

# Nerve Blocks for Pain Management in Patients With Hip Fractures: A Rapid Review

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Clinical questions are developed by the Division of Evidence Development and Standards 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 (RCTs) and guidelines. Systematic reviews are evaluated using a rating scale developed for this purpose. If the 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 included in the systematic review are retrieved and a maximum of two outcomes are graded. If no well-conducted systematic reviews are available, RCTs and/or guidelines are evaluated. Because rapid reviews are completed in very short timeframes, other publication types are not included. All rapid reviews are developed and finalized in consultation with experts.

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Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. Health Quality Ontario works with clinical experts, scientific collaborators, and field evaluation partners to develop and publish research that evaluates the effectiveness and cost-effectiveness of health technologies and services in Ontario.

Based on the research conducted by Health Quality Ontario and its partners, the Ontario Health Technology Advisory Committee (OHTAC)—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.

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## **List of Abbreviations**

AMSTAR	Assessment of Multiple Systematic Reviews
CI	Confidence interval(s)
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HQO	Health Quality Ontario
OR	Odds ratio
RCT	Randomized controlled trial

## 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 <u>www.hqontario.ca</u>.

### **Objective of Analysis**

The objective of this rapid review is to identify the effectiveness of nerve blocks versus systemic analgesic for pain management when administered prior to hip fracture surgery.

### **Clinical Need and Target Population**

Pain management for patients with a hip fracture is a key concern as pain associated with a hip fracture is typically significant, may lead to exacerbations of delirium or depression, and may extend postsurgical lengths of stay. (1-3) Hip fracture patients are often elderly with multiple chronic conditions, raising potential concerns about using high doses of systemic analgesics in patients already taking multiple medications. (4) As a result, local analgesics, or nerve blocks, are being prescribed for pain management before, during, and after surgery. (5) How nerve blocks compare with systemic analgesics in this context is an important consideration because patients who receive nerve blocks sometimes also require pharmaceutical analgesics to help control their pain.

## **Rapid Review**

### **Research Question**

Is there evidence of the benefits and effectiveness of nerve blocks compared with systemic analgesics for pain control when administered prior to hip fracture surgery?

### **Research Methods**

#### Literature Search

A literature search was performed on January 29, 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 (CRD) database, for studies published up to January 29, 2013 (no startdate limit applied). Appendix 1 provides details of the search strategies used. 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 reports)
- published up to January 29, 2013
- systematic reviews, meta-analyses, and health technology assessments
- hip fracture population

#### **Exclusion Criteria**

• studies where outcomes of interest cannot be abstracted

#### **Outcomes of Interest**

- pain
- use of additional pain medication

#### **Expert Panel**

In December 2012, an Expert Advisory Panel on Episodes of Care for Hip Fractures was struck. The panel was comprised of physicians, personnel from the Ministry of Health and Long-Term Care, and representation from the community.

The role of the Expert Advisory Panel on Episode of Care for Hip Fractures was to contextualize the evidence produced by Health Quality Ontario and provide advice on the appropriate clinical pathway for a hip fracture 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.

#### **Statistical Analysis**

Where appropriate, a meta-analysis was performed using Review Manager Version 5. (6) A fixed-effect model was used, unless significant heterogeneity was observed ( $P \le 0.10$ ); then, a random-effects model was used to address significant heterogeneity. A *P* value of < 0.05 was considered statistically significant.

### **Quality of Evidence**

The Assessment of Multiple Systematic Reviews (AMSTAR) tool was used to assess the quality of the final selection of the systematic reviews. (7) Details on the outcomes of interest were abstracted from the selected review and primary studies were reviewed as needed.

The quality of the body of evidence for each outcome was examined according to the GRADE Working Group criteria. (8) 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. (8) For more detailed information, please refer to the latest series of GRADE articles. (8)

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 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 Literature Search**

The database search yielded 275 citations published up to January 29, 2013 (no start-date limit applied, 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.

Three systematic reviews met the inclusion criteria. (9-11) One of the identified reviews was updated in 2008 and this version was used for this rapid review. (9)

#### Quality Assessment of Reviews

As assessed by the AMSTAR scoring of reviews, (7), the quality of the reviews ranged from 2 to 11 out of a possible 11 (Appendix 2, Table A1). The Abou-Setta et al (11) paper received the highest possible AMSTAR score, was recently published, and included all studies referenced in the other two reviews identified. Therefore, for the purposes of this analysis, the Abou-Setta et al paper is examined.

#### **Summary of Review**

The systematic review by Abou-Setta et al was conducted to identify and synthesize the evidence on pain management for non-pathological hip fracture patients across 13 different interventions. (11) A total of 83 studies were included (69 RCTs) with a majority being comprised of older (> 75 years) women without cognitive impairment. The authors determined that, due to the sparseness of the available data, they could not draw firm conclusions to support the selection of one pain management approach over others. (11)

#### Pain

Abou-Setta et al identified 13 RCTs that examined the impact of nerve blocks versus systemic analgesics on acute pain post-treatment. (11) They found significant heterogeneity among the studies and therefore did not provide a summary estimate of the impact on pain among patients who received a nerve block versus no nerve block. The authors comment that the heterogeneity is largely related to the timing of administration of the nerve blocks and that limiting the meta-analysis to only those studies that randomized the pre-operative administration of pain medications (versus administration during or after surgery) minimizes some of the observed heterogeneity ( $I^2 = 92\%$  becomes  $I^2 = 53\%$ ). However, they do not report the effect estimate of this sensitivity analysis. (11) Because the analysis of pre-operatively administered pain management is of interest for this rapid review, the individual effect estimates as published by Abou-Setta et al (11) were applied to a meta-analysis of studies that administered the nerve blocks pre-operatively (Figure 1).

The random-effects model comparing the standardized mean difference of nerve blocks versus systemic analgesics administered pre-operatively identified a statistically significant decrease in postoperative pain among patients who received nerve blocks (standardized mean difference, -0.90; 95% confidence interval [CI], -1.18 to -0.62).

	Ner	ve Blo	ck	System	ic Analg	esic	:	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 3-in-1 nerve blo	ck								
Fletcher, 2003	0.57	0.53	24	1.34	0.53	26	11.4%	-1.43 [-2.06, -0.80]	
Subtotal (95% CI)			24			26	11.4%	-1.43 [-2.06, -0.80]	$\bullet$
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 4.47	′ (P < 0	.00001	)					
1.1.2 Epidural analge	sia								
Matot, 2003	1.16	0.45	34	1.71	0.64	34	14.2%	-0.98 [-1.49, -0.48]	
Scheinin, 2000	2.2	1.6	38	3.5	2	39	15.3%	-0.71 [-1.17, -0.25]	
Subtotal (95% CI)			72			73	29.5%	-0.83 [-1.17, -0.49]	$\bullet$
Heterogeneity: Tau <sup>2</sup> =	0.00; Cł	ni² = 0.0	61, df =	1 (P = 0.4	43); l² = (	0%			
Test for overall effect:	Z = 4.80	) (P < 0	.00001	)					
1.1.3 Fascia iliaca ne	rve bloo	:k							
Mouzopoulos, 2009	6.46	1.6	102	7.26	2	105	20.8%	-0.44 [-0.72, -0.16]	
Subtotal (95% CI)			102			105	20.8%	-0.44 [-0.72, -0.16]	•
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 3.12	2 (P = 0	.002)						
1.1.4 Femoral nerve	block								
Haddad, 1995	3.7	3.02	25	5.9	3.02	25	12.5%	-0.72 [-1.29, -0.14]	
Henderson, 2008	2.7	3.07	6	6.1	3.07	8	4.9%	-1.04 [-2.19, 0.11]	
Murgue, 2006	2.1	2.1	16	6.45	3.45	29	10.3%	-1.40 [-2.08, -0.72]	
Subtotal (95% CI)			47			62	27.7%	-1.01 [-1.46, -0.57]	$\bullet$
Heterogeneity: Tau <sup>2</sup> =	0.02; Cł	ni² = 2.2	28, df =	2 (P = 0.3	32); l² =	12%			
Test for overall effect:	Z = 4.45	5 (P < 0	.00001	)					
1.1.5 Psoas compart	ment ne	erve blo	ock						
Chudinov, 1999	1.4	0.6	20	2.1	0.7	20	10.6%	-1.05 [-1.72, -0.39]	- <b>-</b> -
Subtotal (95% CI)			20			20	10.6%	-1.05 [-1.72, -0.39]	$\bullet$
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 3.10	) (P = 0	.002)						
									•
Total (95% CI)			265			286	100.0%	-0.90 [-1.18, -0.62]	•
Heterogeneity: Tau <sup>2</sup> =	0.08; Cł	ni² = 14	.76, df	= 7 (P = 0	0.04); l² =	53%			
Test for overall effect:	Z = 6.24	↓ (P < 0	.00001	)					-4 -2 U Z 4 Favours perve block Favours sys analoesic
Fest for subgroup differences: Chi2 = 11.74, df = 4 (P = 0.02), I2 = 65.9%									

#### Figure 1: Comparison of Postoperative Pain in Groups Receiving Nerve Blocks Versus Systemic Analgesics Pre-operatively

Abbreviations: CI, confidence interval; df, degrees of freedom; IV, inverse variance; Random, random effects model; SD, standard deviation; Std, standardized; sys, systemic.

#### Quality Assessment

The quality assessment was conducted based on details published in the Abou-Setta et al systematic review. (11) A number of sources of risk of bias were identified; notably, 7 of the 8 included studies did not report details on their methods of allocation concealment, while the eighth study reported that patients were not blinded. Given the subjectivity of pain as an outcome, this risk of bias contributed to our assessment that the effect estimate for the outcome of pain is based on low quality of evidence (Appendix 2, Table A2).

#### **Use of Additional Pain Medication**

Abou-Setta et al conducted a meta-analysis of the 7 RCTs that reported an evaluation of additional pain medication required. (11) This meta-analysis concluded that patients who received nerve blocks requested additional pain medication less frequently than patients who did not receive nerve blocks (odds ratio [OR], 0.32; 95% CI, 0.14–0.72). (11) However, this analysis did not differentiate the timing of the administration of nerve blocks, and so a sensitivity analysis was conducted of the 4 studies that administered nerve blocks pre-operatively, based on the effect estimates published in Abou-Setta et al (11) (Figure 2).

The comparison of nerve blocks versus systemic analgesics administered pre-operatively identified no statistically significant difference in the need for additional pain medications between the two study groups (OR, 0.63; 95% CI, 0.29–1.38).

	Nerve Blo	ck	Systemic Analg	gesic		Odds Ratio		Odds	Ratio	
Study or Subgroup	Events 1	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	M-H, Fixe	ed, 95% CI	
1.4.1 3-in-1 nerve blo	ck									
Fletcher, 2003	1	24	1	26	5.7%	1.09 [0.06, 18.40]				
Subtotal (95% CI)		24		26	5.7%	1.09 [0.06, 18.40]				
Total events	1		1							
Heterogeneity: Not app	olicable									
Test for overall effect:	Z = 0.06 (P =	0.95)								
1.4.3 Fascia iliaca ne	rve block									
Foss. 2007	3	24	3	24	16.4%	1.00 [0.18, 5.53]				
Subtotal (95% CI)	-	24	-	24	16.4%	1.00 [0.18, 5.53]				
Total events	3		3							
Heterogeneity: Not app	olicable									
Test for overall effect:	Z = 0.00 (P =	= 1.00)								
1.4.4 Femoral nerve b	olock							_		
Gille, 2006	5	50	12	50	67.3%	0.35 [0.11, 1.09]			-	
Subtotal (95% CI)		50		50	67.3%	0.35 [0.11, 1.09]				
Total events	5		12							
Heterogeneity: Not app	olicable									
Test for overall effect:	Z = 1.81 (P =	= 0.07)								
1.4.6 Psoas compartr	nent nerve k	block								
Chudinov, 1999	3	20	2	20	10.6%	1.59 [0.24, 10.70]			•	
Subtotal (95% CI)		20		20	10.6%	1.59 [0.24, 10.70]				
Total events	3		2							
Heterogeneity: Not app	olicable									
Test for overall effect:	Z = 0.48 (P =	= 0.63)								
Total (95% CI)		118		120	100.0%	0.63 [0.29, 1.38]		•	•	
Total events	12		18							
Heterogeneity: Chi <sup>2</sup> = 2	2.35, df = 3 (I	P = 0.	50); l² = 0%				⊢			
Test for overall effect:	Z = 1.16 (P =	= 0.25)					0.01	0.1	1 10	100
Test for subaroup diffe	rences: Chi <sup>2</sup>	= 2.3	5, df = 3 (P = 0.5	0), l <sup>2</sup> = 0	)%		Favou	rs nerve block	ravours sys. a	algesic

#### Figure 2: Comparison of Need for Postoperative Analgesics in Groups Receiving Nerve Blocks Versus Systemic Analgesics Pre-operatively

Abbreviations: CI, confidence interval; df, degrees of freedom; Fixed, fixed effects model; M-H, Mantel-Haenszel; sys, systemic.

#### **Quality Assessment**

The quality assessment was conducted based on details published in the Abou-Setta et al systematic review. (11) A number of sources of risk of bias were identified: notably, 5 of the 7 included studies did not report details on the methods of allocation concealment, while 5 had other limitations including no source of funding declared. In addition, the need for additional pain medication is reported as a count of the number of times a patient required it, and no details are provided regarding the doses or total intake of additional analgesics. These limitations contributed to our assessment that the effect estimate for the outcome of additional pain medications is based on very low quality of evidence (Appendix 2, Table A2).

#### Delirium

At a meeting of the Expert Advisory Panel on Episodes of Care for Hip Fractures, it was determined that the addition of a third outcome, delirium, would be important to add to the examination of nerve blocks and pain management. The Abou-Setta et al systematic review identified 4 RCTs and 2 cohort studies that looked at mental status. (11) A statistically significant improvement in mental status was observed among patients who received a nerve block versus the control groups (RCT meta-analysis: OR, 0.33; 95% CI, 0.16–0.66; cohort study meta-analysis: OR, 0.24; 95% CI, 0.08–0.72). (11) However, this analysis included studies that administered nerve blocks before, during, and after surgery, and a sensitivity analysis limited to studies that used nerve blocks pre-operatively is not possible for this outcome based on the data provided in the Abou-Setta et al paper.

#### **Quality Assessment**

The quality of evidence for the outcome of delirium was assessed as moderate, as evaluated by Abou-Setta et al. (11) The authors state there is a medium risk of bias. They identified 1 study as having limitations with allocation concealment, 3 with blinding, and 2 with the complete accounting of patients and outcome events. No study had limitations with the selective reporting bias, 3 had other limitations including unclear declarations of the funding source, and 1 had limitations with the outcome of interest and comparability of cohorts. (11) No limitations were detected with respect to the consistency, directness, precision or other considerations identified. (11)

## Conclusions

- Based on low quality of evidence, there was a significant reduction in postoperative pain among hip fracture patients who pre-operatively received a nerve block versus systemic analgesic.
- Based on very low quality of evidence, there was no significant difference in the use of additional pain medications by hip fracture patients who received nerve block pre-operatively compared to patients who did not.
- Based on moderate quality of evidence, there was a statistically significant difference in mental status in favour of patients who received nerve blocks at any point in their hip fracture care (pre- or postoperatively) versus comparator groups.

## Acknowledgements

#### **Editorial Staff**

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Name	Role	Organization
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## Appendices

### **Appendix 1: Literature Search Strategies**

#### Search date: January 29, 2013

Databases searched: Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; Cochrane Library; Centre for Reviews and Dissemination database (CRD)

Database: Ovid MEDLINE(R) <1946 to January Week 3 2013>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <January 28, 2013>, EMBASE <1980 to 2013 Week 04> Search Strategy:

#	Searches	Results
1	exp Hip Fractures/ use mesz	16201
2	exp Hip Fracture/ use emez	26440
3	((hip* or femur* or femoral* or trochant* or petrochant* or intertrochant* or subtrochant* or intracapsular* or extracapsular*) adj4 fracture*).ti,ab.	55669
4	((hip* or ((femur* or femoral*) adj3 (head or neck or proximal))) adj4 fracture*).ti,ab.	38463
5	or/1-4	69110
6	exp nerve block/	38259
7	exp femoral nerve/	5061
8	block*.ti,ab.	1185299
9	7 and 8	1595
10	(block* adj4 (ascia iliaca* or compartment* or epidural* or fascia iliaca* or femoral* or iliofascial* or lateral* or lumbar plexus or nerve* or neural* or peripheral* or psoas or sacral* or sciatic* or subcostal* or triple* or local an?esthe* or local analges*)).ti,ab.	37358
11	or/6,9-10	60669
12	5 and 11	489
13	limit 12 to english language	402
14	remove duplicates from 13	274

#### **Cochrane Library**

ID	Search	Hits
#1	MeSH descriptor: [Hip Fractures] explode all trees	955
#2	((hip* or femur* or femoral* or trochant* or petrochant* or intertrochant* or subtrochant* or intracapsular* or	1407
	extracapsular*) near/4 fracture*):ti (Word variations have been searched)	
#3	((hip* or ((femur* or femoral*) adj3 (head or neck or proximal))) near/4 fracture*):ti (Word variations have been	792
	searched)	
#4	#1 or #2 or #3	1699
#5	MeSH descriptor: [Nerve Block] explode all trees	2334
#6	MeSH descriptor: [Femoral Nerve] explode all trees	202
#7	block*:ti (Word variations have been searched)	9538
#8	#6 and #7	160
#9	(block* near/4 (ascia iliaca* or compartment* or epidural* or fascia iliaca* or femoral* or iliofascial* or lateral* or	1474
	lumbar plexus or nerve* or neural* or peripheral* or psoas or sacral* or sciatic* or subcostal* or triple* or local	
	an?esthe* or local analges*)):ti (Word variations have been searched)	
#10	#5 or #8 or #9	2953
#11	#4 and #8	13

#### CRD

Line	Search	Hits
1	MeSH DESCRIPTOR hip fractures EXPLODE ALL TREES	161
2	((hip* or femur* or femoral* or trochant* or petrochant* or intertrochant* or subtrochant* or intracapsular* or extracapsular*) adj4 fracture*)):TI	125
3	((hip* or ((femur* or femoral*) adj3 (head or neck or proximal))) adj4 fracture*)):TI	103
4	#1 OR #2 OR #3	205
5	MeSH DESCRIPTOR nerve block EXPLODE ALL TREES	85
6	MeSH DESCRIPTOR femoral nerve EXPLODE ALL TREES	9
7	(block*):TI	375
8	#6 AND #7	9
	(block* adj4 (ascia iliaca* or compartment* or epidural* or fascia iliaca* or femoral* or iliofascial* or lateral* or lumbar	
9	plexus or nerve* or neural* or peripheral* or psoas or sacral* or sciatic* or subcostal* or triple* or local an?esthe* or	8
	local analges*)):TI	
10	#5 OR #8 OR #9	91
11	#4 AND #10	1

### **Appendix 2: Quality Assessment Tables**

#### Table A1: AMSTAR Score of Reviews<sup>a</sup>

Author, Year	AMSTAR score <sup>a</sup>	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
Parker, 2009 (9)	9	~	$\checkmark$	$\checkmark$		√	$\checkmark$	~	~	$\checkmark$		~
Abou-Setta, 2011 (11)	11	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	~	~	$\checkmark$	$\checkmark$	~
O'Malley, 2011 (10)	2			$\checkmark$			~					

<sup>a</sup> Details of AMSTAR method are described in Shea et al. (7)

#### Table A2: GRADE Evidence Profile for Comparison of Nerve Blocks and Systemic Analgesics

No. of Studies (Design)	Risk of Bias <sup>a</sup>	Inconsistency Indirectness		Imprecision	Publication Bias	Upgrade Considerations	Quality		
Pain (postoperative)									
8 (RCTs)	Very serious limitations (-2) <sup>b</sup>	No serious limitations	No serious limitations	No serious limitations	Undetected	None detected	⊕⊕ Low		
Additional pain medications required									
7 (RCTs)	Very serious limitations (-2) <sup>c</sup>	No serious limitations	Serious limitations (-1) <sup>d</sup>	No serious limitations	Undetected	None detected	⊕ Very low		

Abbreviations: No., number; RCT, randomized controlled trial.

<sup>a</sup>Assessment based on details provided in Abou-Setta et al review. (11)

<sup>b</sup>Of the 8 studies included in the analysis on pain, 7 had limitations with allocation concealment, 6 with blinding, 1 with the complete accounting of patients and outcomes, 1 with selective reporting bias, and all 8 had other limitations including not reporting the source of funding or unbalanced baseline characteristics. (11)

<sup>c</sup>Of the 7 studies included in the analysis on additional pain medications required, 5 had limitations with allocations concealment, 4 with blinding, 1 with the complete accounting of all patients and outcomes, 2 with selective reporting bias, and 5 had other limitations including not reporting the source of funding. (11) <sup>d</sup>Assessment of additional pain medication is reported as a count of the number of times a patient required pain medications, and no details are provided regarding dose or total intake of additional systemic

analgesics.

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