stud.* 2019;98:94-106. doi:10.1016/j.ijnurstu.2019.06.010

28. Soffin EM, Wu CL. Regional and Multimodal Analgesia to Reduce Opioid Use After Total Joint Arthroplasty: A Narrative Review. *HSS J*. 2019;15(1):57-65. <u>doi:10.1007/s11420-018-9652-2</u>

29. Goplen CM, Verbeek W, Kang SH, et al. Preoperative opioid use is associated with worse patient outcomes after total joint arthroplasty: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2019;20(1):234. doi:10.1186/s12 891-019-2619-8 30. Sing DC, Barry JJ, Cheah JW, Vail TP, Hansen EN. Long-Acting Opioid Use Independently Predicts Perioperative Complication in Total Joint Arthroplasty. *J Arthroplasty*. 2016;31(9):170-174.e1. <u>d</u> <u>oi:10.1016/j.arth.2016.02.068</u>

31. Kim SC, Choudhry N, Franklin JM, et al. Patterns and predictors of persistent opioid use following hip or knee arthroplasty. *Osteoarthr Cartil.*2017;25(9):1399-1406. doi:10.1016/j.joca.2017.04.002

32. Kim K, Chen KK, Roof M, Anoushiravani AA, Vigdorchik J, Schwarzkopf R. The effects of preoperative chronic opioid use in total hip arthroplasty. *J Clin Orthop Trauma*. 2020;11(1):73-78. doi:10.1016/j.jcot.2019.04.027

33. Nguyen LCL, Sing DC, Bozic KJ. Preoperative Reduction of Opioid Use Before Total Joint Arthroplasty. *J Arthroplasty*. 2016;31(9 Suppl):282-287. doi:10.1016/j.arth.2016.01.068

34. Pivec R, Issa K, Naziri Q, Kapadia BH, Bonutti PM, Mont MA. Opioid use prior to total hip arthroplasty leads to worse clinical outcomes. *Int Orthop*. 2014;38(6):1159-1165. <u>doi:10.1007/s00264-014-229</u> <u>8-x</u>

35. Williams J, Kester BS, Bosco JA, Slover JD, Iorio R, Schwarzkopf R. The Association Between Hospital Length of Stay and 90-Day Readmission Risk Within a Total Joint Arthroplasty Bundled Payment Initiative. *J Arthroplasty*. 2017;32(3):714-718. doi:10.1 016/j.arth.2016.09.005

36. Ramos NL, Karia RJ, Hutzler LH, Brandt AM, Slover JD, Bosco JA. The Effect of Discharge Disposition on 30-Day Readmission Rates After Total Joint Arthroplasty. *J Arthroplasty*. 2014;29(4):674-677. doi:10.1016/j.arth.2013.09.010

37. Inacio MCS, Pratt NL, Roughead EE, Paxton EW, Graves SE. Opioid use after total hip arthroplasty surgery is associated with revision surgery. *BMC Musculoskelet Disord*. 2016;17:122. doi:10.1186/s1289 1-016-0970-6

38. Bonner BE, Castillo TN, Fitz DW, Zhao JZ, Klemt C, Kwon YM. Preoperative Opioid Use Negatively Affects Patient-reported Outcomes After Primary Total Hip Arthroplasty. *J Am Acad Orthop Surg.* 2019;27(22):e1016-e1020. doi:10.5435/JAAOS-D-18-0 0658

39. Hoskins W, Bingham R, Lorimer M, Hatton A, de Steiger RN. Early Rate of Revision of Total Hip Arthroplasty Related to Surgical Approach: An Analysis of 122,345 Primary Total Hip Arthroplasties. *J Bone Joint Surg Am*. 2020;102(21):1874-1882. doi:1 0.2106/JBJS.19.01289 40. Aggarwal VK, Elbuluk A, Dundon J, et al. Surgical approach significantly affects the complication rates associated with total hip arthroplasty. *Bone Jt J*. 2019;101 B(6):646-651. <u>doi:10.1302/0301-620X.101B</u> 6.BJJ-2018-1474.R1

41. Petis S, Howard JL, Lanting BL, Vasarhelyi EM. Surgical approach in primary total hip arthroplasty: anatomy, technique and clinical outcomes. *Can J Surg.* 2015;58(2):128-139. doi:10.1503/cjs.007214

42. Rozell JC, Courtney PM, Dattilo JR, Wu CH, Lee GC. Preoperative Opiate Use Independently Predicts Narcotic Consumption and Complications After Total Joint Arthroplasty. *J Arthroplasty*. 2017;32(9):2658-2662. doi:10.1016/j.arth.2017.04.002

43. Aasvang EK, Luna IE, Kehlet H. Challenges in postdischarge function and recovery: the case of fast-track hip and knee arthroplasty. *Br J Anaesth*. 2015;115(6):861-866. doi:10.1093/bja/aev257

44. Zhang Y, Johnson P, Jeng PJ, et al. First Opioid Prescription and Subsequent High-Risk Opioid Use: a National Study of Privately Insured and Medicare Advantage Adults. *J Gen Intern Med*. 2018;33(12):2156-2162. <u>doi:10.1007/s11606-018-462</u> <u>8-y</u>

45. Deyo RA, Hallvik SE, Hildebran C, et al. Association Between Initial Opioid Prescribing Patterns and Subsequent Long-Term Use Among Opioid-Naïve Patients: A Statewide Retrospective Cohort Study. *J Gen Intern Med*. 2017;32(1):21-27. do i:10.1007/s11606-016-3810-3

46. Delaney LD, Gunaseelan V, Rieck H, Dupree JM, Hallstrom BR, Waljee JF. High-Risk Prescribing Increases Rates of New Persistent Opioid Use in Total Hip Arthroplasty Patients. *J Arthroplasty*. 2020;35(9):2472-2479.e2. doi:10.1016/j.arth.2020.0 4.019

47. Singh V, Kugelman DN, Rozell JC, Meftah M, Schwarzkopf R, Davidovitch RI. Impact of preoperative opioid use on patient outcomes following primary total hip arthroplasty. *Orthopedics*. 2021;44(2):77-84. doi:10.3928/01477447-20210217-0
3

48. Chaudhary MA, Dalton MK, Koehlmoos TP, Schoenfeld AJ, Goralnick E. Identifying Patterns and Predictors of Prescription Opioid Use after Total Joint Arthroplasty. *Mil Med*. 2021;186(5-6):587-592. <u>doi:1</u> 0.1093/milmed/usaa573

49. Naylor JM, Pavlovic N, Farrugia M, et al. Associations between pre-surgical daily opioid use and short-term outcomes following knee or hip arthroplasty: a prospective, exploratory cohort study. *BMC Musculoskelet Disord*. 2020;21(1):398. doi:10.118 6/s12891-020-03413-z 50. Tan TL, Rondon AJ, Wilt Z, et al. Understanding Opioid Use After Total Hip Arthroplasty: A Comprehensive Analysis of a Mandatory Prescription Drug Monitoring Program. *J Am Acad Orthop Surg.* 2020;28(20):e917-e922. <u>doi:10.5435/JAAOS-D-19-006</u> <u>76</u>

51. Bernstein JA, Feng J, Mahure SA, Schwarzkopf R, Long WJ. Revision total hip arthroplasty is associated with significantly higher opioid consumption as compared to primary total hip arthroplasty in the acute postoperative period. *HIP Int*. 2020;30(1\_suppl):59-63. doi:10.1177/1120700020938 324

52. Prentice HA, Inacio MCS, Singh A, Namba RS, Paxton EW. Preoperative Risk Factors for Opioid Utilization After Total Hip Arthroplasty. *J Bone Joint Surg Am*. 2019;101(18):1670-1678. doi:10.2106/JBJS.1 8.01005

53. Soffin EM, Wilson LA, Liu J, Poeran J, Memtsoudis SG. Association between sex and perioperative opioid prescribing for total joint arthroplasty: a retrospective population-based study. *Br J Anaesth*. 2021;126(6):1217-1225. doi:10.1016/j.bja.2020.12.046

54. Lanzillotta-Rangeley J, Clark A, Christianson A, Kalarchian MA. Association of Prescription Opioid Exposure and Patient Factors With Prolonged Postoperative Opioid Use in Opioid-Naive Patients. *AANA J*. 2020;88(1):18-26. http://ovidsp.ovid.com/ovi dweb.cgi?T=JS&PAGE=reference&D=med17&NEW S=N&AN=32008614

55. Roebke AJ, Via GG, Everhart JS, et al. Inpatient and outpatient opioid requirements after total joint replacement are strongly influenced by patient and surgical factors. *Bone Jt Open*. 2020;1(7):398-404. do i:10.1302/2633-1462.17.bjo-2020-0025.r1

56. Anoushiravani AA, Kim KY, Roof M, et al. Risk factors associated with persistent chronic opioid use following THA. *Eur J Orthop Surg Traumatol*. 2020;30(4):681-688. doi:10.1007/s00590-019-0261 <u>8-w</u>

57. Cryar KA, Hereford T, Edwards PK, Siegel E, Barnes CL, Mears SC. Preoperative Smoking and Narcotic, Benzodiazepine, and Tramadol Use are Risk Factors for Narcotic Use After Hip and Knee Arthroplasty. *J Arthroplasty*. 2018;33(9):2774-2779. <u>d</u> oi:10.1016/j.arth.2018.03.066

58. Bardram L, Funch-Jensen P, Jensen P, Kehlet H, Crawford ME. Recovery after laparoscopic colonic surgery with epidural analgesia, and early oral nutrition and mobilisation. *Lancet*. 1995;345(8952):763-764. <u>doi:10.1016/S0140-6736(9</u> 5)90643-6 59. Kaye A, Urman R, Cornett E, et al. Enhanced recovery pathways in orthopedic surgery. *J Anaesthesiol Clin Pharmacol*. 2019;35(5):35-39. <u>doi:1</u> 0.4103/joacp.JOACP\_35\_18

60. Sharrock NE, Cazan MG, Hargett MJL, Williams-Russo P, Wilson PD. Changes in mortality after total hip and knee arthroplasty over a ten- year period. *Anesth Analg.* 1995;80(2):242-248. doi:10.1097/00000 539-199502000-00008

61. Memtsoudis SG, Fiasconaro M, Soffin EM, et al. Enhanced recovery after surgery components and perioperative outcomes: a nationwide observational study. *Br J Anaesth*. 2020;124(5):638-647. doi:10.101 6/j.bja.2020.01.017

62. Wainwright TW, Gill M, McDonald DA, et al. Consensus statement for perioperative care in total hip replacement and total knee replacement surgery: Enhanced Recovery After Surgery (ERAS R) Society recommendations. *Acta Orthop*. 2020;91(1):3-19. do i:10.1080/17453674.2019.1683790

63. Oppedal K, Møller AM, Pedersen B, Tønnesen H. Preoperative alcohol cessation prior to elective surgery. *Cochrane Database Syst Rev.* 2012;2012(7). do i:10.1002/14651858.CD008343.pub2

64. Basques BA, Toy JO, Bohl DD, Golinvaux NS, Grauer JN. General compared with spinal anesthesia for total hip arthroplasty. *J Bone Jt Surg - Am Vol.* 2015;97(6):455-461. doi:10.2106/JBJS.N.00662

65. Shah R, Kuo YF, Westra J, Lin YL, Raji MA. Opioid Use and Pain Control after Total Hip and Knee Arthroplasty in the US, 2014 to 2017. *JAMA Netw open*. 2020;3(7):e2011972. <u>doi:10.1001/JAMANETWO</u> <u>RKOPEN.2020.11972</u>

66. Elvir-Lazo OL, White PF. The role of multimodal analgesia in pain management after ambulatory surgery. *Curr Opin Anaesthesiol*. 2010;23(6):697-703. doi:10.1097/ACO.0b013e32833fad0a

67. Sinatra RS, Jahr JS, Reynolds LW, Viscusi ER, Groudine SB, Payen-Champenois C. Efficacy and safety of single and repeated administration of 1 gram intravenous acetaminophen injection (paracetamol) for pain management after major orthopedic surgery. *Anesthesiology*. 2005;102(4):822-831. doi:10.1097/00000542-2005040 00-00019

68. Huang YM, Wang CM, Wang CT, Lin WP, Horng LC, Jiang CC. Perioperative celecoxib administration for pain management after total knee arthroplasty - a randomized, controlled study. *BMC Musculoskelet Disord*. 2008;9. <u>doi:10.1186/1471-2474-9-77</u>

69. Chincholkar M. Analgesic mechanisms of gabapentinoids and effects in experimental pain models: a narrative review. *Br J Anaesth*. 2018;120(6):1315-1334. doi:10.1016/j.bja.2018.02.066

70. Han C, Li X dan, Jiang H qiang, Ma J xiong, Ma X long. The use of gabapentin in the management of postoperative pain after total hip arthroplasty: a meta-analysis of randomised controlled trials. *J Orthop Surg Res.* 2016;11(1). doi:10.1186/s13018-01 6-0412-z

71. Goode VM, Morgan B, Muckler VC, Cary MP, Zdeb CE, Zychowicz M. Multimodal Pain Management for Major Joint Replacement Surgery. *Orthop Nurs*. 2019;38(2):150-156. <u>doi:10.1097/NOR.00000000000000000525</u>

72. Wick EC, Grant MC, Wu CL. Postoperativemultimodal analgesia pain management with nonopioid analgesics and techniques a review. *JAMA Surg.* 2017;152(7):691-697. doi:10.1001/jamasurg.2017.0898

73. Memtsoudis SG, Poeran J, Zubizarreta N, et al.
Association of multimodal pain management strategies with perioperative outcomes and resource utilization a population-based study. *Anesthesiology*.
2018;128(5):891-902. doi:10.1097/ALN.00000000000 2132

74. Choi P, Bhandari M, Scott J, Douketis JD, Cracknell J. Epidural analgesia for pain relief following hip or knee replacement. *Cochrane Database Syst Rev.* 2003;2003(3). <u>doi:10.1002/1465185</u> <u>8.CD003071</u>

75. Martin G, Hartmannsgruber M, Riley E, Manvelian G. Single-dose extended-release epidural morphine for pain after hip arthroplasty. *J Opioid Manag.* 2006;2(4):209-218. doi:10.5055/jom.2006.0033

76. Tyagi A, Salhotra R. Total hip arthroplasty and peripheral nerve blocks: limited but salient role? *J Anaesthesiol Clin Pharmacol*. 2018;34(3):379-380. do i:10.4103/joacp.JOACP\_114\_18

77. Nishio S, Fukunishi S, Fukui T, et al. Comparison of continuous femoral nerve block with and without combined sciatic nerve block after total hip arthroplasty: a prospective randomized study. *Orthop Rev (Pavia)*. 2017;9(2). doi:10.4081/or.2017.7063

78. Ueshima H, Hiroshi O. Incidence of lowerextremity muscle weakness after quadratus lumborum block. *J Clin Anesth*. 2018;44:104. <u>doi:10.1</u> 016/J.JCLINANE.2017.11.020 79. Becker P, Bosch J, Smith F. Analgesia after total hip replacement: epidural versus psoas compartment block. *South African J Anaesth Analg*. 2007;13(2):21-25. <u>doi:10.1080/22201173.2007.108724</u> 70

80. Opioid prescription limits and policies by state -Ballotpedia. Accessed August 20, 2021. <u>https://ballot pedia.org/Opioid\_prescription\_limits\_and\_policies\_b</u> <u>y\_state</u>  Pannu TS, Villa JM, Fleites J, Patel PD, Higuera CA, Riesgo AM. Florida State Opioid Prescription Restriction Law: Impact on Opioid Utilization After Total Joint Arthroplasty. *J Arthroplasty*. 2021;36(8):2742-2745. doi:10.1016/j.arth.2021.03.055

82. Chalmers BP, Lebowitz J, Chiu YF, et al. Reduction of Opioid Quantities at Discharge After TKA Did Not Increase the Risk of Manipulation Under Anesthesia: An Institutional Experience. *J Arthroplasty.* 2021;36(7):2307-2312. doi:10.1016/j.arth.2021.02.045