

CADTH Health Technology Review

# Mepivacaine Versus Bupivacaine for Patients Undergoing Total Joint Arthroplasty

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**ISSN:** 2563-6596

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**Funding:** CADTH receives funding from Canada's federal, provincial, and territorial governments, except for Quebec.

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## Table of Contents

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<b>Abbreviations</b> .....	<b>5</b>
<b>Key Messages</b> .....	<b>6</b>
<b>Context and Policy Issues</b> .....	<b>6</b>
<b>Research Questions</b> .....	<b>7</b>
<b>Methods</b> .....	<b>7</b>
Literature Search Methods.....	7
Selection Criteria and Methods .....	7
Exclusion Criteria.....	7
Critical Appraisal of Individual Studies .....	8
<b>Summary of Evidence</b> .....	<b>8</b>
Quantity of Research Available.....	8
Summary of Study Characteristics.....	8
Summary of Critical Appraisal.....	10
Summary of Findings .....	11
<b>Limitations</b> .....	<b>14</b>
<b>Conclusions and Implications for Decision- or Policy-Making</b> .....	<b>15</b>
<b>References</b> .....	<b>17</b>
<b>Appendix 1: Selection of Included Studies</b> .....	<b>18</b>
<b>Appendix 2: Characteristics of Included Publications</b> .....	<b>19</b>
<b>Appendix 3: Critical Appraisal of Included Publications</b> .....	<b>22</b>
<b>Appendix 4: Main Study Findings</b> .....	<b>24</b>

## List of Tables

---

Table 1: Selection Criteria.....	8
Table 2: Characteristics of Included Systematic Review.....	19
Table 3: Characteristics of Included Primary Clinical Studies .....	19
Table 4: Strengths and Limitations of the Systematic Review and Meta-Analysis Using AMSTAR 2 .....	22
Table 5: Strengths and Limitations of Clinical Studies Using the Downs and Black Checklist <sup>13</sup> .....	22
Table 6: Summary of Findings by Outcome – Neurologic Symptoms .....	24
Table 7: Summary of Findings by Outcome – Mobility .....	24
Table 8: Summary of Findings by Outcome – Pain .....	27
Table 9: Summary of Findings by Outcome – Length of Stay .....	29
Table 10: Summary of Findings by Outcome – Urinary Retention .....	30
Table 11: Summary of Findings by Outcome – Additional Clinical Outcomes.....	31
Table 12: Summary of Findings by Outcome – Adverse Events and Safety.....	33

## List of Figures

---

Figure 1: Selection of Included Studies .....	18
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## Abbreviations

<b>AM-PAC</b>	Activity Measure for Post-Acute Care
<b>CI</b>	confidence interval
<b>ED</b>	emergency department
<b>HOOS, JR</b>	Hip disability and Osteoarthritis Outcome Score for Joint Replacement
<b>LOS</b>	length of stay
<b>MA</b>	meta-analysis
<b>OR</b>	odds ratio
<b>RCT</b>	randomized controlled trial
<b>SR</b>	systematic review
<b>THA</b>	total hip arthroplasty
<b>TJA</b>	total joint arthroplasty
<b>TKA</b>	total knee arthroplasty

## Key Messages

- Mepivacaine was found to have statistically significantly better results than bupivacaine for various specific measurements related to neurologic symptoms, mobility, length of stay, urinary retention, and adverse events and safety; however, for the overall evidence, the difference in outcomes between the 2 did not consistently reach the level of statistical significance.
- The overall evidence for postoperative pain largely found no statistically significant difference between mepivacaine and bupivacaine, except for proportion of postoperative zero pain, where mepivacaine resulted in a statistically greater proportion of patients reporting zero pain postoperatively than bupivacaine.
- Evidence was only identified for individuals who received either total hip arthroplasty or total knee arthroplasty, and thus the findings presented in this report may not be generalizable to other total joint reconstruction or replacement surgeries.
- No evidence was identified regarding the cost-effectiveness or evidence-based guidelines for the use of mepivacaine versus bupivacaine for total joint arthroplasty.

## Context and Policy Issues

Total joint arthroplasty (TJA) or total joint replacement is a surgical procedure to restore the function of a joint by removing parts of an arthritic or damaged joint and replacing them with prosthetic materials.<sup>1,2</sup> Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are the 2 most common arthroplasty procedures, but replacement surgery can be performed on other joints including the ankle, wrist, shoulder, and elbow.<sup>1</sup> From 2020 to 2021, approximately 110,000 joint replacement surgeries were performed in Canada, with 55,300 and 55,285 of these surgeries being THA or TKA procedures, respectively.<sup>3</sup> For the previous 10 years, the number of TJA surgeries increased each year in Canada, but the COVID-19 pandemic resulted in 20% fewer surgeries from 2020 to 2021.<sup>3</sup> Recovery after TJA procedures may be painful and can result in limited mobility, depending on the location of the surgery.<sup>2</sup> It is common for patients to stay in hospital for several days post-surgery, and adverse events may prolong total recovery time.<sup>2</sup>

Pain control for TJA is often multimodal and can include perioperative anesthesia, acetaminophen, and nonsteroidal anti-inflammatory drugs.<sup>4</sup> Perioperative anesthesia is important for enhancing recovery pathways to minimize pain, and also offers benefits like early postoperative mobilization and decreased length of stay in hospital.<sup>5</sup> Bupivacaine is a common perioperative anesthesia used in arthroplasty procedures and is indicated for local or regional anesthesia use.<sup>6</sup> Bupivacaine for arthroplasty can be given as a hyperbaric solution or isobaric solution in a spinal administration; the anesthesia onset is rapid (approximately 5 minutes) and has a typical duration of 3 to 9 hours, but can last up to 72 hours.<sup>6,9</sup> Hyperbaric bupivacaine solutions have a greater density than the cerebrospinal fluid, allowing for a quicker onset and shorter duration of motor and sensory block, whereas isobaric bupivacaine solutions have an equal density to the cerebrospinal fluid allowing for a slower onset and longer duration of action.<sup>10</sup> Mepivacaine is another common perioperative anesthesia indicated for local or regional anesthesia use.<sup>11</sup> It has a rapid onset of anesthesia (3 to 20 minutes), and a duration of 2 to 2.5 hours.<sup>11</sup> The more rapid nature of mepivacaine has been reported to translate to quicker postoperative mobilization and shorter length of

stay.<sup>7</sup> It has also been noted that drowsiness and lassitude have not been commonly reported in mepivacaine use, and it has been shown to have preferable tissue compatibility with minimal irritation or tissue damage from administration.<sup>11</sup>

Because mepivacaine use provides more rapid anesthesia, there is question as to whether mepivacaine may be a more appropriate form of anesthetic for TJA than bupivacaine. The aim of the current report is to summarize the evidence regarding the clinical effectiveness, cost-effectiveness, and recommendations from evidence-based guidelines for the use of mepivacaine versus bupivacaine for patients undergoing TJA.

## Research Questions

1. What is the comparative clinical effectiveness of mepivacaine versus bupivacaine for patients undergoing total joint arthroplasty?
2. What is the cost-effectiveness of mepivacaine versus bupivacaine for patients undergoing total joint arthroplasty?
3. What are the evidence-based guidelines for the use of mepivacaine for patients undergoing total joint arthroplasty?

## Methods

### Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International HTA Database, and the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were mepivacaine and joint arthroplasty. No filters were applied to limit the retrieval by study type. Conference abstracts were excluded from the search results. The search was completed on August 8, 2022, and limited to English-language documents published since January 1, 2017.

### Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in [Table 1](#).

### Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in [Table 1](#), they were duplicate publications, or they were published before 2017. Primary studies retrieved by the search were excluded if they were captured in at least 1 included systematic review.

## Critical Appraisal of Individual Studies

The included publications were critically appraised by 1 reviewer using the following tools as a guide: A Measurement Tool to Assess systematic Reviews 2 (AMSTAR 2)<sup>12</sup> for systematic reviews and the Downs and Black checklist<sup>13</sup> for randomized and non-randomized studies. Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

## Summary of Evidence

### Quantity of Research Available

A total of 50 citations were identified in the literature search. Following screening of titles and abstracts, 35 citations were excluded and 15 potentially relevant reports from the electronic search were retrieved for full-text review. One potentially relevant publication was retrieved from the grey literature search for full-text review. Of the 16 potentially relevant articles, 13 publications were excluded for various reasons, and 3 publications met the inclusion criteria and were included in this report. These comprised 1 systematic review (SR) with meta-analysis (MA) and 2 non-randomized studies. Appendix 1 presents the PRISMA<sup>14</sup> flow chart of the study selection.

### Summary of Study Characteristics

One SR with MA<sup>15</sup> and 2 non-randomized studies<sup>9,10</sup> were included in this report.

Additional details regarding the characteristics of included publications are provided in [Appendix 2](#).

**Table 1: Selection Criteria**

Criteria	Description
Population	Patients undergoing total joint arthroplasty
Intervention	Mepivacaine
Comparator	Q1 and Q2: Bupivacaine Q3: Not applicable
Outcomes	Q1: Clinical effectiveness (e.g., postoperative pain, postoperative length of stay, opioid use, return of motor function, safety [e.g., adverse events]) Q2: Cost-effectiveness (e.g., cost per quality-adjusted life-year gained, incremental cost-effectiveness ratios) Q3: Recommendations regarding the administration and use of mepivacaine
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines

Q = question.



## Study Design

The SR by Siddiqi et al. (2022)<sup>15</sup> included 3 randomized controlled trials (RCTs) and 2 retrospective cohort studies in the MA. The search for relevant studies had no restrictions on time frame, but the included primary studies were published between 2018 and 2020.

Two non-randomized studies included in this report were published in 2022<sup>10</sup> and 2021.<sup>9</sup> Both were retrospective cohort studies. One retrospective cohort study did not report follow-up findings after discharge, while 1 retrospective cohort study included follow-up times of 2 weeks, 6 weeks, and 3 months for applicable outcomes.<sup>9</sup>

## Country of Origin

The SR<sup>15</sup> and 2 retrospective cohort studies<sup>9,10</sup> were conducted in the US.

## Patient Population

The primary studies in the SR included patients who received spinal anesthesia for THA or TKA, with a total number of 1,550 patients included in the review.<sup>15</sup> The primary studies of the SR either reported on both THA and TKA (1 RCT and 1 non-randomized study), only THA (1 RCT), or only TKA (1 RCT and 1 non-randomized study).<sup>15</sup>

One retrospective cohort study<sup>10</sup> included patient data from 1,328 patients who underwent primary unilateral THA or TKA with spinal anesthesia performed at either an acute care hospital or affiliated ambulatory surgery centre from September 2020 to September 2021. The second retrospective cohort study<sup>9</sup> included 141 patients who received spinal anesthesia for anterior approach THA from an ambulatory surgery centre between November 2018 and July 2020.

## Interventions and Comparators

The primary studies of the SR<sup>15</sup> compared mepivacaine and bupivacaine for spinal anesthesia in THA and TKA. The range of doses for 4 primary studies was 52.5 mg to 70 mg, and 10 mg to 12.5 mg, for mepivacaine and bupivacaine, respectively.<sup>15</sup> Doses for 1 primary study were not reported. In addition, the number of patients that received mepivacaine and bupivacaine for each primary study ranged from 15 to 563 and 16 to 491, respectively.<sup>15</sup>

One retrospective cohort study<sup>10</sup> compared mepivacaine and hyperbaric or isobaric bupivacaine. The mean dose and standard deviation for THA patients that received mepivacaine, hyperbaric bupivacaine, or isobaric bupivacaine was 63.4 ( $\pm$  75.3) mg, 10.9 ( $\pm$  1.7) mg, and 12.7 ( $\pm$  2.1) mg, respectively.<sup>10</sup> The mean dose and standard deviation for TKA patients that received mepivacaine, hyperbaric bupivacaine, or isobaric bupivacaine was 65.2 ( $\pm$  54.5) mg, 10.7 ( $\pm$  1.6) mg, and 11.0 ( $\pm$  2.4) mg, respectively.<sup>10</sup> The second retrospective cohort study<sup>9</sup> compared 2% mepivacaine (40 to 60 mg) to 0.75% hyperbaric bupivacaine (10.5 mg to 15 mg) for spinal anesthesia in THA.

## Outcomes

The SR<sup>15</sup> assessed surgical outcomes related to time of full neurologic motor return, pain levels, mobility, postoperative length of stay in hospital (LOS), and complications, including transient neurologic symptoms and urinary retention.

One retrospective cohort study<sup>10</sup> assessed LOS in days, postoperative day 0 ambulation, failed same-day discharge attempt, first mobility using the Activity Measure for Post-Acute Care

(AM-PAC) 6-Clicks mobility score,<sup>16</sup> first physical therapy documented ambulation distance, urinary retention, home discharge, 30-day readmission, and 30-day emergency department (ED) return. The second retrospective cohort study<sup>9</sup> assessed time in each phase of care, pain scores (0 to 10 scale), pain medication received, time to ambulation, ambulation distance, time to controlled void, bethanechol doses, and postoperative nausea or vomiting. In addition, the second retrospective cohort study<sup>9</sup> assessed pain (visual analogue scale) and Hip disability and Osteoarthritis Outcome Score for Joint Replacement (HOOS, JR) scores at 2 weeks, 6 weeks, and 3 months; and 90-day postoperative outcomes, including complications, ED visits, hospital readmissions, and reoperations.

### Summary of Critical Appraisal

The SR<sup>15</sup> clearly described the objective and provided details related to the literature search strategy, including time frame of the search, study designs included, and search terms applied, which allows for potential reproducibility for this review. The authors of the SR<sup>15</sup> also indicated that manual screening of bibliographic references was done to identify any potentially relevant studies. The authors did not state if a research protocol was established before conducting the SR, which may make it challenging to determine if appropriate and reliable methods were followed to produce the findings of this study. It is unclear if literature screening, study selection, or data extraction was performed in duplicate, to minimize potential errors for study selection and data extraction. It was stated that risk of bias assessments for included primary studies was performed in duplicate using the Cochrane Collaboration Tool for RCTs and A Cochrane Risk of Bias Assessment Tool: for Non-Randomized Studies of Interventions. Each included study was reported to have a low risk of bias. Duplicate assessments may reduce missing or erroneous information in determining the risk of bias. The authors of this review did not provide a list of excluded studies, reasons for exclusion, and information related to funding for primary studies that were included in the review. Without this information, it is difficult to determine if relevant studies have been excluded, leading to increased risk of selection bias, or if there was a potential risk to editorial independence due to funding sources. Limited details of the study characteristics of the included studies were presented, which included information related to study year, design, population, intervention, comparison, dosing, results, and limitations. The authors of this review used appropriate methods for statistical analysis based on the Cochrane Handbook for Systematic Review of Interventions. They assessed heterogeneity using  $I^2$  statistics and Cochrane chi-square tests, and considered heterogeneity in the discussion of results for each reported outcome. This is helpful to interpret the reliability of results across studies. The MA compared results from both RCTs and non-randomized studies, but the author did not discuss how results should be interpreted due to the variation in study design. Given the reported low risk of bias of the included studies, no assessment of potential impact of risk of bias on the results of the MA was conducted. Finally, though the authors provided a conflict-of-interest declaration, they did not report funding information for this study.

The objective, main outcome, patient characteristics, and interventions received were clearly described in both retrospective cohort studies.<sup>9,10</sup> One retrospective cohort study<sup>10</sup> described principal confounders and used multivariate linear and regression models to compare outcomes while controlling for confounders. The other retrospective cohort study<sup>9</sup> did not adequately describe principal confounders or control for confounders, but the authors noted that any confounding factors were unlikely to be significant. Because confounding factors were not controlled for, it is unclear if the reported finding could be solely attributed to the interventions used. One retrospective cohort study<sup>10</sup> did not adequately report details

regarding included patients, if patient data were obtained from the same population, and the reasons for excluding patients, which may create concern over selection bias and impact generalizability of findings. The other retrospective cohort study<sup>9</sup> did provide details related to patient recruitment and data use, and stated that patient data were drawn from the same population group at a single institution from 2018 to 2020. The study population appeared to be representative of the entire population from which they were recruited, and a justification was given for excluding any patient data. The main findings from both retrospective cohort studies<sup>9,10</sup> were clearly described and included appropriate estimates of variability where applicable. Actual P values were also reported for both retrospective cohort studies, except where the P value was less than 0.001.<sup>9,10</sup> Appropriate statistical analyses were used in both retrospective cohort studies for dichotomous, continuous, and multiple variables.<sup>9,10</sup> In addition, 1 retrospective cohort study<sup>10</sup> provided a subgroup analysis for same-day discharge groups and risk-adjust analysis to control for principal confounders. Providing appropriate statistical analyses helps determine accurate interpretation for main findings. Both retrospective cohort studies lack the randomization effect of RCTs to balance confounding factors across study groups and reduce associated risk of bias.<sup>9,10</sup> Finally, both retrospective cohort studies reported that no funding was received to conduct their study.<sup>9,10</sup> One retrospective cohort study<sup>10</sup> reported no conflict of interest, while the other retrospective cohort study<sup>9</sup> did declare potential conflicts of interest, and it appeared unlikely that funding and other interest inappropriately influenced the outcomes and interpretation of findings in either study.

Additional details regarding the strengths and limitations of included publications are provided in [Appendix 3](#).

## Summary of Findings

[Appendix 4](#) presents the main study findings of the SR<sup>15</sup> and 2 retrospective cohort studies.<sup>9,10</sup> The findings are presented by main outcomes, which are neurologic symptoms ([Table 6](#)), mobility ([Table 7](#)), pain ([Table 8](#)), LOS ([Table 9](#)), urinary retention ([Table 10](#)), additional clinical outcomes ([Table 11](#)), and adverse events and safety ([Table 12](#)).

### Clinical Effectiveness of Mepivacaine Versus Bupivacaine for Patients Undergoing TJA

One SR<sup>15</sup> and 2 retrospective cohort studies<sup>9,10</sup> were found regarding the clinical effectiveness of mepivacaine versus bupivacaine for patients undergoing TJA.

#### *Neurologic Symptoms*

The SR<sup>15</sup> identified 3 studies that compared the time to postoperative motor function return for mepivacaine versus bupivacaine spinal anesthesia. The pooled overall effect for time to postoperative motor function return significantly favoured mepivacaine (154 minutes) compared to bupivacaine (170 minutes) with a mean difference of -27.34 (95% confidence interval [CI], -41.12 to -13.56; P = 0.0472; I<sup>2</sup> = 0%).<sup>15</sup> The SR<sup>15</sup> also identified transient neurologic symptoms (defined as pain or abnormal sensation in the lower back, buttocks, and lower extremities) from 1 included study that reported transient neurologic symptoms in 10%, 11.3%, and 3.9% of patients treated with mepivacaine, hyperbaric bupivacaine, and isobaric bupivacaine, respectively. The difference between the groups was not statistically significant (P = 0.36).<sup>15</sup> One retrospective cohort study<sup>9</sup> reported that transient neurologic symptoms occurred in 2 patients who received bupivacaine versus none among those who received mepivacaine (P = 0.489).

### **Mobility**

Four studies in the SR<sup>15</sup> reported outcomes for mobilization distance on postoperative day 0, while 3 studies reported outcome for mobilization distance on postoperative day 1. Combined early mobilization for postoperative day 0 and day 1 was shown to be greater for the patients who received mepivacaine (94.2 ft) compared to patients who received bupivacaine (89.1 ft), with a mean difference of 5.1 ft (95% CI, -15 to 25.2).<sup>15</sup> This difference was not statistically significant ( $P = 0.61$ ) and the heterogeneity among studies was significant ( $I^2 = 54\%$ ).<sup>15</sup> One retrospective cohort study<sup>9</sup> reported ambulation distances in postoperative recovery room for recipients of mepivacaine and bupivacaine. Mepivacaine recipients had a greater average ambulation distance (69 ft) compared to bupivacaine recipients (64.4 ft); however, this difference was not statistically significant ( $P = 0.611$ ).

One retrospective cohort study<sup>10</sup> reported the number of patients ambulated on postoperative day 0. The authors found that patients who received mepivacaine were more likely to be ambulated on postoperative day 0 compared to patients who received bupivacaine, for both THA and TKA procedures ( $P < 0.001$  in each comparison). Mepivacaine still showed a greater likelihood than bupivacaine of patients ambulated on postoperative day 0, with an odds ratio (OR) of 2.391 (95% CI, 1.789 to 3.197;  $P < 0.001$ ) after controlling for confounding factors.<sup>10</sup> The authors also found significant differences in both THA and TKA procedures for first physical therapy ambulation distance for those who received mepivacaine compared to bupivacaine ( $P < 0.001$ ).<sup>10</sup> However, a subgroup analysis of same-day discharge patients did not find a statistically significant difference between mepivacaine and bupivacaine for first physical therapy ambulation distance, following either THA ( $P = 0.144$ ) or TKA ( $P = 0.757$ ).<sup>10</sup> When controlling for confounding factors, patients who received mepivacaine had a greater first physical therapy ambulation distance with an OR of 21.785 (95% CI, 10.459 to 33.111;  $P < 0.001$ ) compared to those who received bupivacaine.<sup>10</sup> This retrospective cohort study<sup>10</sup> also assessed AM-PAC 6-Clicks mobility scores and found that mepivacaine recipients and hyperbaric bupivacaine recipients has statistically significantly higher scores compared to isobaric bupivacaine recipients for those who underwent THA ( $P = 0.003$ ), but not for those who underwent TKA ( $P = 0.607$ ). A subgroup analysis for patients discharged the same day of procedure found that mepivacaine recipients had higher AM-PAC 6 Click mobility scores for both THA and TKA ( $P < 0.001$  in each comparison).<sup>10</sup> However, the difference between mepivacaine and bupivacaine for this outcome was not statistically significant after controlling for confounding factors ( $P = 0.192$ ).<sup>10</sup>

One retrospective cohort study<sup>9</sup> compared time to postoperative mobilization outcomes between mepivacaine and bupivacaine. No significant difference was found for the number of hours to ankle plantar or dorsiflexion ( $P = 0.502$ ). However, mepivacaine recipients had a significant decrease in number of hours to sitting up ( $P < 0.001$ ) and number of hours to ambulation ( $P < 0.001$ ) compared to bupivacaine.<sup>9</sup>

### **Pain**

Three studies in the SR<sup>15</sup> reported on pain scores on postoperative day 0, while 4 studies reported on pain scores on postoperative day 1. Combined pain scores during the early postoperative period showed lower average pain scores for those who received mepivacaine (3.57) compared to those who received bupivacaine (3.68), with a mean difference of -0.1 (95% CI, -2.1 to 1.9).<sup>15</sup> The difference was not statistically significant ( $P = 0.91$ ), and no heterogeneity was detected between the studies for this assessment ( $I^2 = 0$ ). One retrospective cohort study<sup>9</sup> reported postoperative pain outcomes from immediately after up to 5 hours after procedure, and found that bupivacaine recipients reported significantly

lower postoperative pain scores at 1 hour ( $P < 0.001$ ), 2 hours ( $P < 0.001$ ), and 3 hours ( $P = 0.003$ ) compared to mepivacaine recipients. Additionally, the authors reported outcomes for the proportion of patients who experienced zero pain immediately postoperative, up to 5 hours postoperative. The authors found that a significantly larger proportion of mepivacaine recipients reported zero postoperative pain at 1 hour ( $P = 0.010$ ), 2 hours ( $P < 0.001$ ), 3 hours ( $P = 0.006$ ), 4 hours ( $P < 0.001$ ), and 5 hours ( $P = 0.043$ ) compared to bupivacaine recipients.<sup>9</sup> There was no significant difference in postoperative pain scores for those who received mepivacaine or bupivacaine at 2 weeks ( $P = 0.308$ ), 6 weeks ( $P = 0.386$ ), or 3 months ( $P = 0.575$ ).<sup>9</sup> Mepivacaine recipients reported significantly higher pain scores at discharge compared to bupivacaine recipients ( $P = 0.004$ ), and postoperative pain medication use was significantly higher in mepivacaine recipients compared to bupivacaine recipients ( $P < 0.001$ ).<sup>9</sup>

### ***Length of Stay***

Three studies in the SR<sup>15</sup> reported on overall LOS and found that mepivacaine recipients had a significantly lower mean LOS of 25.95 hours, compared to a mean LOS of 29.96 hours for bupivacaine recipients. The mean difference in overall LOS was  $-7.03$  hours (95% CI,  $-10.02$  to  $-4.04$ ;  $P = 0.0057$ ); however, the between-studies heterogeneity was high for this assessment ( $I^2 = 53\%$ ).<sup>15</sup> One retrospective cohort study<sup>10</sup> reported that those who received mepivacaine showed significantly lower LOS days compared to those who received bupivacaine for both THA ( $P < 0.001$ ) and TKA ( $P < 0.001$ ) procedures. When controlling for confounders, LOS was significantly lower for those who received mepivacaine compared to those who received bupivacaine (OR =  $-0.421$ ; 95% CI,  $-0.502$  to  $-0.330$ ;  $P < 0.001$ ).<sup>10</sup> In addition, the authors of this retrospective cohort study<sup>10</sup> reported significantly higher numbers of 0-day LOS for those who received mepivacaine compared to those who received bupivacaine for both THA ( $P < 0.001$ ) and TKA ( $P < 0.001$ ) procedures. When controlling for confounding factors, those who received mepivacaine had higher odds of 0-day LOS, with an OR of 5.767 (95% CI, 4.357 to 7.634;  $P < 0.001$ ).<sup>10</sup> One retrospective cohort study<sup>9</sup> reported the time spent in each ambulatory phase while in hospital and found a significantly lower number of hours for mepivacaine recipients in the postoperative phase ( $P < 0.001$ ) and total facility time ( $P < 0.001$ ) compared to bupivacaine recipients.

### ***Urinary Retention***

Five studies in the SR<sup>15</sup> found that the incidence of postoperative urinary retention was significantly lower in those who received mepivacaine compared to those who received bupivacaine ( $P = 0.0181$ ); however, there was moderate heterogeneity among studies reporting urinary retention as a postoperative complication ( $I^2 = 49\%$ ). One retrospective cohort study<sup>10</sup> reported no significant difference in the rates of urinary retention for mepivacaine recipients compared to bupivacaine recipients, for both THA ( $P = 0.097$ ) and TKA ( $P = 0.734$ ) procedures. Controlling for confounding factors, this did not change the statistical significance in the difference between mepivacaine and bupivacaine for this outcome ( $P = 0.452$ ).<sup>10</sup> Finally, 1 retrospective cohort study<sup>9</sup> reported a significantly lower number of hours to controlled void for mepivacaine recipients compared to bupivacaine recipients ( $P < 0.001$ ), and the number of patients who required bethanechol doses (used to manage voiding) was significantly lower with mepivacaine than with bupivacaine ( $P < 0.001$ ).

### ***Additional Clinical Outcomes***

One retrospective cohort study<sup>10</sup> found that significantly more patients who underwent THA and received mepivacaine were discharged to their homes compared to those who received bupivacaine ( $P = 0.001$ ). No significant difference was observed for patients who underwent TKA and received either mepivacaine or bupivacaine ( $P = 0.106$ ).<sup>10</sup> When controlling for

confounding factors, patients who received mepivacaine were more likely to be discharged home with an OR of 6.537 (95% CI, 1.540 to 27.743;  $P = 0.011$ ) compared to patients who received bupivacaine.<sup>10</sup>

One retrospective cohort study<sup>9</sup> found no significant difference between mepivacaine and bupivacaine in HOOS, JR scores, which measured hip disability and osteoarthritis outcomes for patients at 2 weeks ( $P = 0.990$ ), 6 weeks ( $P = 0.704$ ), and 3 months ( $P = 0.604$ ) postoperative.

### ***Adverse Events and Safety***

One retrospective cohort study<sup>10</sup> reported on the number of failed same-day discharge attempts between mepivacaine recipients compared to bupivacaine recipients and found no significant difference for both THA ( $P = 0.334$ ) and TKA ( $P = 0.449$ ) procedures. Similarly, when controlling for confounding factors, this difference between mepivacaine and bupivacaine for failed same-day discharge attempts was not statistically significant (OR = 0.801; 95% CI, 0.458 to 1.400;  $P = 0.436$ ).<sup>10</sup> The same retrospective cohort study<sup>10</sup> reported that mepivacaine recipients had a significantly lower 30-day readmissions rate than bupivacaine recipients for TKA ( $P = 0.008$ ), but not for THA ( $P = 0.699$ ).<sup>10</sup> The odds of a 30-day readmission was not significantly different in mepivacaine versus bupivacaine recipients after controlling for confounding factors (OR = 0.494; 95% CI, 0.226 to 1.083;  $P = 0.078$ ).<sup>10</sup> No significant difference was found for mepivacaine recipients compared to bupivacaine recipients for 30-day ED returns in either THA ( $P = 0.305$ ) or TKA ( $P = 0.599$ ) cohorts.<sup>10</sup> The odds of 30-day ED returns was not significantly different between mepivacaine and bupivacaine recipients after adjusting for confounding factors (OR = 1.068; 95% CI, 0.552 to 2.067;  $P = 0.845$ ).<sup>10</sup>

One retrospective cohort study<sup>9</sup> reported on 90-day adverse events between mepivacaine recipients and bupivacaine recipients and found no difference between total complications ( $P = 1.00$ ), ED visits ( $P = 1.00$ ), hospital admissions ( $P = 1.00$ ), and reoperations ( $P = 1.00$ ). In addition, the retrospective cohort study<sup>9</sup> found no statistically significant difference between mepivacaine and bupivacaine recipients in the incidence of postoperative nausea or vomiting ( $P = 0.223$ ) and hypotension requiring treatment ( $P = 0.153$ ).<sup>9</sup>

### **Cost-Effectiveness of Mepivacaine Versus Bupivacaine for Patients Undergoing TJA**

No evidence was identified regarding the cost-effectiveness of mepivacaine versus bupivacaine for patients undergoing TJA; therefore, no summary can be provided.

### **Guidelines Regarding the Use of Mepivacaine Versus Bupivacaine for Patients Undergoing TJA**

No evidence-based guidelines were identified regarding the use of mepivacaine for patients undergoing TJA; therefore, no summary can be provided.

## **Limitations**

The main limitations were related to the generalizability and applicability of the findings. The SR<sup>15</sup> reported findings for combined surgical outcomes, which included data from patients

who underwent THA or TKA, but the authors did not provide a subgroup analysis for surgical outcomes related only to THA or TKA. This may be a concern for accurately interpreting findings and may impact generalizability depending on the arthroplasty procedure (e.g., findings for patients who only received THA may not be applicable to those who received TKA or may undergo another form of TJA). In addition, the authors reported considerable heterogeneity for mobility, LOS, and urinary retention outcomes, but did not provide details on how heterogeneity may impact findings for these outcomes.<sup>15</sup> These limitations should be considered when interpreting findings drawn from the SR.

Although many outcomes (e.g., neurologic symptoms, mobility, pain, LOS, urinary retention, and adverse events and safety) were reported across multiple studies, there was a high degree of heterogeneity for the methods used to collect relevant outcome data, making it challenging to compare outcomes across the studies.

The included studies were all conducted in the US and therefore it is unclear how generalizable these findings may be to the Canadian context. In addition, this report could not identify evidence related to the cost-effectiveness of mepivacaine versus bupivacaine for patients undergoing TJA, or evidence-based guidelines providing recommendations regarding the use of mepivacaine versus bupivacaine for patients undergoing TJA.

## Conclusions and Implications for Decision- or Policy-Making

This report identified 1 SR with MA<sup>15</sup> and 2 retrospective cohort studies<sup>9,10</sup> regarding the clinical effectiveness of mepivacaine versus bupivacaine for patients undergoing TJA.

The included studies provided findings for a variety of clinical outcomes regarding the use of mepivacaine compared to bupivacaine spinal anesthesia. These outcomes were found in similar populations, being adults who underwent either THA or TKA. Overall, some clinical evidence regarding the use of mepivacaine versus bupivacaine for patients undergoing TJA was identified that may be in favour of mepivacaine, depending on the outcome being measured. Patients who received mepivacaine for THA or TKA were shown to have significantly better neurologic symptom outcomes for postoperative motor function return.<sup>15</sup> Mepivacaine recipients showed significantly better mobility outcomes for being ambulated on postoperative day 0,<sup>10</sup> first physical therapy ambulation distance,<sup>10</sup> AM-PAC 6-Clicks mobility scores for those who underwent THA,<sup>10</sup> number of hours to sitting up,<sup>9</sup> and number of hours to ambulation.<sup>9</sup> Mepivacaine recipients showed significantly better pain outcomes when assessing zero postoperative pain at 1, 2, 3, 4, and 5 hours;<sup>9</sup> however, no significant difference was found for combined pain scores during the early postoperative period.<sup>15</sup> For those who did report having postoperative pain, bupivacaine was found to have significantly better outcomes for postoperative pain at 1, 2, and 3 hours.<sup>9</sup> Mepivacaine recipients were shown to have significantly better outcomes for overall LOS,<sup>15</sup> LOS days,<sup>10</sup> 0-day LOS,<sup>10</sup> hours in postoperative phase,<sup>9</sup> and total facility time.<sup>9</sup> Mepivacaine recipients were shown to have significantly better urinary retention outcomes for number of urinary events,<sup>15</sup> number of hours to controlled void,<sup>9</sup> and number of patients who required bethanechol doses.<sup>9</sup> Mepivacaine recipients were shown to have significantly better outcomes for home discharge outcomes when controlling for confounding factors.<sup>10</sup> Mepivacaine recipients were shown



to have significantly better 30-day readmission outcomes for patients who underwent TKA<sup>10</sup>; however, no difference was found for failed same-day discharge attempts,<sup>10</sup> 30-day readmissions when controlling for confounding factors,<sup>10</sup> 30-day ED returns,<sup>10</sup> 90-day adverse events,<sup>9</sup> postoperative nausea or vomiting,<sup>9</sup> and hypotension requiring treatment.<sup>9</sup>

These findings are based on reported outcomes found in the identified studies and should be interpreted with considerations for their methodological limitations and heterogeneity of outcome measurements. Given that the findings of these studies are only related to patients who have received either THA or TKA, the generalizability of the results for other TJA procedures is unknown. Patient satisfaction or quality of life measurements were not captured in any of the identified studies. Despite these concerns, the studies identified do provide multiple findings for major clinical outcomes related to neurologic symptoms, mobility, pain, LOS, urinary retention, and adverse events and safety that should be considered for future decisions around the use of mepivacaine. Future high-quality studies that also evaluate other forms of TJA, patient satisfaction with mepivacaine or bupivacaine, and changes in health-related quality of life would help stakeholders' decisions concerning the use of either for TJA procedures. In addition, evidence on the cost-effectiveness and evidence-based recommendations for using mepivacaine versus bupivacaine in TJA are needed to inform treatment selection decisions for optimal patient outcomes.

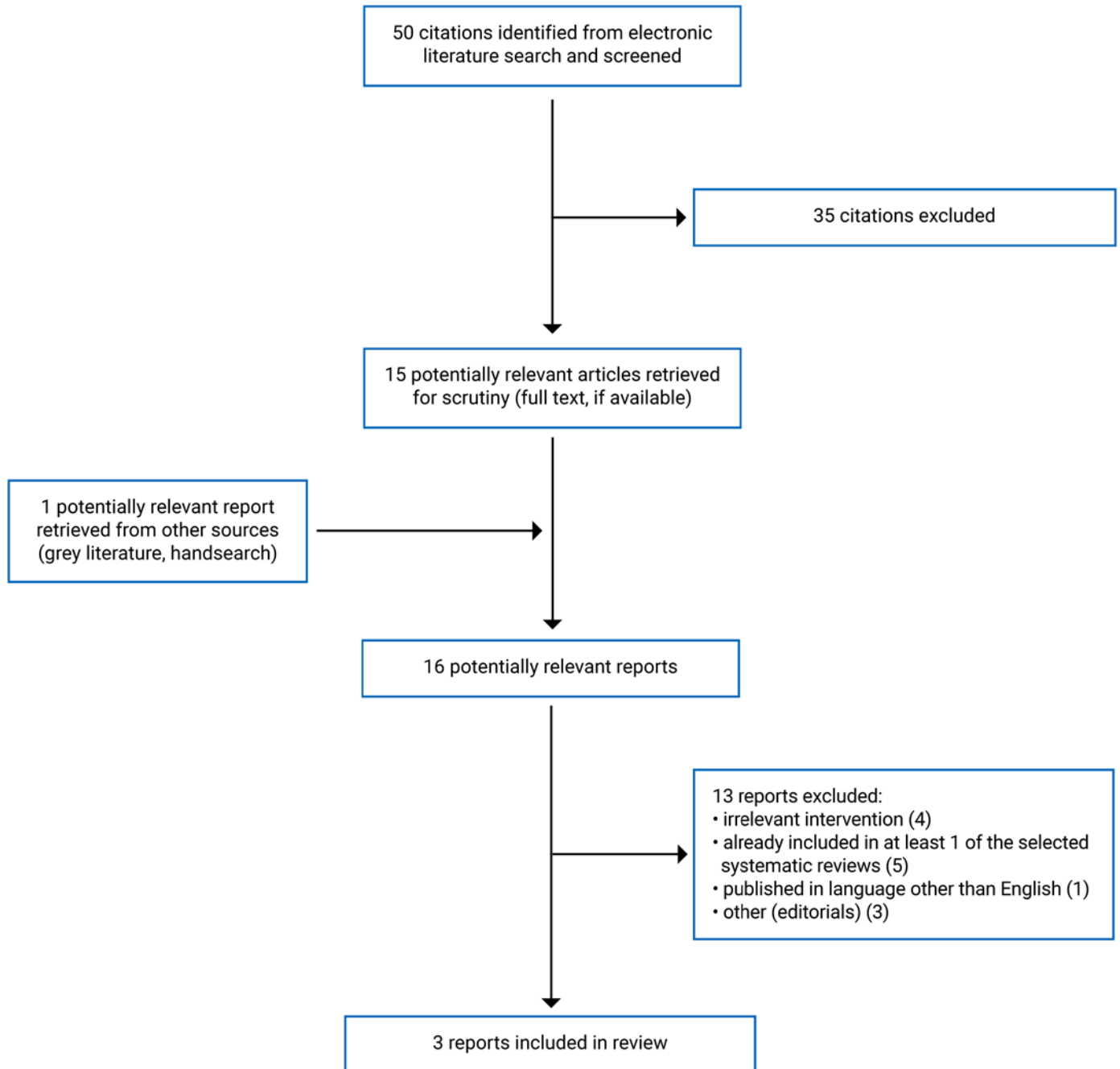


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## Appendix 1: Selection of Included Studies

Figure 1: Selection of Included Studies



## Appendix 2: Characteristics of Included Publications

Note that this appendix has not been copy-edited.

**Table 2: Characteristics of Included Systematic Review**

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics for included primary studies	Intervention and comparator	Clinical outcomes, length of follow-up
Siddiqi et al. (2022) <sup>15</sup> US Funding source: NR	<b>Number of included studies:</b> 5 (3 RCTs and 2 non-randomized studies)	<b>Eligibility criteria:</b> Patients who received spinal anesthesia for THA or TKA <b>Total number of patients included:</b> 1550 <b>Sample size (range):</b> 31 to 1054	<b>Intervention (dosage range):</b> Mepivacaine (52.5 mg to 70 mg) <sup>a</sup> <b>Comparator (dosage range):</b> Bupivacaine (10 mg to 12 mg) <sup>a</sup>	<b>Outcomes:</b> <ul style="list-style-type: none"> <li>• neurologic motor return</li> <li>• mobility</li> <li>• pain</li> <li>• length of stay</li> <li>• urinary retention</li> <li>• transient neurologic symptoms</li> </ul> <b>Follow-up:</b> Follow-up details NR for included studies

mg = milligram; NR = not reported; RCT = randomized controlled trial; THA = total hip arthroplasty; TKA = total knee arthroplasty.

<sup>a</sup>One included study did not provide dosages for intervention or comparator.

**Table 3: Characteristics of Included Primary Clinical Studies**

Study citation, country, funding source	Study design, setting, number of patients included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Stock et al. (2022) <sup>10</sup> US Funding source: No funding	<b>Study design:</b> Retrospective cohort study <b>Setting:</b> Joint Replacement Centre <b>N = 1328</b>	<b>Eligibility criteria:</b> Patients who received spinal anesthesia for primary unilateral THA or TKA from September 2020 to September 2021 <b>Number of patients in each TJA cohort:</b> <ul style="list-style-type: none"> <li>• THA mepivacaine = 232</li> <li>• THA hyperbaric bupivacaine = 401</li> <li>• THA isobaric bupivacaine = 34</li> <li>• TKA mepivacaine = 131</li> <li>• TKA hyperbaric bupivacaine = 502</li> </ul>	<b>Intervention (mean dose for THA and TKA):</b> Mepivacaine (63.4 mg; 65.2 mg) <b>Comparator (mean dose for THA and TKA):</b> <ul style="list-style-type: none"> <li>• Hyperbaric bupivacaine (10.9 mg; 10.7 mg)</li> <li>• Isobaric bupivacaine (12.7 mg; 11.0 mg)</li> </ul>	<b>Outcomes:</b> <ul style="list-style-type: none"> <li>• 0-day length of stay</li> <li>• length of stay days</li> <li>• postoperative day 0 ambulation</li> <li>• failed same-day discharge attempt</li> <li>• first AM-PAC 6-Clicks mobility score</li> <li>• the first physical therapy documented ambulation distance</li> <li>• urinary retention</li> <li>• home discharge</li> <li>• 30-day readmission</li> <li>• 30-day ED return</li> </ul> <b>Follow-up:</b> NA

Study citation, country, funding source	Study design, setting, number of patients included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
		<ul style="list-style-type: none"> <li>TKA isobaric bupivacaine = 28</li> </ul> <p><b>Mean age (SD):</b></p> <ul style="list-style-type: none"> <li>THA mepivacaine = 63.2 (9.6)</li> <li>THA hyperbaric bupivacaine = 66.7 (11.4)</li> <li>THA isobaric bupivacaine = 65.3 (12.)</li> <li>TKA mepivacaine = 66.1 (8.5)</li> <li>TKA hyperbaric bupivacaine = 68.9 (8.3)</li> <li>TKA isobaric bupivacaine = 68.9 (8.2)</li> </ul>		
<p>Calkins et al. (2021)<sup>9</sup> US <b>Funding source:</b> No funding</p>	<p><b>Study design:</b> Retrospective cohort study <b>Setting:</b> Ambulatory surgery centre <b>N = 282</b></p>	<p><b>Eligibility criteria:</b> Patients who received spinal anesthesia for anterior approach THA between November 2018 and July 2020</p> <p><b>Mean age (SD):</b></p> <ul style="list-style-type: none"> <li>Mepivacaine = 56.2 (8.8)</li> <li>Bupivacaine = 55.2 (8.6)</li> </ul> <p><b>Number of females (%):</b></p> <ul style="list-style-type: none"> <li>Mepivacaine = 57 (40.4)</li> <li>Bupivacaine = 55.2 (8.6)</li> </ul>	<p><b>Intervention (dosage):</b> Mepivacaine (40 mg to 60 mg) <b>Comparator (dosage):</b> Hyperbaric bupivacaine (10.5 mg to 15 mg)</p>	<p><b>Outcomes:</b></p> <ul style="list-style-type: none"> <li>time spent in phases of ambulatory care</li> <li>pain scores</li> <li>pain medications received in morphine equivalent doses</li> <li>time to ambulation</li> <li>ambulation distance</li> <li>time to controlled void</li> <li>bethanechol doses</li> <li>PONV</li> <li>complications</li> <li>90-day postoperative outcomes</li> </ul> <p><b>Follow-up:</b></p> <ul style="list-style-type: none"> <li>2 weeks, 6 weeks, and 3 months for pain and HOOS Jr outcomes</li> <li>90-day complications, ED visits, hospital</li> </ul>

Study citation, country, funding source	Study design, setting, number of patients included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
				admissions, and reoperations

AM-PAC = Activity Measure for Post-Acute Care; ED = emergency department; HOOS, JR = Hip Disability and Osteoarthritis Outcome Score for Joint Replacement; mg = milligram; NA = not applicable; PONV = postoperative nausea/vomiting; SD = standard deviation; THA = total hip arthroplasty; TJA = total joint arthroplasty; TKA = total knee arthroplasty.

## Appendix 3: Critical Appraisal of Included Publications

Note that this appendix has not been copy-edited.

**Table 4: Strengths and Limitations of the Systematic Review and Meta-Analysis Using AMSTAR 2<sup>12</sup>**

Strengths	Limitations
<b>Siddiqi et al. (2022)<sup>15</sup></b>	
<ul style="list-style-type: none"> <li>• The objective of the review was clearly described.</li> <li>• Multiple databases were searched, including manual screening of bibliographic references, and search terms were provided.</li> <li>• There were no restrictions on time frame or study design of primary studies included in the review.</li> <li>• Details regarding study year, design, population, intervention, comparator, dosing, results, and limitations were provided for each included study.</li> <li>• Risk of bias was assessed in duplicate for all individual studies using the Cochrane Collaboration Tool for RCTs and A Cochrane Risk of Bias Assessment Tool: for Non-Randomized Studies of Interventions for non-randomized studies.</li> <li>• Appropriate methods were used for statistical combination of results based on the Cochrane Handbook for Systematic Reviews of Interventions. Unpaired t-tests using summary data were used to compare outcomes across individual studies.</li> <li>• All included studies were reported to have low risk of bias, and therefore assessment of potential impact of risk of bias in individual studies on the results of the meta-analysis was not performed.</li> <li>• Heterogeneity was assessed using <math>I^2</math> statistic and Cochrane chi-square test. Heterogeneity was included in the discussion of results for each reported outcome.</li> <li>• The review authors declared conflicts of interest.</li> </ul>	<ul style="list-style-type: none"> <li>• The research questions and inclusion criteria were not outlined or did not include any PICO components.</li> <li>• No statement was provided to indicate that review methods were established prior to conducting the review.</li> <li>• The reviewer authors did not provide a clear explanation for their selection of study designs for inclusion in the reviews.</li> <li>• It is unclear if screening, study selection and data extraction was done in duplicate.</li> <li>• A list of excluded studies and reason for exclusion was not provided.</li> <li>• Publication bias was not discussed which may be a concern for interpreting the impact of study results.</li> <li>• The review authors did not provide information related to funding received for the systematic review or its included primary studies, which may be a concern for determining potential external influence.</li> <li>• The meta-analysis included both randomized and non-randomized studies for comparison, which may impact the ability to properly interpret findings.</li> </ul>

AMSTAR 2 = A Measurement Tool to Assess Systematic Reviews 2; PICO = patients, interventions, comparators, and outcomes; RCT = randomized controlled trial.

**Table 5: Strengths and Limitations of Clinical Studies Using the Downs and Black Checklist<sup>13</sup>**

Strengths	Limitations
<b>Stock et al. (2022)<sup>10</sup></b>	
<ul style="list-style-type: none"> <li>• The objective, main outcomes assessed, patient characteristics, and interventions received was clearly described in the introduction and methods sections.</li> <li>• Principal confounders were described, and multivariate linear and regression models were used to compare outcomes while controlling for confounders.</li> <li>• The main findings of the study were clearly described and include appropriate estimates of variability with standard</li> </ul>	<ul style="list-style-type: none"> <li>• It is unclear if all important adverse events have been reported.</li> <li>• It is unclear whether patients were recruited from the same population and reasons for excluding patients were not outlined, which may contribute to selection bias and impact whether this patient population was representative of the whole population.</li> <li>• Because the study design did not involve randomization, it has</li> </ul>

Strengths	Limitations
<p>deviation where applicable. Actual probability values have been reported for main outcomes except where the probability value is less than 0.001.</p> <ul style="list-style-type: none"> <li>• Procedures were performed by board-certified orthopedic surgeons at an acute care hospital or ambulatory surgery centre, which would be representative of the procedures received by this population.</li> <li>• Appropriate statistical analyses were used for comparing outcomes across intervention groups. Univariate analysis was used for categorical variables, and two-sided independent sample t-tests and 1-way ANOVA was used for continuous measures across intervention groups. Relevant subgroup analyses were also conducted for intervention and comparison groups for same-day discharge patients and risk-adjusted analyses were done for controlling for confounders.</li> <li>• Outcome measures were clearly described. Any subjective type outcomes were provided with a description and justification for use.</li> <li>• No funding was received for this study and no conflict of interests were declared.</li> </ul>	<p>a risk of bias due to confounding factors that could impact its findings.</p>
<b>Calkins et al. (2021)<sup>9</sup></b>	
<ul style="list-style-type: none"> <li>• The objective, main outcomes, patient characteristics, and interventions received was clearly described in the introduction and methods sections.</li> <li>• All outcomes and main findings of the study are clearly described and include appropriate estimates of variability with standard deviation where applicable. Actual probability values have been reported for main outcomes except where the probability value is less than 0.001.</li> <li>• Patient data from a single site was used between 2018 and 2020 and may have been representative of the entire population from which they were recruited.</li> <li>• Patient data from different intervention groups were used from the same population and justification was given for excluding patient data, which may address selection bias.</li> <li>• Appropriate statistical tests were used to assess outcomes. Continuous variables were assessed using 2-tailed independent means t-test and all dichotomous categorical variables were assessed using Fisher's exact test or ANOVA for multiple variables.</li> <li>• No funding was received for this study and any conflicts of interests were declared.</li> </ul>	<ul style="list-style-type: none"> <li>• Distribution of principal confounding factors were not clearly described or controlled for throughout the study, but it was noted that any confounding factors were not likely to be significant.</li> <li>• It is unclear if all important adverse events have been reported.</li> <li>• Because the study design did not involve randomization, it has a risk of bias due to confounding factors that could impact its findings.</li> </ul>

ANOVA = analysis of variance.

## Appendix 4: Main Study Findings

Note that this appendix has not been copy-edited.

**Table 6: Summary of Findings by Outcome – Neurologic Symptoms**

Study citation and design	Study Findings
<b>Postoperative Motor Function Return</b>	
Siddiqi et al. (2022) <sup>15</sup> Systematic Review and Meta Analysis (outcome based on 3 included studies)	<p><b>Combined values for N, Mean and SD for 3 included studies (minutes)</b></p> <p><b>Mepivacaine</b></p> <ul style="list-style-type: none"> <li>• N =139</li> <li>• Mean = 154.05</li> <li>• SD = 63.13</li> </ul> <p><b>Bupivacaine</b></p> <ul style="list-style-type: none"> <li>• N = 200</li> <li>• Mean = 170.335</li> <li>• SD = 80.765</li> </ul> <p>Mean difference (95% CI) = -27.34 (-41.12 to -13.56); P = 0.0472; I<sup>2</sup> = 0%</p>
<b>Transient Neurologic Symptoms</b>	
Siddiqi et al. (2022) <sup>15</sup> Systematic Review and Meta Analysis (outcome based on 1 included study)	<p><b>Occurrence of transient neurologic symptoms (%)</b></p> <p><b>Mepivacaine:</b> Occurrence = 10</p> <p><b>Hyperbaric Bupivacaine:</b> Occurrence = 11.3</p> <p><b>Isobaric Bupivacaine:</b> Occurrence = 3.9</p> <p>P = 0.36</p>
Calkins et al. (2021) <sup>9</sup> Retrospective cohort study (N = 282)	<p><b>Transient neurological symptoms</b></p> <p><b>Mepivacaine (n = 141):</b> n (%) = 0 (0)</p> <p><b>Bupivacaine (n = 141):</b> n (%) = 2 (1.4)</p> <p>P = 0.498</p>

CI = confidence interval; N = number; SD = standard deviation.

**Table 7: Summary of Findings by Outcome – Mobility**

Study citation and design	Study Findings
<b>Mobilization Distance Postoperative Day 0</b>	
Siddiqi et al. (2022) <sup>15</sup> Systematic Review and Meta Analysis (outcome based on 4 included studies)	<p><b>Combined total distance for 4 included studies (feet)</b></p> <p><b>Mepivacaine:</b> Total = 195</p> <p><b>Bupivacaine:</b> Total = 300</p> <p>Mean difference (95% CI) = 12.01 (-9.04 to 33.05); P = 0.26; I<sup>2</sup> = 55%</p>
Calkins et al. (2021) <sup>9</sup> Retrospective cohort study (N = 282)	<p><b>Ambulation distance in postoperative recovery room (feet)</b></p> <p><b>Mepivacaine (n = 141):</b> Mean (SD) = 69 (30.4)</p>



Study citation and design	Study Findings	
	<b>Bupivacaine (n = 141): Mean (SD) = 64.4 (58.4)</b> P = 0.661	
<b>Mobilization Distance Postoperative Day 1</b>		
Siddiqi et al. (2022) <sup>15</sup> Systematic Review and Meta Analysis (outcome based on 3 included studies)	<b>Combined total distance for 3 included studies (feet)</b> <b>Mepivacaine: Total = 145</b> <b>Bupivacaine: Total = 196</b> Mean difference (95% CI) = 5.04 (-24.38 to 34.46); P = 0.76; I <sup>2</sup> = 54%	
<b>Number of Patients Ambulated Postoperative Day 0</b>		
Stock et al. (2022) <sup>10</sup> Retrospective cohort study (N = 1328)	<b>Unadjusted postoperative THA</b> <b>Mepivacaine (n = 232): n (%) = 196 (84.5)</b> <b>Hyperbaric Bupivacaine (n = 401): n (%) = 282 (70.3)</b> <b>Isobaric Bupivacaine (n = 34): n (%) = 19 (55.9)</b> P < 0.001	<b>Unadjusted postoperative TKA</b> <b>Mepivacaine (n = 131): n (%) = 225 (85.9)</b> <b>Hyperbaric Bupivacaine (n = 502): n (%) = 328 (65.3)</b> <b>Isobaric Bupivacaine (n = 28): n (%) = 17 (60.7)</b> P < 0.001
	<b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients THA</b> <b>Mepivacaine (n = 141): n (%) = 141 (100.0)</b> <b>Bupivacaine (n = 104): n (%) = 104 (100.0)</b> P = NA	<b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients TKA</b> <b>Mepivacaine (n = 138): n (%) = 138 (100.0)</b> <b>Bupivacaine (n = 59): n (%) = 59 (100.0)</b> P = NA
	<b>Risk-adjusted mepivacaine vs. bupivacaine (n)<sup>a</sup></b> <b>Mepivacaine: OR (95% CI) = 2.391 (1.789 to 3.197); P &lt; 0.001</b>	
<b>First Physical Therapy Ambulation Distance</b>		
Stock et al. (2022) <sup>10</sup> Retrospective cohort study (N = 1328)	<b>Unadjusted postoperative THA (feet)</b> <b>Mepivacaine (n = 232): Mean (SD) = 184 (±84.84)</b> <b>Hyperbaric Bupivacaine (n = 401): Mean (SD) = 151 (±97.51)</b> <b>Isobaric Bupivacaine (n = 34): Mean (SD) = 142.55 (±114.21)</b> P < 0.001	<b>Unadjusted postoperative TKA (feet)</b> <b>Mepivacaine (n = 131): Mean (SD) = 165.24 (±101.79)</b> <b>Hyperbaric Bupivacaine (n = 502): Mean (SD) = 134.57 (±98.89)</b> <b>Isobaric Bupivacaine (n = 28): Mean (SD) = 111.67 (±77.44)</b> P < 0.001
	<b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients THA (feet)</b> <b>Mepivacaine (n = 141): Mean (SD) = 208.93 (±66.60)</b> <b>Bupivacaine (n = 104): Mean (SD) = 193.81 (±73.84)</b> P = 0.144	<b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients TKA (feet)</b> <b>Mepivacaine (n = 138): Mean (SD) = 215.53 (±82.85)</b> <b>Bupivacaine (n = 59): Mean (SD) = 220.25 (±90.13)</b> P = 0.757

Study citation and design	Study Findings	
	<b>Risk-adjusted mepivacaine vs. bupivacaine (feet)<sup>a</sup></b> <b>Mepivacaine: OR (95% CI) = 21.785 (10.459 to 33.111); P &lt; 0.001</b>	
<b>Activity Measure for Post-Acute Care 6-Clicks Mobility Score</b>		
Stock et al. (2022) <sup>10</sup> Retrospective cohort study (N = 1328)	<b>Unadjusted postoperative THA score</b> <b>Mepivacaine (n = 232): Mean (SD) = 20.43 (±2.51)</b> <b>Hyperbaric Bupivacaine (n = 401): Mean (SD) = 20.48 (±2.75)</b> <b>Isobaric Bupivacaine (n = 34): Mean (SD) = 18.82 (±2.92)</b> <b>P = 0.003</b>	<b>Unadjusted postoperative TKA score</b> <b>Mepivacaine (n = 131): Mean (SD) = 19.98 (±2.50)</b> <b>Hyperbaric Bupivacaine (n = 502): Mean (SD) = 20.13 (±2.75)</b> <b>Isobaric Bupivacaine (n = 28): Mean (SD) = 20.5 (±2.5)</b> <b>P = 0.607</b>
	<b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients THA score</b> <b>Mepivacaine (n = 141): Mean (SD) = 20.16 (±2.38)</b> <b>Bupivacaine (n = 104): Mean (SD) = 21.26 (±2.28)</b> <b>P = 0.001</b>	<b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients TKA score</b> <b>Mepivacaine (n = 138): Mean (SD) = 19.96 (±2.54)</b> <b>Bupivacaine (n = 59): Mean (SD) = 22.08 (±2.15)</b> <b>P &lt; 0.001</b>
	<b>Risk-adjusted mepivacaine vs. bupivacaine score<sup>a</sup></b> <b>Mepivacaine: OR (95% CI) = -0.209 (-0.523 to 0.105); P = 0.192</b>	
	<b>Time to Postoperative Mobilization</b>	
Calkins et al. (2021) <sup>9</sup> Retrospective cohort study (N = 282)	<b>Hours to ankle dorsi/plantar flexion</b> <b>Mepivacaine (n = 141): Mean (SD) = 1.6 (0.7)</b> <b>Bupivacaine (n = 141): Mean (SD) = 1.8 (1.2)</b> <b>P = 0.502</b> <b>Hours to sitting up</b> <b>Mepivacaine (n = 141): Mean (SD) = 2.5 (0.7)</b> <b>Bupivacaine (n = 141): Mean (SD) = 3.3 (1.1)</b> <b>P &lt; 0.001</b> <b>Hours to ambulation</b> <b>Mepivacaine (n = 141): Mean (SD) = 3.2 (1.0)</b> <b>Bupivacaine (n = 141): Mean (SD) = 4.5 (1.6)</b> <b>P = &lt; 0.001</b>	

CI = confidence interval; N = number; NA = not applicable; OR = odds ratio; SD = standard deviation; THA = total hip arthroplasty; TKA = total knee arthroplasty; vs. = versus.  
<sup>a</sup>Risk-adjusted comparison controls for age, body mass index, sex, American Society of Anesthesiologists score, and procedure type (THA or TKA).

**Table 8: Summary of Findings by Outcome – Pain**

Study citation and design	Study Findings
<b>Pain Postoperative Day 0</b>	
<p>Siddiqi et al. (2022)<sup>15</sup> Systematic Review and Meta Analysis (outcome based on 3 included studies)</p>	<p><b>Combined total pain scores for 3 included studies (VAS<sup>a</sup>)</b>  <b>Mepivacaine:</b> Total = 118  <b>Bupivacaine:</b> Total = 172  Mean difference (95% CI) = 1.44 (0.94 to 1.94); P = 0.75; I<sup>2</sup> = 0%</p>
<p>Calkins et al. (2021)<sup>9</sup> Retrospective cohort study (N = 282)</p>	<p><b>Immediate postoperative pain (0-10 scale)</b>  <b>Mepivacaine (n = 141):</b> Mean (SD) = 0.1 (0.8)  <b>Bupivacaine (n = 141):</b> Mean (SD) = 0.1 (0.8)  P = 0.83</p> <p><b>1-hour postoperative pain (0-10 scale)</b>  <b>Mepivacaine (n = 141):</b> Mean (SD) = 1.6 (2.7)  <b>Bupivacaine (n = 141):</b> Mean (SD) = 0.6 (1.6)  P &lt; 0.001</p> <p><b>2-hour postoperative pain (0-10 scale)</b>  <b>Mepivacaine (n = 141):</b> Mean (SD) = 1.7 (2.5)  <b>Bupivacaine (n = 141):</b> Mean (SD) = 0.9 (1.9)  P &lt; 0.001</p> <p><b>3-hour postoperative pain (0-10 scale)</b>  <b>Mepivacaine (n = 141):</b> Mean (SD) = 1.3 (2.1)  <b>Bupivacaine (n = 141):</b> Mean (SD) = 0.9 (1.9)  P = 0.003</p> <p><b>4-hour postoperative pain (0-10 scale)</b>  <b>Mepivacaine (n = 141):</b> Mean (SD) = 0.8 (1.9)  <b>Bupivacaine (n = 141):</b> Mean (SD) = 0.8 (1.7)  P = 0.945</p> <p><b>5-hour postoperative pain (0-10 scale)</b>  <b>Mepivacaine (n = 141):</b> Mean (SD) = 0.3 (1.0)  <b>Bupivacaine (n = 141):</b> Mean (SD) = 0.7 (1.6)  P = 0.099</p>
	<p><b>Zero pain immediately postoperative (% only)</b>  <b>Mepivacaine (n = 141):</b> = 99%  <b>Bupivacaine (n = 141):</b> = 99%  P = 1.000</p> <p><b>Zero pain at 1-hour postoperative (% only)</b>  <b>Mepivacaine (n = 141):</b> = 69%  <b>Bupivacaine (n = 141):</b> = 86%  P = 0.010</p>

Study citation and design	Study Findings
	<p><b>Zero pain at 2-hour postoperative (% only)</b>  <b>Mepivacaine (n = 141): = 58%</b>  <b>Bupivacaine (n = 141): = 79%</b>            P &lt; 0.001</p> <p><b>Zero pain at 3-hour postoperative (% only)</b>  <b>Mepivacaine (n = 141): = 57%</b>  <b>Bupivacaine (n = 141): = 73%</b>            P = 0.006</p> <p><b>Zero pain at 4-hour postoperative (% only)</b>  <b>Mepivacaine (n = 141): = 39%</b>  <b>Bupivacaine (n = 141): = 61%</b>            P &lt; 0.001</p> <p><b>Zero pain at 5-hour postoperative (% only)</b>  <b>Mepivacaine (n = 141): = 28%</b>  <b>Bupivacaine (n = 141): = 45%</b>            P = 0.043</p>
<b>Pain Postoperative Day 1</b>	
Siddiqi et al. (2022) <sup>15</sup> Systematic Review and Meta Analysis (outcome based on 4 included studies)	<p><b>Combined total pain scores for 4 included studies (VAS<sup>a</sup>)</b>  <b>Mepivacaine: Total = 219</b>  <b>Bupivacaine: Total = 276</b>            Mean difference (95% CI) = 0.04 (-0.32 to 0.39); P = 0.84; I<sup>2</sup> = 0%</p>
<b>Postoperative Pain at 2 Weeks, 6 weeks, and 3 Months</b>	
Calkins et al. (2021) <sup>9</sup> Retrospective cohort study (N = 282)	<p><b>Postoperative pain at 2 weeks (VAS<sup>a</sup>)</b>  <b>Mepivacaine: Mean = 2.2</b>  <b>Bupivacaine: Mean = 1.9</b>            P = 0.308</p> <p><b>Postoperative pain at 6 weeks (VAS<sup>a</sup>)</b>  <b>Mepivacaine: Mean = 1.6</b>  <b>Bupivacaine: Mean = 1.8</b>            P = 0.386</p> <p><b>Postoperative pain at 3 months (VAS<sup>a</sup>)</b>  <b>Mepivacaine: Mean = 1.3</b>  <b>Bupivacaine: Mean = 1.3</b>            P = 0.575</p>
<b>Discharge Pain</b>	
Calkins et al. (2021) <sup>9</sup> Retrospective cohort study (N = 282)	<p><b>Discharge Pain (0-10 scale)</b>  <b>Mepivacaine (n = 141): Mean (SD) = 1.1 (1.9)</b></p>

Study citation and design	Study Findings
	<b>Bupivacaine (n = 141): Mean (SD) = 0.5 (1.2)</b> P = 0.004
<b>Pain Medication Use</b>	
Calkins et al. (2021) <sup>9</sup> Retrospective cohort study (N = 282)	<b>Morphine equivalents given (mg)</b> <b>Mepivacaine (n = 141): Mean (SD) = 7.8 (6.2)</b> <b>Bupivacaine (n = 141): Mean (SD) = 3.7 (5.8)</b> P < 0.001

CI = confidence interval; mg = milligram; N = number; SD = standard deviation; VAS = visual analogue scale.

<sup>a</sup>Scale range for VAS measurement was not reported.

**Table 9: Summary of Findings by Outcome – Length of Stay**

Study citation and design	Study Findings	
<b>Postoperative Length of Stay</b>		
Siddiqi et al. (2022) <sup>15</sup> Systematic Review and Meta Analysis (outcome based on 3 included studies)	<b>Combined values for total, mean and SD for 3 included studies (hours)</b> <b>Mepivacaine</b> <ul style="list-style-type: none"> <li>• Total = 118</li> <li>• Mean = 25.95</li> <li>• SD = 12.275</li> </ul> <b>Bupivacaine</b> <ul style="list-style-type: none"> <li>• Total = 223</li> <li>• Mean = 29.96</li> <li>• SD = 12.895</li> </ul> Mean difference (95% CI) = -7.03 (-10.02 to -4.04); P = 0.0057; I <sup>2</sup> = 53%	
Stock et al. (2022) <sup>10</sup> Retrospective cohort study (N = 1328)	<b>Unadjusted postoperative THA (days)</b> <b>Mepivacaine (n = 232): Mean (SD) = 0.43 (±0.59)</b> <b>Hyperbaric Bupivacaine (n = 401): Mean (SD) = 0.92 (±0.79)</b> <b>Isobaric Bupivacaine (n = 34): Mean (SD) = 1.12 (±1.00)</b> P < 0.001	<b>Unadjusted postoperative TKA (days)</b> <b>Mepivacaine (n = 131): Mean (SD) = 0.51 (±0.59)</b> <b>Hyperbaric Bupivacaine (n = 502): Mean (SD) = 1.09 (±0.91)</b> <b>Isobaric Bupivacaine (n = 28): Mean (SD) = 1.00 (±0.61)</b> P < 0.001
	<b>Risk-adjusted mepivacaine vs. bupivacaine (days)<sup>a</sup></b> <b>Mepivacaine: OR (95% CI) = -0.421 (-0.502 to -0.330); P &lt; 0.001</b>	
<b>0 Day Length of Stay</b>		
Stock et al. (2022) <sup>10</sup> Retrospective cohort study (N = 1328)	<b>Unadjusted postoperative THA</b> <b>Mepivacaine (n = 232): n (%) = 141 (60.8)</b> <b>Hyperbaric Bupivacaine (n = 401): n (%) = 96 (23.9)</b>	<b>Unadjusted postoperative TKA</b> <b>Mepivacaine (n = 131): n (%) = 138 (52.7)</b> <b>Hyperbaric Bupivacaine (n = 502): n (%) = 55 (11.0)</b>

Study citation and design	Study Findings	
	<b>Isobaric Bupivacaine (n = 34):</b> n (%) = 8 (23.5) P < 0.001	<b>Isobaric Bupivacaine (n = 28):</b> n (%) = 4 (14.3) P < 0.001
<b>Risk-adjusted mepivacaine vs. bupivacaine (n)<sup>a</sup></b> <b>Mepivacaine: OR (95% CI) = 5.767 (4.357 to 7.634); P &lt; 0.001</b>		
<b>Time Spent in Each Ambulatory Phase</b>		
Calkins et al. (2021) <sup>9</sup> Retrospective cohort study (N = 282)	<b>Preoperative unit (hours)</b> <b>Mepivacaine (n = 141):</b> Mean (SD) = 1.5 (0.6) <b>Bupivacaine (n = 141):</b> Mean (SD) = 1.7 (0.5) P = 0.18 <b>Operating room (hours)</b> <b>Mepivacaine (n = 141):</b> Mean (SD) = 1.5 (0.2) <b>Bupivacaine (n = 141):</b> Mean (SD) = 1.6 (0.2) P = 0.25 <b>Postoperative unit (hours)</b> <b>Mepivacaine (n = 141):</b> Mean (SD) = 4.0 (1.1) <b>Bupivacaine (n = 141):</b> Mean (SD) = 5.7 (1.6) P < 0.001 <b>Total facility time (hours)</b> <b>Mepivacaine (n = 141):</b> Mean (SD) = 7.0 (1.3) <b>Bupivacaine (n = 141):</b> Mean (SD) = 8.8 (2.0) P < 0.001	

CI = confidence interval; N = number; OR = odds ratio; SD = standard deviation; THA = total hip arthroplasty; TKA = total knee arthroplasty; vs. = versus.

<sup>a</sup>Risk-adjusted comparison controls for age, body mass index, sex, American Society of Anesthesiologists score, and procedure type (THA or TKA).

**Table 10: Summary of Findings by Outcome – Urinary Retention**

Study citation and design	Study Findings	
<b>Postoperative Urinary Retention</b>		
Siddiqi et al. (2022) <sup>15</sup> Systematic Review and Meta Analysis (outcome based on 5 included studies)	<b>Combined occurrence of urinary events (%)</b> <b>Mepivacaine:</b> Occurrence = 7.15 <b>Bupivacaine:</b> Occurrence = 10.58 Overall difference (95% CI) = -3.43 (0.48 to 1.01); P = 0.0181; I <sup>2</sup> = 49%	
Stock et al. (2022) <sup>10</sup> Retrospective cohort study (N = 1328)	<b>Unadjusted postoperative THA<sup>a</sup></b> <b>Mepivacaine (n = 232):</b> n (%) = 3 (1.3) <b>Hyperbaric Bupivacaine (n = 401):</b> n (%) = 5 (1.2) <b>Isobaric Bupivacaine (n = 34):</b> n (%) = 2 (5.9) P = 0.097	<b>Unadjusted postoperative TKA<sup>a</sup></b> <b>Mepivacaine (n = 131):</b> n (%) = 2 (0.8) <b>Hyperbaric Bupivacaine (n = 502):</b> n (%) = 6 (1.2) <b>Isobaric Bupivacaine (n = 28):</b> n (%) = 0 (0.0) P = 0.734

Study citation and design	Study Findings	
	<p><b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients THA<sup>a</sup></b></p> <p>Mepivacaine (n = 141): n (%) = 2 (1.4)                      Bupivacaine (n = 104): n (%) = 1 (1.0)                      P = 1.000</p>	<p><b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients TKA<sup>a</sup></b></p> <p>Mepivacaine (n = 138): n (%) = 0 (0.0)                      Bupivacaine (n = 59): n (%) = 1 (1.7)                      P = 0.299</p>
<p>Calkins et al. (2021)<sup>9</sup>                      Retrospective cohort study                      (N = 282)</p>	<p><b>Risk-adjusted mepivacaine vs. bupivacaine (n)<sup>ab</sup></b>                      Mepivacaine: OR (95% CI) = 0.661 (0.225 to 1.942); P = 0.452</p> <p><b>Hours to controlled void</b></p> <p>Mepivacaine (n = 141): Mean (SD) = 3.1 (1.1)                      Bupivacaine (n = 141): Mean (SD) = 4.9 (1.6)                      P &lt; 0.001</p> <p><b>Required bethanechol</b></p> <p>Mepivacaine (n = 141): n (%) = 27 (19.1)                      Bupivacaine (n = 141): n (%) = 54 (38.3)                      P &lt; 0.001</p> <p><b>Straight urinary catheter use</b></p> <p>Mepivacaine (n = 141): n (%) = 0 (0)                      Bupivacaine (n = 141): n (%) = 0 (0)                      P = NA</p>	

CI = confidence interval; N = number; NA = not applicable; OR = odds ratio; SD = standard deviation; THA = total hip arthroplasty; TKA = total knee arthroplasty; vs = versus.

<sup>a</sup>Urinary retention was defined as any instance of postoperative straight or foley catheter use.

<sup>b</sup>Risk-adjusted comparison controls for age, body mass index, sex, American Society of Anesthesiologists score, and procedure type (THA or TKA).

**Table 11: Summary of Findings by Outcome – Additional Clinical Outcomes**

Study citation and design	Study Findings	
<b>Home Discharge</b>		
<p>Stock et al. (2022)<sup>10</sup>                      Retrospective cohort study                      (N = 1328)</p>	<p><b>Unadjusted postoperative THA</b></p> <p>Mepivacaine (n = 232): n (%) = 232 (100)                      Hyperbaric Bupivacaine (n = 401): n (%) = 389 (97.0)                      Isobaric Bupivacaine (n = 34): n (%) = 31 (91.2)                      P = 0.001</p>	<p><b>Unadjusted postoperative TKA</b></p> <p>Mepivacaine (n = 131): n (%) = 260 (99.2)                      Hyperbaric Bupivacaine (n = 502): n (%) = 486 (96.8)                      Isobaric Bupivacaine (n = 28): n (%) = 27 (96.4)                      P = 0.106</p>
	<p><b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients THA</b></p> <p>Mepivacaine (n = 141): n (%) = 141 (100)                      Bupivacaine (n = 104): n (%) = 104 (100)                      P = NA</p>	<p><b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients TKA</b></p> <p>Mepivacaine (n = 138): n (%) = 138 (100)                      Bupivacaine (n = 59): n (%) = 59 (100)                      P = NA</p>

Study citation and design	Study Findings
	<b>Risk-adjusted mepivacaine vs. bupivacaine (n)<sup>x</sup></b> <b>Mepivacaine: OR (95% CI) = 6.537 (1.540 to 27.743); P = 0.011</b>
<b>HOOS, JR</b>	
Calkins et al. (2021) <sup>9</sup> Retrospective cohort study (N = 282)	<b>HOOS, JR at 2 weeks</b> <b>Mepivacaine: Mean = 71.5</b> <b>Bupivacaine: Mean = 71.5</b> P = 0.990 <b>HOOS, JR at 6 weeks:</b> <b>Mepivacaine: Mean = 78.6</b> <b>Bupivacaine: Mean = 77.9</b> P = 0.704 <b>HOOS, JR at 3 months</b> <b>Mepivacaine: Mean = 85.7</b> <b>Bupivacaine: Mean = 84.5</b> P = 0.604

CI = confidence interval; HOOS, JR = Hip Disability and Osteoarthritis Outcome Score for Joint Replacement; N = number; NA = not applicable; OR = odds ratio; THA = total hip arthroplasty; TKA = total knee arthroplasty; vs. = versus.

<sup>a</sup>Risk-adjusted comparison controls for age, body mass index, sex, American Society of Anesthesiologists score, and procedure type (THA or TKA).



**Table 12: Summary of Findings by Outcome – Adverse Events and Safety**

Study citation and design	Study Findings	
<b>Failed Same-Day Discharge Attempt</b>		
Stock et al. (2022) <sup>10</sup> Retrospective cohort study (N = 1328)	<b>Unadjusted postoperative THA</b> <b>Mepivacaine (n = 232): n (%) = 14 (6.0)</b> <b>Hyperbaric Bupivacaine (n = 401): n (%) = 22 (5.5)</b> <b>Isobaric Bupivacaine (n = 34): n (%) = 4 (11.8)</b> P = 0.334	<b>Unadjusted postoperative TKA</b> <b>Mepivacaine (n = 131): n (%) = 6 (2.3)</b> <b>Hyperbaric Bupivacaine (n = 502): n (%) = 17 (3.4)</b> <b>Isobaric Bupivacaine (n = 28): n (%) = 0 (0.0)</b> P = 0.449
	<b>Risk-adjusted mepivacaine vs. bupivacaine (n)<sup>x</sup></b> <b>Mepivacaine: OR (95% CI) = 0.801 (0.458 to 1.400); P = 0.436</b>	
<b>30-Day Readmission</b>		
Stock et al. (2022) <sup>10</sup> Retrospective cohort study (N = 1328)	<b>Unadjusted postoperative THA</b> <b>Mepivacaine (n = 232): n (%) = 4 (1.7)</b> <b>Hyperbaric Bupivacaine (n = 401): n (%) = 8 (2.0)</b> <b>Isobaric Bupivacaine (n = 34): n (%) = 0 (0.0)</b> P = 0.699	<b>Unadjusted postoperative TKA</b> <b>Mepivacaine (n = 131): n (%) = 4 (1.5)</b> <b>Hyperbaric Bupivacaine (n = 502): n (%) = 30 (6.0)</b> <b>Isobaric Bupivacaine (n = 28): n (%) = 0 (0.0)</b> P = 0.008
	<b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients THA</b> <b>Mepivacaine (n = 141): n (%) = 2 (1.4)</b> <b>Bupivacaine (n = 104): n (%) = 0 (0.0)</b> P = 0.509	<b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients TKA</b> <b>Mepivacaine (n = 138): n (%) = 2 (1.4)</b> <b>Bupivacaine (n = 59): n (%) = 2 (3.4)</b> P = 0.585
	<b>Risk-adjusted mepivacaine vs. bupivacaine (n)<sup>x</sup></b> <b>Mepivacaine: OR (95% CI) = 0.494 (0.226 to 1.083); P = 0.078</b>	
<b>30-Day ED Return</b>		
Stock et al. (2022) <sup>10</sup> Retrospective cohort study (N = 1328)	<b>Unadjusted postoperative THA</b> <b>Mepivacaine (n = 232): n (%) = 5 (2.2)</b> <b>Hyperbaric Bupivacaine (n = 401): n (%) = 15 (3.7)</b> <b>Isobaric Bupivacaine (n = 34): n (%) = 0 (0.0)</b> P = 0.305	<b>Unadjusted postoperative TKA</b> <b>Mepivacaine (n = 131): n (%) = 9 (3.4)</b> <b>Hyperbaric Bupivacaine (n = 502): n (%) = 15 (3.0)</b> <b>Isobaric Bupivacaine (n = 28): n (%) = 0 (0.0)</b> P = 0.599
	<b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients THA</b> <b>Mepivacaine (n = 141): n (%) = 4 (2.8)</b> <b>Bupivacaine (n = 104): n (%) = 0 (0.0)</b> P = 0.138	<b>Subgroup analysis of mepivacaine vs. bupivacaine for same-day discharge patients TKA</b> <b>Mepivacaine (n = 138): n (%) = 2 (3.6)</b> <b>Bupivacaine (n = 59): n (%) = 2 (3.4)</b> P = 1.000

Study citation and design	Study Findings			
	<b>Risk-adjusted mepivacaine vs. bupivacaine (n)<sup>x</sup></b> <b>Mepivacaine: OR (95% CI) = 1.068 (0.552 to 2.067); P = 0.845</b>			
<b>Total 90-Day Adverse Events</b>				
Calkins et al. (2021) <sup>9</sup> Retrospective cohort study (N = 282)	<b>Total complications</b> <b>Mepivacaine: n = 5</b> <b>Bupivacaine: n = 5</b> P = 1.00	<b>ED Visits</b> <b>Mepivacaine: n = 4</b> <b>Bupivacaine: n = 4</b> P = 1.00	<b>Hospital admissions</b> <b>Mepivacaine: n = 1</b> <b>Bupivacaine: n = 1</b> P = 1.00	<b>Reoperations</b> <b>Mepivacaine: n = 1</b> <b>Bupivacaine: n = 1</b> P = 1.00
<b>Postoperative Nausea/Vomiting</b>				
Calkins et al. (2021) <sup>9</sup> Retrospective cohort study (N = 282)	<b>Postoperative nausea or vomiting</b> <b>Mepivacaine (n = 141): n (%) = 31 (22.0)</b> <b>Bupivacaine (n = 141): n (%) = 22 (15.6)</b> P = 0.223			
<b>Hypotension Requiring Treatment</b>				
Calkins et al. (2021) <sup>9</sup> Retrospective cohort study (N = 282)	<b>Hypotension requiring treatment</b> <b>Mepivacaine (n = 141): n (%) = 13 (9.2)</b> <b>Bupivacaine (n = 141): n (%) = 6 (4.3)</b> P = 0.153			

CI = confidence interval; ED = emergency department; N = number; OR = odds ratio; THA = total hip arthroplasty; TKA = total knee arthroplasty; vs. = versus.

<sup>a</sup>Risk-adjusted comparison controls for age, body mass index, sex, American Society of Anesthesiologists score, and procedure type (THA or TKA).