Ontario
Health Quality Ontario
Qualité des services de santé Ontario

Local Infiltration Analgesia in Hip and Knee Arthroplasty: A Rapid Review

S Brener

November 2013

Evidence Development and Standards Branch at Health Quality Ontario

Suggested Citation

This report should be cited as follows:

Brener, S. Local infiltration analgesia in hip and knee arthroplasty: a rapid review. Toronto: Health Quality Ontario; 2013 November. 22 p. Available from: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/rapid-reviews.

Permission Requests

All inquiries regarding permission to reproduce any content in Health Quality Ontario reports should be directed to EvidenceInfo@hqontario.ca.

How to Obtain Rapid Reviews From Health Quality Ontario

All rapid reviews are freely available in PDF format at the following URL:
http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/rapid-reviews.

Conflict of Interest Statement

All reports prepared by the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses; if none are located, the search is expanded to include randomized controlled trials and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If a systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to a maximum of 2 outcomes. Because rapid reviews are completed in very short time frames, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

About Health Quality Ontario

Health Quality Ontario is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series*, which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

About Health Quality Ontario Publications

To conduct its rapid reviews, Evidence Development and Standards and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Division of Evidence Development and Standards at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current to the date of the literature search specified in the Research Methods section, as appropriate. This rapid review may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Table of Contents

List of Abbreviations

AMSTAR	Assessment of Multiple Systematic Reviews
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
LIA	Local infiltration analgesia
RCT	Randomized controlled trial
THA	Total hip arthroplasty
TKA	Total knee arthroplasty

Background

As legislated in Ontario's *Excellent Care for All Act*, Health Quality Ontario's mandate includes the provision of objective, evidence-informed advice about health care funding mechanisms, incentives, and opportunities to improve quality and efficiency in the health care system. As part of its Quality-Based Funding (QBF) initiative, Health Quality Ontario works with multidisciplinary expert panels (composed of leading clinicians, scientists, and administrators) to develop evidence-based practice recommendations and define episodes of care for selected disease areas or procedures. Health Quality Ontario's recommendations are intended to inform the Ministry of Health and Long-Term Care's Health System Funding Strategy.

For more information on Health Quality Ontario's Quality-Based Funding initiative, visit www.hqontario.ca.

Objective of Analysis

The objective of this rapid review was to examine the effectiveness of local infiltration analgesia in patients who have undergone primary hip arthroplasty or primary knee arthroplasty.

Clinical Need and Target Population

Primary hip or knee arthroplasty surgery requires appropriate anesthesia and analgesia to minimize patient discomfort and promote recovery. Multimodal pain management strategies are common and may include a combination of analgesics, such as opioids and nonsteroidal anti-inflammatory drugs (NSAIDs), and/or regional anesthetics, such as epidurals and femoral nerve blocks. (1-3) Pain management medications for patients undergoing total knee arthroplasty (TKA) or total hip arthroplasty (THA) can be administered through a number of different modalities such as oral, local injection, or epidural injection. (4) Local infiltration analgesia (LIA) is one such modality of pain management administered as a "cocktail" of a combination of many pain medications into the intra-articular space of the joints or other tissues at the site of the joint. The cocktail may be administered directly or through a catheter. (5) What remains uncertain, however, is if LIA provides superior pain management compared with other pain management strategies.

Rapid Review

Research Question

What is the effectiveness of local infiltration analgesia (LIA) in primary hip arthroplasty and primary knee arthroplasty?

Research Methods

Literature Search

Search Strategy

A literature search was performed on May 16, 2013, using OVID MEDLINE, OVID MEDLINE In-Process and Other Non-Indexed Citations, OVID Embase, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), and EBM Reviews for studies published from January 1, 2008, until May 16, 2013. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English language full-text publications
- published between January 1, 2008, and May 16, 2013
- systematic reviews, meta-analyses, and health technology assessments
- primary hip arthroplasty or primary knee arthroplasty
- local infiltration analgesia at the surgical joint site

Exclusion Criteria

- studies from which results on outcomes of interest cannot be abstracted

Outcomes of Interest

- pain
- hospital length of stay

Expert Panel

In April 2013, an Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was struck. Members of the panel included physicians, personnel from the Ministry of Health and Long-Term Care, and representatives from community laboratories.

The role of the Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was to contextualize the evidence produced by Health Quality Ontario and provide advice on the appropriate clinical pathway for a hip and knee arthroplasty in the Ontario health care setting. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of Expert Advisory Panel members.

Quality of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool is used to assess the methodological quality of the final selection of systematic reviews. (6) Primary studies were abstracted from the selected reviews and referenced for quality assessment of the body of the evidence for the 2 outcomes of interest.

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (7) The overall quality was determined to be very low, low, moderate, or high using a step-wise, structural methodology.

Study design was the first consideration; the starting assumption was that randomized controlled trials are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: large magnitude of effect, dose response gradient, and accounting for all residual confounding factors. (7) For more detailed information, please refer to the latest series of GRADE articles. (7)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Rapid Review

The database search yielded 349 citations published between January 1, 2008, and May 16, 2013 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

Four systematic reviews met the inclusion criteria. The reference lists of the included studies, health technology assessment websites, and other resources were hand searched to identify other relevant studies, and no additional citations were identified.

Quality Assessment of Reviews

The included reviews are summarized in Table 1 below. The AMSTAR scores of the identified reviews, ranged from 1 to 8 out of a possible 11. (6) Only 3 of the reviews specifically examined LIA in patients undergoing TKA or THA. (5;8;9) The other review examined pain management in the target population more broadly and included local infiltration as one of the pain management strategies reviewed. (4)

Table 1: Summary of Included Reviews

Author, Year	Search Dates	Study Designs Included	Population	Objective of Review	AMSTAR[a]
Fischer et al, 2008 (4)	1966–2005	RCT	TKA	An examination of various analgesics	8
Gibbs et al, 2012 (8)	Not reported	RCT and observational	TKA	An examination of local administration analgesics	1
McCarthy & Iohom, 2012 (9)	1966–2012	RCT and observational	THA	An examination of intraoperative local anesthetic infiltration for pain management postoperatively	5
Starks et al, 2011 (5)	Not reported	RCT	TKA and THA	An examination of the role of local anesthetics in joint replacement surgery	1

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; RCT, randomized controlled trial; THA, total hip arthroplasty; TKA, total knee arthroplasty.
[a] Out of a possible 11, with higher scores representing higher methodological quality; details of scores are shown in Appendix 2, Table A1.

The low AMSTAR scores indicate a number of methodological flaws in the Gibbs et al (8) and Starks et al (5) reviews, and for this reason these 2 reviews were excluded from this rapid review and were only used as additional references for supplementary details on the primary studies. As a result, the Fischer et al (4) review of LIA in patients undergoing total knee arthroplasty (TKA) and the McCarthy and Iohom (9) review of LIA in patients undergoing total hip arthroplasty (THA) were included.

Summary of Included Reviews

The Fischer et al (4) review identified 112 studies, of which 74 studies evaluated pharmacological mechanisms of pain management; of these, 8 randomized controlled trails (RCTs) examined LIA. (4) The review by McCarthy and Iohom (9) included 8 RCTs and 2 observational studies.

The Fischer et al (4) and McCarthy and Iohom (9) reviews concluded that intra-articular analgesic techniques are not recommended due to the inconsistency of the results, and that, while there are some advantages when compared to placebo, there is no additive benefit when combined with a multimodal analgesic approach.

Infiltration Cocktails of Included Primary Studies

There were a number of differences in the intervention and control protocols in the primary studies included in the Fischer et al (4) and McCarthy and Iohom (9) reviews. Some of the differences included variations in the timing and method of administration of the LIA (before/during/after closure of the surgical wound; with or without a catheter); variations in the control group (other analgesics, saline combined with other analgesics, saline alone with postoperative analgesics only or no control); and variations in the LIA cocktails (see Table 2).

Table 2: Summary of Interventions in the Included Primary Studies

Author, Year	Intervention (LIA cocktail)[a]	Control
TKA population		
Badner et al, 1996 (10)	150 mg bupivacaine 0.15 mg epinephrine	Saline
Badner et al, 1997 (11)	150 mg bupivacaine 1.5 mg adrenaline 1 mg morphine	Saline
Browne et al, 2004 (12)	100 mg bupivacaine	Saline
Klasen et al, 1999 (13)	1 mg morphine	No local infiltration
Mauerhan et al, 1997 (14)	50 mg bupivacaine 5 mg morphine	Saline
Nechleba et al, 2005 (15)	100 mg bupivacaine Plus bolus of 10.25 mg bupivacaine per hour	Saline
Ritter et al, 1999 (16)	10 mg morphine 25 mg bupivacaine	Saline
Tanaka et al, 2001 (17)	75 mg bupivacaine 0.15 mg epinephrine 5 mg morphine	Saline and epinephrine
THA population		
Andersen et al, 2007 (18)	200 mg ropivacaine 0.5 mg epinephrine 30 mg ketorolac Plus bolus at 8 hours of 20 mL of 150 mg ropivacaine, 0.5 mg epinephrine, and 30 mg ketorolac	Epidural to 20 hours
Andersen et al, 2007 (19)	300 mg ropivacaine 30 mg ketorolac 0.5 mg epinephrine Plus bolus in the morning of 20 mL of the cocktail	Saline
Andersen et al, 2011 (20)	340 mg ropivacaine 1.7 mg epinephrine	Saline
Bianconi et al, 2003 (21)	200 mg ropivacaine Plus extra-articular infusion ropivacaine 10 mg per hour for 55 hours	Extra-articular saline infusion
Busch et al, 2010 (22)	400 mg ropivacaine 0.6 mg epinephrine 30 mg ketorolac 5 mg morphine	No local infusion

Kerr & Lohan, 2008 (23)	300 mg ropivacaine 1.5 mg epinephrine 30 mg ketorolac Plus bolus at 15–20 hours of 50 mL of the cocktail	No control group
Lunn et al, 2011 (24)	300 mg ropivacaine 1.5 mg epinephrine Plus a multimodal analgesic management of pain	Saline and a multimodal analgesic management of pain
Otte et al, 2008 (25)	300 mg ropivacaine 1.5 mg epinephrine	No control group
Parvateneni et al, 2007 (26)	200–400 mg bupivacaine 4–10 mg morphine 0.3 mg epinephrine 40 mg methylprednisolone 750 mg cefuroxime	No local infusion
Specht et al, 2011 (27)	200 mg ropivacaine 30 mL ketorolac 1 mg epinephrine Plus bolus of 51 mL with IA catheter at 10 and 22 hours of the cocktail and a multimodal analgesic management of pain	Saline and a multimodal analgesic management of pain

Abbreviations: IA, intra-articular; LIA, local infiltration analgesia; THA, total hip arthroplasty; TKA, total knee arthroplasty.
[a] The details of the interventions were pulled from the Fischer et al (4), Gibbs et al (8), McCarthy & Iohom (9), and Starks et al (5) reviews and were further supplemented by the individual primary studies only on an as-needed basis.

Results for the Outcomes of Interest

Pain

All of the individual studies included in the two reviews reported pain as an outcome measure, but neither review conducted a meta-analysis or other quantitative summary of the results for this outcome. Table 3 shows a summary from the reviews of the results for the outcome of pain.

Table 3: Summary of Results for Pain

Author, Year	Population	Intervention/ Comparator	Included Studies	Results	GRADE
Fischer et al, 2008 (4)	TKA	Intra-articular LIA / placebo or no treatment	8 RCTs	Mixed results Significant decrease in pain in 2 studies; no statistically significant difference in 5 studies; inconclusive results in 1 study	Very low
McCarthy & Iohom, 2012 (9)	THA	LIA/ placebo or usual care or no comparator	8 RCTs; 2 observational studies	Mixed results Significant decrease in pain in 8 studies; no statistically significant difference in 2 studies	Very low

Abbreviations: LIA, local infiltration analgesia; RCT, randomized controlled trail; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Overall, the results for the effectiveness of LIA to manage pain were inconsistent. This result was based on very low quality of evidence (Appendix 2, Table A2).

Hospital Length of Stay

Only the McCarthy and Iohom review (9) examined hospital length of stay as an outcome measure. A summary of the results is described in Table 4.

Table 4: Summary of Results for Length of Stay

Author, Year	Population	Intervention/ Comparator	Included Studies	Results	GRADE
McCarthy & Iohom, 2012 (9)	THA	LIA / placebo or usual care or no treatment	5 RCTs	Mixed results Significant ↓in LOS in 3 studies; no statistically significant difference in 2 studies	Very low

Abbreviations: LIA, local infiltration analgesia; LOS, length of stay; RCT, randomized controlled trial; THA, total hip arthroplasty.

Overall, the results for the impact of LIA on hospital length of stay were inconsistent. This result was based on very low quality of evidence (Appendix 2, Table A2).

Conclusions

Based on very low quality of evidence:

- The results for the impact of local infiltration analgesia on pain in patients undergoing either total hip or knee arthroplasty were inconsistent.
- The results for the impact of local infiltration analgesia on hospital length of stay in patients undergoing total hip arthroplasty, based on very low quality of evidence, were inconsistent.

Acknowledgements

Editorial Staff
Joanna Odrowaz, BSc (Hons.)

Medical Information Services
Kellee Kaulback, BA(H), MISt

Expert Panel for Health Quality Ontario: Episodes of Care for Primary Hip/Knee Replacement

Panel Member	Affiliation(s)	Appointment(s)
Panel Chair		
Dr James Waddell	St. Michaels Hospital; University of Toronto	Orthopaedic Surgeon Professor, Division of Orthopaedic Surgery
Orthopaedic Surgery		
Dr John Rudan	Queens University Kingston General Hospital	Head of Department of Surgery Orthopaedic Surgeon
Dr Jeffrey Gollish	Sunnybrook Health Sciences Centre University of Toronto	Medical Director of the Holland Orthopaedic & Arthritic Centre Associate Professor, Division of Orthopaedic Surgery
Dr Maurice Bent	North York General Hospital	Chief, Division Orthopedic Surgery
Dr David Backstein	Mount Sinai Hospital University of Toronto	Division Head of Orthopaedic Surgery Associate Professor
Dr Paul E. Beaulé	University of Ottawa	Professor of Surgery, Head of Adult Reconstruction
Dr Steven MacDonald	London Health Science Centre University of Western Ontario	Site Chief of Orthopaedic Surgery Professor, Division of Orthopaedic Surgery
Dr Mitchell Winemaker	Hamilton Health Sciences – Chief of Orthopedic Surgery	Juravinski Hospital McMaster University Associate Professor
Dr Andrew Van Houwellingen	Orthopaedic Surgeon	St. Thomas Elgin General Hospital
Primary Care		
Dr Tatiana Jevremovic	University of Western Ontario Fowler Kennedy Sport Medicine Clinic	Assistant Professor Department of Family Medicine
Dr Christopher Jyu	Rouge Valley Health System The Scarborough Hospital	Primary Care Lead
Internal Medicine		

Panel Member	Affiliation(s)	Appointment(s)
Dr Valerie Palda	St. Michael's Hospital University of Toronto	General Internist Associate Professor, Department of Medicine
Anesthesiology		
Dr Nick Lo	St. Michael's Hospital University of Toronto	Staff Anesthesiologist Assistant Professor, Department of Anesthesiology
Dr Colin McCartney	Sunnybrook Health Sciences Centre University of Toronto	Staff Anesthesiologist Associate Professor
Geriatric Medicine		
Dr Anna Byszewski	The Ottawa Hospital Regional Geriatric Program of Eastern Ontario	Staff Geriatrician Full Professor, University of Ottawa
Physiotherapy and Rehabilitation		
Caroline Fanti	Thunder Bay Regional Health Sciences Centre	Physiotherapist
Deborah Marie Kennedy	Sunnybrook Holland Orthopaedic and Arthritic Centre	Manager, Rehabilitation and MSK Program Development
Raymond Kao	St. Michael's Hospital	Case Manager, Inpatient Mobility Program
Dr Peter Nord	Providence Healthcare Foundation University of Toronto	Vice President, Chief Medical Officer and Chief of Staff
Executive Administration		
Anne Marie MacLeod	Sunnybrook Health Science Centre	Operations Director
Tiziana Silveri	North Bay Regional Health Centre	Vice President, Clinical Services
Rhona McGlasson	Bone and Joint Canada	Executive Director
Brenda Flaherty	Hamilton Health Sciences	EVP and Chief Operating Officer
Charissa Levy	GTA Rehab Network	Executive Director
Jane DeLacy	William Osler Health System	Executive Director Clinical Services
Kathy Sabo	University Health Network Toronto Western Hospital	Senior Vice President Executive Head

Appendices

Appendix 1: Literature Search Strategies

Search date: May 16, 2013
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; All EBM Reviews

#	Searches	Results
1	exp Arthroplasty, Replacement, Hip/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or Arthroplasty, Replacement/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	20435
2	exp hip arthroplasty/ use emez or exp Hip Prosthesis/	55638
3	((hip* adj2 (replacement* or arthroplast*)) or ((femoral head* or hip*) adj2 prosthes?s) or THR).mp.	115083
4	or/1-3	119434
5	exp Arthroplasty, Replacement, Knee/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or Arthroplasty, Replacement/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	16304
6	exp knee arthroplasty/ use emez or exp Knee Prosthesis/	33189
7	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR).mp.	50406
8	or/5-7	54230
9	4 or 8	158633
10	exp Analgesia/	131354
11	exp Analgesics/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	452034
12	exp analgesic agent/ use emez	596408
13	exp Anesthesia/	412137
14	exp anesthetic agent/ use emez	204605
15	exp Anesthetics/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	219860
16	or/10-13	1426782
17	(infiltra* or instill* or infus* or lia).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw, tn, dm, mf, dv, nm, kf, ps, rs, ui]	983304
18	16 and 17	87227
19	((Intraarticular or knee* or hip? or intra-articular or periarticular or peri-articular or wound* or joint*) adj2 (injection* or infiltat* or infus* or instill*)).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw, tn, dm, mf, dv, nm, kf, ps, rs, ui]	18114
20	((infiltra* or instill* or infus*) adj2 (analgesi* or an?esthesia*or ropivacaine or ketorolac or adrenaline or steroid* or magnesium sulphate or morphine or nonsteroidal anti-inflammatory or nsaid* or opiod* or anti-hyperalgesic* or pregabalin or s-ketamine or epinephrine or bupivacaine)).mp. [mp=ti, ab, tx, kw, ct, ot, sh, hw, tn, dm, mf, dv, nm, kf, ps, rs, ui]	15585
21	lia.mp.	1474
22	19 or 20 or 21	34538
23	18 or 22	111906
24	9 and 23	2053
25	limit 24 to (english language and yr="2008 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	997
26	remove duplicates from 25	691
27	(Meta Analysis or Controlled Clinical Trial or Randomized Controlled Trial).pt.	867226
28	Meta-Analysis/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Technology Assessment, Biomedical/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	49681
29	Meta Analysis/ use emez or Biomedical Technology Assessment/ use emez	82162
30	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane or ((health technolog* or biomedical technolog*) adj2 assess*)).ti,ab.	354090
31	exp Random Allocation/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Double-Blind Method/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Control Groups/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Placebos/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	331119
32	Randomized Controlled Trial/ use emez or exp Randomization/ use emez or exp RANDOM SAMPLE/ use emez or Double Blind Procedure/ use emez or exp Triple Blind Procedure/ use emez or exp Control Group/ use emez or exp PLACEBO/ use emez	613192
33	(random* or RCT or placebo* or sham* or (control* adj2 clinical trial*)).ti,ab.	2090938
34	exp Standard of Care/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Guideline/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Guidelines as Topic/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	130082
35	exp Practice Guideline/ use emez or exp Professional Standard/ use emez	545615
36	(guideline* or guidance or consensus statement* or standard or standards).ti.	234585
37	or/27-36	3641482
38	26 and 37	352

Appendix 2: Quality Assessment Tables

Table A1: AMSTAR score of Reviews[a]

Author, Year	AMSTAR score[a]	1) Provided Study Design	2) Duplicate Study Selection	3) Broad Literature Search	4) Considered Status of Publication	5) Listed Excluded Studies	6) Provided Characteristics of Studies	7) Assessed Scientific Quality	8) Considered Quality in Report	9) Methods to Combine Appropriate	10) Assessed Publication Bias	11) Stated Conflict of Interest
Fischer et al, 2008 (4)	8	✓		✓		✓	✓	✓	✓	✓		✓
Gibbs et al, 2012 (8)	1						✓					
McCarthy & Iohom, 2012 (9)	5	✓		✓			✓	✓	✓			
Starks, 2011 (5)	1						✓					

[a] Details of AMSTAR method are described in Shea et al. (6)

Table A2: GRADE Evidence Profile for Local Infiltration Analgesia in Primary Hip and Knee Arthroplasty

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Pain in TKA population							
8 (RCTs)	No serious limitations[a]	Serious limitations (−1)[b]	Very serious limitations (−2)[c]	No serious limitations[d]	Undetected	None	⊕ Very Low
Pain in THA population							
8 (RCTs)	Serious limitations (−1)[a]	Serious limitations (−1)[b]	Very serious limitations (−2)[c]	No serious limitations[e]	Undetected	None	⊕ Very Low
2 (observational)	Serious limitations (−1)[a]	Serious limitations (−1)[b]	Very serious limitations (−2)[c]	No serious limitations[e]	Undetected	None	⊕ Very Low
Length of Stay in THA population							
5 (RCTs)	Serious limitations (−1)[a]	Serious limitations (−1)[b]	Very serious limitations (−2)[c]	No serious limitations[f]	Undetected	None	⊕ Very Low

Abbreviations: RCT, randomized controlled trial; THA, total hip arthroplasty; TKA, total knee arthroplasty

[a] For details about risk of bias of individual studies see Table A3 and Table A4.

[b] Some studies identified a statistically significant difference while others found no difference or had inconclusive results.

[c] All studies had differences in protocols for the administration of local infiltration analgesics with variations in medication types, dosage, and timing of administration as well as differences in control groups including the use of a placebo, usual care, or no control arm.

[d] No meta-analysis was conducted; using the power calculation provided in the publication by Bianconi et al (21), all study samples were sufficiently large.

[e] No meta-analysis was conducted; using the power calculation provided in the publication by Bianconi et al (21), all but 2 of the study samples were sufficiently large.

[f] No meta-analysis was conducted; appropriate power calculation for outcome of length of stay is unknown.

Table A3: Risk of Bias Among Randomized Controlled Trials for the Examination of Local Infiltration Analgesia

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
TKA population					
Badner et al, 1996 (10)	No limitations	No limitations	No limitations	No limitations	None
Badner et al, 1997 (11)	No limitations	No limitations	No limitations	No limitations	None
Browne et al, 2004 (12)	No limitations	No limitations	No limitations	No limitations	None
Klasen et al, 1999 (13)	Limitations[a]	Limitations[b]	Limitations[c]	No limitations	None
Mauerhan et al, 1997 (14)	No limitations	No limitations	No limitations	No limitations	None
Nechleba et al, 2005 (15)	No limitations	No limitations	No limitations	No limitations	None
Ritter et al, 1999 (16)	No limitations	No limitations	No limitations	No limitations	None
Tanaka et al, 2001 (17)	No limitations	No limitations	No limitations	No limitations	None
THA population					
Andersen et al, 2007 (18)	Limitations[d]	Limitations[b]	Limitations[c]	No limitations	None
Andersen et al, 2007 (19)	No limitations	No limitations	Limitations[c]	No limitations	None
Andersen et al, 2011 (20)	No limitations[e]	No limitations	No limitations	No limitations	None
Bianconi et al, 2003 (21)	Limitations[d]	No limitations	No limitations	No limitations	None
Busch et al, 2010 (22)	Limitations[a]	No limitations	No limitations	No limitations	None
Lunn et al, 2011 (24)	No limitations	No limitations	No limitations	No limitations	None
Parvateneni et al, 2007 (26)	Limitations[a]	Limitations[e]	No limitations	No limitations	None
Specht et al, 2011 (27)	No limitations	No limitations	No limitations	No limitations	None

Abbreviations: THA, total hip arthroplasty; TKA, total knee arthroplasty.

[a] Surgeons were not blinded though the assessors were.

[b] Patients were not blinded; catheter placement location differed between study groups.

[c] Per protocol analysis, as opposed to intention-to-treat analysis, was conducted.

[d] Surgeons were not blinded.

[e] Patient blinding may be compromised due to differences in the protocols for the various arms of the study.

Table A4: Risk of Bias Among Observational Trials for the Examination of Local Infiltration Analgesia

Author, Year	Appropriate Eligibility Criteria	Appropriate Measurement of Exposure	Appropriate Measurement of Outcome	Adequate Control for Confounding	Complete Follow-Up
THA population					
Kerr & Lohan, 2008 (23)	Limitations[a]	No limitations	Limitations[b]	Limitations[c]	No limitations
Otte et al, 2008 (25)	No limitations	No limitations	Limitations[b]	Limitations[c]	No limitations

Abbreviations: THA, total hip arthroplasty.

[a] Unclear eligibility criteria.

[b] Patients were not blinded, which may bias the measurement of subjective outcomes such as pain.

[c] Inadequate controlling for potential confounding conducted in analysis.

References

(1) British Orthopaedic Association. Primary total hip replacement: a guide to good practice. London: British Orthopaedic Association, 1999; revised August 2006. pp. 1-37. Chandlers Printers Ltd., East Sussex, England.

(2) Bone and Joint Canada. Hip and knee replacement surgery toolkit. Canada: Bone & Joint Canada; 2009 pp. 79.

(3) Mak JC, Fransen M, Jennings M, March L, Mittal R, Harris IA. Evidence-based review for patients undergoing elective hip and knee replacement. ANZ J Surg. 2013 Mar 15.

(4) Fischer HB, Simanski CJ, Sharp C, Bonnet F, Camu F, Neugebauer EA, et al. A procedure-specific systematic review and consensus recommendations for postoperative analgesia following total knee arthroplasty. Anaesthesia. 2008 Oct;63(10):1105-23.

(5) Starks I, Wainwright T, Middleton R. Local anaesthetic infiltration in joint replacement surgery: What is its role in enhanced recovery? ISRN Anesthesiology. 2011:doi: 10.5402/2011/742927.

(6) Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol. 2007;7:10.

(7) Guyatt GH, Oxman AD, Schunemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol. 2011 Apr;64(4):380-2.

(8) Gibbs DM, Green TP, Esler CN. The local infiltration of analgesia following total knee replacement: a review of current literature. J Bone Joint Surg Br. 2012 Sep;94(9):1154-9.

(9) McCarthy D, Iohom G. Local infiltration analgesia for postoperative pain control following total hip arthroplasty: a systematic review. Anesthesiol Res Pract. 2012;2012:709531.

(10) Badner NH, Bourne RB, Rorabeck CH, MacDonald SJ, Doyle JA. Intra-articular injection of bupivacaine in knee-replacement operations. Results of use for analgesia and for preemptive blockade. J Bone Joint Surg Am. 1996 May;78(5):734-8.

(11) Badner NH, Bourne RB, Rorabeck CH, Doyle JA. Addition of morphine to intra-articular bupivacaine does not improve analgesia following knee joint replacement. Reg Anesth. 1997 Jul;22(4):347-50.

(12) Browne C, Copp S, Reden L, Pulido P, Colwell C, Jr. Bupivacaine bolus injection versus placebo for pain management following total knee arthroplasty. J Arthroplasty. 2004 Apr;19(3):377-80.

(13) Klasen JA, Opitz SA, Melzer C, Thiel A, Hempelmann G. Intraarticular, epidural, and intravenous analgesia after total knee arthroplasty. Acta Anaesthesiol Scand. 1999 Nov;43(10):1021-6.

(14) Mauerhan DR, Campbell M, Miller JS, Mokris JG, Gregory A, Kiebzak GM. Intra-articular morphine and/or bupivacaine in the management of pain after total knee arthroplasty. J Arthroplasty. 1997 Aug;12(5):546-52.

(15) Nechleba J, Rogers V, Cortina G, Cooney T. Continuous intra-articular infusion of bupivacaine for postoperative pain following total knee arthroplasty. J Knee Surg. 2005 Jul;18(3):197-202.

(16) Ritter MA, Koehler M, Keating EM, Faris PM, Meding JB. Intra-articular morphine and/or bupivacaine after total knee replacement. J Bone Joint Surg Br. 1999 Mar;81(2):301-3.

(17) Tanaka N, Sakahashi H, Sato E, Hirose K, Ishii S. The efficacy of intra-articular analgesia after total knee arthroplasty in patients with rheumatoid arthritis and in patients with osteoarthritis. J Arthroplasty. 2001 Apr;16(3):306-11.

(18) Andersen KV, Pfeiffer-Jensen M, Haraldsted V, Soballe K. Reduced hospital stay and narcotic consumption, and improved mobilization with local and intraarticular infiltration after hip arthroplasty: a randomized clinical trial of an intraarticular technique versus epidural infusion in 80 patients. Acta Orthop. 2007 Apr;78(2):180-6.

(19) Andersen LJ, Poulsen T, Krogh B, Nielsen T. Postoperative analgesia in total hip arthroplasty: a randomized double-blinded, placebo-controlled study on peroperative and postoperative ropivacaine, ketorolac, and adrenaline wound infiltration. Acta Orthop. 2007 Apr;78(2):187-92.

(20) Andersen LO, Otte KS, Husted H, Gaarn-Larsen L, Kristensen B, Kehlet H. High-volume infiltration analgesia in bilateral hip arthroplasty. A randomized, double-blind placebo-controlled trial. Acta Orthop. 2011 Aug;82(4):423-6.

(21) Bianconi M, Ferraro L, Traina GC, Zanoli G, Antonelli T, Guberti A, et al. Pharmacokinetics and efficacy of ropivacaine continuous wound instillation after joint replacement surgery. Br J Anaesth. 2003 Dec;91(6):830-5.

(22) Busch CA, Whitehouse MR, Shore BJ, MacDonald SJ, McCalden RW, Bourne RB. The efficacy of periarticular multimodal drug infiltration in total hip arthroplasty. Clin Orthop Relat Res. 2010 Aug;468(8):2152-9.

(23) Kerr DR, Kohan L. Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. Acta Orthop. 2008 Apr;79(2):174-83.

(24) Lunn TH, Husted H, Solgaard S, Kristensen BB, Otte KS, Kjersgaard AG, et al. Intraoperative local infiltration analgesia for early analgesia after total hip arthroplasty: a randomized, double-blind, placebo-controlled trial. Reg Anesth Pain Med. 2011 Sep;36(5):424-9.

(25) Otte KS, Husted H, Andersen LØ, Kristensen BB, Kehlet H. Local infiltration analgesia in total knee arthroplasty and hip resurfacing: a methodological study. Acute Pain. 2008;10(3-4):111-6.

(26) Parvataneni HK, Shah VP, Howard H, Cole N, Ranawat AS, Ranawat CS. Controlling pain after total hip and knee arthroplasty using a multimodal protocol with local periarticular injections: a prospective randomized study. J Arthroplasty. 2007 Sep;22(6 Suppl 2):33-8.

(27) Specht K, Leonhardt JS, Revald P, Mandoe H, Andresen EB, Brodersen J, et al. No evidence of a clinically important effect of adding local infusion analgesia administrated through a catheter in pain treatment after total hip arthroplasty. Acta Orthop. 2011 Jun;82(3):315-20.

Health Quality Ontario
130 Bloor Street West, 10th Floor
Toronto, Ontario
M5S 1N5
Tel: 416-323-6868
Toll Free: 1-866-623-6868
Fax: 416-323-9261
Email: EvidenceInfo@hqontario.ca
www.hqontario.ca

© Queen's Printer for Ontario, 2013