Ontario
Health Quality Ontario
Qualité des services de santé Ontario

Anesthesia Among Patients Undergoing 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. Anesthesia among patients undergoing knee arthroplasty: a rapid review. Toronto, ON: 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 branch 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 as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. 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
NR	Not reported
RCT	Randomized controlled trial
SD	Standard deviation

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 is to examine the safety and effectiveness of regional anesthesia versus general anesthesia among patients undergoing primary knee arthroplasty.

Clinical Need and Target Population

Anesthesia is required among patients undergoing knee arthroplasty. The 2 main categories of anesthesia are general and regional. According to definitions from the Canadian Anesthesiologists' Society, general anesthesia is a reversible state of complete unconsciousness with loss of memory, pain relief, and muscle relaxation induced by drugs typically administered intravenously or by inhaled induction. (1) Regional anesthesia is the injection of a local anesthetic to an area of the body close to a nerve or group of nerves that supply function or feeling to the area of body involved in an operation. (1)

When deciding what anesthesia is to be used, several factors are considered by the surgical team. With all things being equal, there is currently uncertainty over potential benefits or risks to patients who receive general versus regional anesthesia when undergoing knee arthroplasty.

Rapid Review

Research Question

What is the safety and effectiveness of regional anesthesia versus general anesthesia among patients undergoing primary knee arthroplasty?

Research Methods

Literature Search

A literature search was performed on April 19, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for studies published from January 1, 2008, until April 19, 2013. 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, until April 19, 2013
- systematic reviews, health technology assessments, and meta-analyses
- primary knee arthroplasty
- compared regional anesthesia to general anesthesia

Exclusion Criteria

- studies where results on outcomes of interest could not be abstracted
- case reports, editorials, letters, comments, and conference abstracts

Outcomes of Interest

- hospital length of stay
- mortality

Expert Panel

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

The role of the Expert Advisory Panel on Episodes of Care for Hip and Knee Arthroplasty was to place the evidence produced by Health Quality Ontario into context and to provide advice on the appropriate clinical pathway for hip and knee arthroplasty in Ontario health care. 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) tool was used to assess the quality of the final selection of systematic reviews. (2) Primary studies were abstracted from the selected reviews and referenced for assessment of 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. (3) The overall quality was determined to be very low, low, moderate, or high via a step-wise, structural method.

Study design was the first consideration; the starting assumption was that randomized controlled trials (RCTs) 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 can raise the quality of evidence were considered: large magnitude of effect, dose-response gradient, and accounting for all residual confounding factors. (3) For more detailed information, please refer to the latest series of GRADE articles. (3)

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

High	Very confident that the true effect lies close to the estimate of the effect;
Moderate	Moderately confident 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	Confidence in the effect estimate is limited—the true effect could 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 Literature Search

The database search yielded 457 citations published between January 1, 2008, and April 19, 2013 (with duplicates removed). Articles were excluded on the basis of information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

One systematic review met the inclusion criteria. The reference lists of studies that were deemed topically relevant and health technology assessment websites were hand searched to identify any potentially relevant studies, and no additional citations were identified.

Quality Assessment of Reviews

As assessed by the AMSTAR score, the quality of the included review was a 7 of a possible 11 (see Appendix 2, Table A1).

Summary of Included Studies

The systematic review by Macfarlane et al was published in 2009 and included RCTs published between 1990 and 2008. (4) Its objective was to determine whether regional anesthesia improves patient outcomes after knee arthroplasty; it identified 28 studies with a total of 1,538 patients. (4) There was no meta-analysis or other qualitative summary of effect estimates. (4) The authors concluded that regional anesthesia reduced pain, morphine consumption, and opioid-related adverse effects. As well, it can reduce length of stay and aid in rehabilitation. (4) Additionally, the authors noted no difference in blood loss or in the length of surgery and insufficient evidence that anesthesia type affected mortality, cardiovascular morbidity or deep vein thrombosis, and pulmonary embolism. (4) The systematic review's scope was larger than the scope of interest for this rapid review, and therefore the reference list was hand searched to identify individual articles that met the review's inclusion criteria. This resulted in a final inclusion of 4 RCTs evaluating the 2 identified outcomes of interest summarized in Table 1. (5-8)

Table 1: Randomized Controlled Trials Assessing General Versus Regional Anesthesia

Author, Year	Population	Sample Size (Intervention/ Control)	Regional Anesthesia Group (Intervention)	General Anesthesia Group (Control)
Mitchell et al, 1991 (5)	Knee arthroplasty	72 (34/38)	Epidural anesthesia (pharmaceutical unspecified)	General anesthesia (sodium thiopental, succinylcholine, halogenated agent, and nitrous oxide in oxygen)
Moiniche et al, 1994 (6)	Hip or knee arthroplasty	Knee group: 20 (10/10)	Continuous epidural (bupivacaine plus morphine) for 48 hours post-surgery and oral piroxacam	General anesthesia and intramuscular opioid (midazolam, fentanyl, and pancuronium) and acetaminophen
Williams-Russo et al, 1995 (7)	Knee arthroplasty	262 (134/128)	Epidural (lidocaine or bupivicaine, and midazolam or fentanyl) and post-surgery epidural analgesia as requested	General anesthesia (thiopental sodium, fentanyl, vecuronium, and nitrous oxide) and post-surgery intravenous analgesia
Williams-Russo et al, 1996[a] (8)	Knee arthroplasty	178 (97/81)	Epidural (lidocaine or bupivicaine, and midazolam or fentanyl) and post-surgery epidural analgesia as requested	General anesthesia (thiopental sodium, fentanyl, vecuronium, and nitrous oxide) and post-surgery intravenous analgesia

[a]Subgroup of Williams-Russo et al, 1995 study (7) of patients who received thromboembolic prophylaxis.

Results for Outcomes of Interest

Mortality

One RCT examined mortality as an outcome of interest, with results described in Table 2.

Table 2: Mortality Among Patients Receiving Regional Versus General Anesthesia When Undergoing Primary Knee Arthroplasty

Author, Year	Sample Size	Results for Outcome of Mortality	Statistical Significance
Williams-Russo et al, 1995 (7)	262	2 months after surgery: Regional anesthesia group: 1 death General anesthesia group: 1 death	Not significant[a]

[a]Not reported in the publication, but based on a calculation of the odds ratio using the raw data presented.

No statistical analysis was provided for this outcome. An odds ratio calculation using the data provided in the publication showed no statistically significant difference between the study groups for the outcome of mortality (odds ratio 0.95, 95% confidence interval 0.06, 15.43). The GRADE for the quality of evidence was evaluated as very low; details are provided in Appendix 2, Table A2.

Hospital Length of Stay

The 4 RCTs all reported on hospital length of stay. Because of limitations in the data available, a meta-analysis was not conducted. Individual study results are described in Table 3. (5-8)

Table 3: Hospital Length of Stay Among Patients Receiving Regional Versus General Anesthesia When Undergoing Primary Knee Arthroplasty

Author, Year	Sample Size	Mean Length of Stay, Days (SD)		Statistical Significance
		Regional Anesthesia Group	General Anesthesia Group	
Mitchell et al, 1991 (5)	72	11.0 (NR)	10.4 (NR)	Not significant[a]
Moinische et al, 1994 (6)	20	12.0 (NR)	13.0 (NR)	Not significant[a]
Williams-Russo et al, 1995 (7)	262	12.7 (5.3)	12.7 (4.3)	Not significant[a]
Williams-Russo et al, 1996 (8)[b]	178	12.1 (4.5)	12.7 (4.3)	*P* = 0.27

Abbreviations: NR, not reported; SD, standard deviation.

[a] As reported in publication, no *P* value was published.

[b] Subgroup of Williams-Russo et al 1995 study (7) of patients who received thromboembolic prophylaxis.

All studies identified no statistically significant difference in the hospital length of stay among knee arthroplasty patients who received regional anesthesia versus those who received general anesthesia. The GRADE for the quality of evidence was evaluated as very low; details are provided in Appendix 2, Table A2.

The Canadian Institute for Health Information stated in 2006 that the average length of stay for Ontario patients undergoing hip or knee replacements was 7 days for men and 8 for women. (9) This was further placed into context by the Expert Advisory Panel, who stated that the current average length of stay for these patients in Ontario is closer to 4 days. Consequently, the evidence on the effect of regional versus

general anesthesia on hospital length of stay among patients undergoing primary knee arthroplasty in Ontario is considered insufficient.

Addendum

On the advice of the Expert Panel, a pivotal observational study comparing regional to general anesthesia in primary total joint arthroplasty had recently been published. These results, along with the very low quality of evidence obtained from the original rapid review, prompted a decision to add and evaluate observational data.

The original literature search was revisited in light of the same inclusion and exclusion criteria as the original rapid review, with the modification of limiting to the last 2 years and including observational studies (search dates from January 1, 2011, to April 19, 2013). Two observational studies were identified, in addition to the 1 study identified by the Expert Panel that was published 1 month after the original literature search dates; 3 observational studies are included in this addendum.

Table 4 briefly describes the included studies. Of the 3 studies 2 used the same administrative data source; the Stundner et al (10) publication is a subgroup of the study by Memtsoudis et al (11).

Table 2: Summary of Observational Studies

Author, Year	Location	Data Source	Population	Sample Size	Study groups
Memtsoudis, 2013 (11)	USA	Premier Perspective, Inc.[a]	All primary lower extremity joint arthroplasty conducted 2006–2010 (TKAs and THAs)	356,028 TKAs; 172,467 THAs	3 groups: -neuraxial anesthesia general anesthesia neuraxial + general anesthesia
Stundner, 2012 (10)	USA	Premier Perspective, Inc.[a]	Bilateral TKAs conducted 2006–2010	15,687	3 groups: -neuraxial anesthesia general anesthesia neuraxial + general anesthesia
Pugely, 2013 (12)	USA	ACS NSQIP[b]	TKAs 2005–2010	14,052	Spinal anesthesia General anesthesia

Abbreviations: ACS NSQIP, American College of Surgeons National Surgical Quality Improvement Program; THA, total hip arthroplasty; TKA, total knee arthroplasty.

[a]Includes data from approximately 400 acute care hospitals throughout the United States.

[b]Includes data from 258 hospitals throughout the United States.

Addendum Results for Outcomes of Interest

Mortality

The Memtsoudis et al (11) study identified a statistically significant decrease in 30-day mortality among patients who underwent TKA and received regional anesthesia compared with those who received general anesthesia (Table 5). The body of evidence for the outcome of 30-day mortality was evaluated as low quality (Appendix 3, Table A4).

Table 3: 30-Day Mortality Results From Observational Studies Among Patients Receiving Regional Versus General Anesthesia When Undergoing Primary Knee Arthroplasty

Author, Year	Sample size (intervention/ control)	Results
Memtsoudis, 2013 (11)	28,426 regional/194,682 general anesthesia	Odds ratio[a] 0.55 (95% confidence interval 0.32–0.93)[b]

[a]Multivariate weighted logistic regression adjusted for age, sex, race, admission type, payer type, hospital size, hospital location, hospital teaching status, surgical pathology, and comorbidity burden.
[b]Calculated inverse of effect estimate reported in original publication.

Given the limitations of the data reported, neither Stundner et al (10) nor Pugely et al (12) were included in the analysis. Both studies reported only unadjusted numbers for the outcome of mortality, and neither found a statistically significant difference between the regional and general anesthesia study groups.

Length of Stay

Stundner et al (10) identified no statistically significant difference between groups in hospital length of stay (Table 6). Evidence for the outcome of length of stay was evaluated as low quality (Appendix 3, Table A4).

Table 4: Length of Stay Results From Observational Studies Among Patients Receiving Regional Versus General Anesthesia When Undergoing Primary Knee Arthroplasty

Author, Year	Sample size (intervention/ control)	Results
Stundner, 2012 (10)	1,066 regional/12,567 general anesthesia	Odds ratio[a] 1.07 (95% confidence interval 0.91–1.26)

[a]Adjusted for age, sex, race, and comorbidity burden.

Memtsoudis et al (11) did not report on length of stay and, due to the limitations of the data reported, the study by Pugely et al (12) was excluded from the current analysis. Pugely et al (12) reported only unadjusted numbers for the outcome of length of stay and reported a statistically significant decrease among patients who received regional versus general anesthesia.

Conclusions

From the examination of 1 systematic review of randomized controlled trials as part of the rapid review:

- Based on very low quality of evidence, there was no significant difference in mortality for patients who received regional anesthesia versus those who received general anesthesia for primary knee arthroplasty.

- Based on very low quality of evidence, there was no significant difference in hospital length of stay for patients who received regional anesthesia versus those who received general anesthesia for primary knee arthroplasty.

From the examination of observational studies as part of the addendum to the rapid review:

- Based on low-quality evidence, there was a statistically significant decrease in 30-day mortality among patients who received regional versus general anesthesia for primary knee arthroplasty.

- Based on low-quality evidence, there was no significant different in hospital length of stay among patients who received regional versus general anesthesia for primary knee arthroplasty.

Acknowledgements

Editorial Staff

Elizabeth Jean Betsch, ELS

Medical Information Services

Corinne Holubowich, BEd, MLIS
Kellee Kaulback, BA(H), MISt

Expert Advisory Panel for Health Quality Ontario on 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

Panel Member	Affiliation(s)	Appointment(s)
Dr Christopher Jyu	Rouge Valley Health System The Scarborough Hospital	Primary Care Lead
Internal Medicine		
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: April 19, 2013
Databases searched: Ovid MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; Cochrane Library; Centre for Reviews and Dissemination
Limits: 2008-current; English; removal of case reports, editorials, letters, comments, conference abstracts
Filters: none

Database: Embase 1980 to 2013 Week 15, Ovid MEDLINE(R) 1946 to April Week 2 2013, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations April 18, 2013
Search Strategy:

#	Searches	Results
1	exp Arthroplasty, Replacement, Knee/ use mesz or Arthroplasty, Replacement/ use mesz	14761
2	exp knee arthroplasty/ use emez or exp Knee Prosthesis/	32528
3	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR).mp.	47547
4	or/1-3	51194
5	exp Anesthesia, Conduction/ use mesz	50849
6	exp regional anesthesia/ use emez or exp epidural anesthesia/ use emez or exp local anesthesia/ use emez or exp spinal anesthesia/ use emez	90421
7	(((an?esthet* or an?esthesia) adj4 (conduction or regional* or local* or spinal or epidural or neuraxial*)) or nerve block*).ti,ab.	127244
8	or/5-7	198034
9	4 and 8	2143
10	limit 9 to english language	1949
11	Case Reports/ or Comment.pt. or Editorial.pt. or Letter.pt. or Congresses.pt.	3976280
12	Case Report/ or Comment/ or Editorial/ or Letter/ or conference abstract.pt.	6638882
13	or/11-12	6709824
14	10 not 13	1342
15	limit 14 to yr="2008 -Current"	660
16	remove duplicates from 15	437

Cochrane

ID	Search	Hits
#1	MeSH descriptor: [Arthroplasty, Replacement, Knee] explode all trees	1279
#2	MeSH descriptor: [Arthroplasty, Replacement] explode all trees	2541
#3	MeSH descriptor: [Knee Prosthesis] explode all trees	501
#4	((knee* near/2 (replacement* or arthroplast*)) or (knee* near/2 prosthes?s) or TKR):ti,ab,kw (Word variations have been searched)	2211
#5	#1 or #2 or #3 or #4	3444
#6	MeSH descriptor: [Anesthesia, Conduction] explode all trees	6954
#7	(((an?esthet* or an?esthesia) near/4 (conduction or regional* or local* or spinal or epidural or neuraxial*)) or nerve block*):ti (Word variations have been searched)	2815
#8	(((an?esthet* or an?esthesia) near/4 (conduction or regional* or local* or spinal or epidural or neuraxial*)) or nerve block*):ab (Word variations have been searched)	4963
#9	#6 or #7 or #8	10133
#10	#5 and #9 from 2008 to 2013	131

Centre for Reviews and Dissemination

Line	Search	Hits
1	MeSH DESCRIPTOR Arthroplasty, Replacement, Knee EXPLODE ALL TREES	242
2	MeSH DESCRIPTOR Arthroplasty, Replacement EXPLODE ALL TREES	480
3	MeSH DESCRIPTOR Knee Prosthesis EXPLODE ALL TREES	60
4	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR)	429
5	#1 OR #2 OR #3 OR #4	666
6	MeSH DESCRIPTOR Anesthesia, Conduction EXPLODE ALL TREES	226
7	(((an?esthet* or an?esthesia) adj4 (conduction or regional* or local* or spinal or epidural or neuraxial*)) or nerve block*)	453
8	#6 OR #7	454
9	#5 AND #8	24
10	(#9) FROM 2008 TO 2013	15

Appendix 2: Quality Assessment Tables

Table A1: AMSTAR Score of Reviews

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
Macfarlane et al, 2009 (4)	7	✓		✓			✓	✓	✓	✓		✓

Abbreviation: AMSTAR, Assessment of Multiple Systematic Reviews.
[a]Details of AMSTAR method are described in Shea et al. (2)

Table A2: GRADE Evidence Profile for Comparison of Regional Anesthesia Versus General Anesthesia

No. of Studies by Design	Risk of Bias[a]	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Mortality							
1 RCT	Serious limitations (−1)	No serious limitations	No serious limitations	Very serious limitations (−2)[d]	Undetected	None	⊕ Very low
Length of Stay							
4 RCTs	Very serious limitations (−2)	No serious limitations	Serious limitations (−1)[b]	Serious limitations (−1)[c]	Undetected	None	⊕ Very low

Abbreviations: GRADE, Grading of Recommendations Assessment, Development and Evaluation; No., number; RCT, randomized controlled trial.
[a]Details on risk of bias are described in Table A3.
[b]Because average hospital length of stay differed, the Episode of Care Expert Advisory Panel considered the body of literature different from the current Ontario context.
[c]Limited data available make confidence intervals around an effect estimate immeasureable.
[d]Sample size does not meet optimal information size criteria, and confidence intervals around the odds are wide.

Table A3: Risk of Bias Among Randomized Controlled Trials for Comparison of Regional Versus General Anesthesia

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Mitchell et al, 1991 (5)	Limitations[a]	Limitations[b]	No limitations	No limitations	Limitations[c]
Moiniche et al, 1994 (6)	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Williams-Russo et al, 1995 (7)	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations
Williams-Russo et al, 1996 (8)[d]	Limitations[a]	Limitations[b]	No limitations	No limitations	No limitations

[a]Health care providers could not be blinded to treatment group and as a result might have biased evaluation of subjective outcomes (e.g., pain).

[b]Patients could not be blinded to their study group of regional or general anesthesia and as a result might have biased evaluation of subjective outcomes (e.g., pain). Length of stay could be influenced by patients' pain.

[c]Treatment protocols differed by sex, but results showed no indication of bias between study groups. Men received 650 mg of acetylsalicylic acid while women were given low-dose warfarin the night before surgery.

[d]Subgroup of Williams-Russo et al,1995 study (7) of patients who received thromboembolic prophylaxis.

Appendix 3: Quality Assessment Tables for Addendum

Table A4: GRADE Evidence Profile for Comparison of Regional Versus General Anesthesia in Observational Studies

No. of Studies (Design)	Risk of Bias[a]	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Mortality							
1 Observational	No serious limitations	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low
Length of Stay							
1 Observational	No serious limitations	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕⊕ Low

[a]Details on risk of bias are available in Table A5

Table A5: Risk of Bias Among Observational Studies for Comparison of Regional Versus General Anesthesia

Author, Year	Appropriate Eligibility Criteria	Appropriate Measurement of Exposure	Appropriate Measurement of Outcome	Adequate Control for Confounding	Complete Follow-Up
Stundner et al, 2012 (10)	No limitations	No limitations	No limitations	No limitations [a]	No limitations
Memtsoudis et al, 2013 (11)	No limitations	No limitations	No limitations	No limitations [b]	No limitations

[a]Multivariate regression model and propensity score matching was conducted for evaluation of certain outcomes.
[b]Multivariate regression model was conducted for evaluation of certain outcomes.

References

(1) van der Vyver M. Anesthesia: general, regional, local [Internet]. Canadian Anesthesiologists' Society; [updated 2010; cited 2013 May 1]. Available from: http://www.cas.ca/English/Types-of-anesthesia.

(2) 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):1-7.

(3) 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.

(4) Macfarlane AJ, Prasad GA, Chan VW, Brull R. Does regional anesthesia improve outcome after total knee arthroplasty? Clin Orthop Relat Res. 2009 Sep;467(9):2379-402.

(5) Mitchell D, Friedman RJ, Baker JD III, Cooke JE, Darcy MD, Miller MC III. Prevention of thromboembolic disease following total knee arthroplasty. Epidural versus general anesthesia. Clin Orthop Relat Res. 1991 Aug;(269):109-12.

(6) Moiniche S, Hjortso NC, Hansen BL, Dahl JB, Rosenberg J, Gebuhr P, et al. The effect of balanced analgesia on early convalescence after major orthopaedic surgery. Acta Anaesthesiol Scand. 1994 May;38(4):328-35.

(7) Williams-Russo P, Sharrock NE, Mattis S, Szatrowski TP, Charlson ME. Cognitive effects after epidural vs general anesthesia in older adults. A randomized trial. JAMA. 1995 Jul 5;274(1):44-50.

(8) Williams-Russo P, Sharrock NE, Haas SB, Insall J, Windsor RE, Laskin RS, et al. Randomized trial of epidural versus general anesthesia: outcomes after primary total knee replacement. Clin Orthop Relat Res. 1996 Oct;(331):199-208.

(9) Canadian Joint Replacement Registry. Hip and Knee Replacements in Canada. Ottawa: Canadian Institute for Health Information; 2006:1-88.

(10) Stundner O, Chiu YL, Sun X, Mazumdar M, Fleischut P, Poultsides L, et al. Comparative perioperative outcomes associated with neuraxial versus general anesthesia for simultaneous bilateral total knee arthroplasty. Reg Anesth Pain Med. 2012 Nov;37(6):638-44.

(11) Memtsoudis SG, Sun X, Chiu YL, Stundner O, Liu SS, Banerjee S, et al. Perioperative comparative effectiveness of anesthetic technique in orthopedic patients. Anesthesiology. 2013 May;118(5):1046-58.

(12) Pugely AJ, Martin CT, Gao Y, Mendoza-Lattes S, Callaghan JJ. Differences in short-term complications between spinal and general anesthesia for primary total knee arthroplasty. J Bone Joint Surg Am. 2013 Feb 6;95(3):193-9.

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