

Antibiotic-Laden Bone Cement for Primary Knee Arthroplasty: A Rapid Review

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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>.

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List of Abbreviations

ALBC	Antibiotic-laden bone cement
AMSTAR	Assessment of Multiple Systematic Reviews
CADTH	Canadian Agency for Drugs and Technologies in Health
CI	Confidence interval
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HTIS	Health Technology Inquiry Service
IV	Intravenous
No.	Number
OA	Osteoarthritis
Op	Operative
OR	Odds ratio
RA	Rheumatoid arthritis
RCT	Randomized controlled trial
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

This rapid review aimed to determine the safety and effectiveness of antibiotic-laden bone cement (ALBC) versus plain bone cement for primary knee arthroplasty.

Clinical Need and Target Population

Deep infection is a serious and potentially devastating complication of knee arthroplasty. The rate of infection after primary knee arthroplasty is estimated to be between 0.5% and 2%, with the incidence rising as the total number of primary knee arthroplasties increases. (1)

Prophylactic use of ALBC in addition to intravenous antibiotic for primary arthroplasty has been suggested to reduce the risk of infection. (2-4) The ALBC is believed to release antibiotic locally to the surrounding knee tissues, thus establishing resistance to bacterial organisms that could cause infection after joint replacement. Commercially available low-dose ALBC contains less than 1 g of antibiotic per 40 g of cement. (1;5) The effectiveness of ALBC in reducing the rate of deep infections for primary knee arthroplasty, however, remains unclear.

Rapid Review

Research Question

What is the safety and effectiveness of antibiotic-laden bone cement (ALBC) in comparison with plain bone cement for patients undergoing primary knee arthroplasty?

Research Methods

Literature Search

A literature search was performed on April 22, 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, 2005, until April 22, 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, 2005, and April 22, 2013
- systematic reviews, meta-analyses, and health technology assessments
- primary knee arthroplasty population
- comparison of ALBC to plain bone cement

Exclusion Criteria

- studies where discrete results for outcomes of interest cannot be abstracted
- evaluation of use of ALBC for revision knee arthroplasty

Outcomes of Interest

- infections
- revisions

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 into context the evidence produced by Health Quality Ontario and to provide advice on the appropriate clinical pathway for hip and knee arthroplasty in Ontario's 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) tool was used to assess the quality of the final selection of systematic reviews. (6) 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. (7) The overall quality was determined to be very low, low, moderate, or high using a step-wise, structural method.

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 can 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	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 192 citations published between January 1, 2005, and April 5, 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 and a Health Technology Inquiry Service (HTIS) report by the Canadian Agency for Drugs and Technologies in Health (CADTH) were identified that included studies evaluating the use of ALBC for knee arthroplasty. (1;8) Reference lists of the studies included in the reviews as well as health technology assessment websites were further hand-searched, and an updated CADTH review was identified. (9) The updated CADTH HTIS report was not considered a formal systematic review, and therefore was used only as a reference source.

Summary of Included Reviews

The identified systematic reviews and health technology assessment reports are summarized in Table 1. (1;8;9) The methodologic quality of both reviews was poor, with AMSTAR ratings ranging from 4 to 5 of a possible 11 (see Appendix 2; Table A1).

Table 1: Systematic Reviews Evaluating Antibiotic-Laden Bone Cement for Knee Arthroplasty

Author, Year	Search Strategy Dates	Population Included in Review	Number of Studies Related to Primary Knee Arthroplasty	AMSTAR Rating
Block and Stubbs, 2005 (8)	1965–2003 (all study types)	Primary joint arthroplasty	2 RCTs	4
CADTH, 2008 and 2010 update (1;9)	2003–2008 (all study types) Update: 2008–2010	Orthopedic surgeries (primary and revisions)	Review by Block and Stubbs and 2 observational studies	5

Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; CADTH, Canadian Agency for Drugs and Technologies in Health; RCT, randomized controlled trial.

The identified reviews and health technology assessment reports included broad search strategies evaluating all joint replacements; however, no analyses were specific to knee arthroplasty. References for individual studies specifically stated by the reviews as evaluating the use of ALBC in primary knee arthroplasty were therefore extracted and analyzed for the current rapid analysis, identifying 2 RCTs and 2 observational studies. Upon further review of the identified studies, 1 observational study was excluded, as few patients in the comparator group did not receive cement (confirmed by personal communication with primary author). (10) The remaining individual studies extracted are summarized in Table 2. (11–13)

Table 2: Studies of Primary Knee Arthroplasty Included in Systematic Reviews

Author, Year	Study Type (Years)	Country	Population	Exclusion Criteria	Intervention (ALBC)	Comparator (Plain Bone Cement)	Additional Antibiotics Received
Chiu et al, 2002 (11)	RCT (1993–1998)	Taiwan	Primary TKA	Diabetes, peripheral arterial occlusive disease, psoriasis, prior knee surgery, lower-extremity infection, osteomyelitis, malignant tumour, or current immunosuppressive treatment	Cefuroxime in Simplex P cement	Simplex P cement	IV cefazolin and gentamicin pre-op and post-op; oral cefazolin 7 d
Chiu et al, 2001 (12)	RCT (1994–1998)	Taiwan	Primary TKA with diabetes and OA	RA, psoriasis, previous knee surgery, infection of the lower limb, osteomyelitis, malignant tumour, or undergoing immunosuppressive treatment	Cefuroxime in Simplex P cement	Simplex P cement	IV cefazolin and gentamicin pre-op and post-op; oral cefazolin 7 d
Gandhi et al, 2009 (13)	Observational with contemporaneous controls (1998–2006)	Canada	Primary TKA with OA or RA	Prior knee sepsis	Simplex T cement (trobramycin impregnated)	Simplex P cement	1 dose systemic antibiotics pre-op and for 24 h after surgery

Abbreviations: ALBC, antibiotic-laden bone cement; IV, intravenous; OA, osteoarthritis; op, operative; RA, rheumatoid arthritis; RCT, randomized controlled trial; TKA, total knee arthroplasty.

Results for Outcomes of Interest

Infections

All 3 of the included studies evaluated deep infections as the primary outcome of interest. None of the included studies evaluated the effect of ALBC on revision surgeries. Results are summarized in Table 3. (11-13)

Table 3: Risk of Deep Infection after Primary Total Knee Arthroplasty for Patients Receiving Antibiotic-Laden Bone Cement versus Plain Bone Cement

Author, Year	Study Type	Mean Length of Follow-up (range)	Deep Infection N (%)		Statistical Significance of Risk of Infection with ALBC versus Plain Bone Cement
			ALBC	Plain Bone Cement	
Chiu et al, 2002 (11)	RCT	49 mo (26–80)	0/178 (0%)	5/162 (3.1%)	$P = 0.024$
Chiu et al, 2001 (12)	RCT	50 mo (26–88)	0/41 (0%)	5/37 (13.5%)	$P = 0.021$
Gandhi et al, 2009 (13)	Observational	1 y	18/814 (2.2%)	25/811 (3.1%)	Unadjusted: $P = 0.27$ Adjusted ^a OR (95% CI): 1.1 (0.4, 3.1); $P = 0.85$

Abbreviations: ALBC, antibiotic-laden bone cement; CI, confidence interval; OR, odds ratio; RCT, randomized controlled trial.

^aMultivariate linear regression model including age, sex, body mass index, Charlson Index, education, diagnosis of rheumatoid arthritis, and preoperative Western Ontario and McMaster Universities Arthritis Index score.

Randomized Controlled Trials

Chiu et al found a decrease in the rate of deep infection among patients with diabetes and osteoarthritis receiving cefuroxime-laden bone cement in comparison with plain bone cement ($P = 0.02$) (11) as well as among patients without diabetes ($P = 0.02$). (12) These studies might not be generalizable to Ontario, as the authors self-identified as having poor operating room environments. The GRADE for this body of evidence was assessed as very low (See Appendix 2, Tables A2 and A3). (11;12)

Observational Studies

Gandhi et al. (13) found no significant difference in the rate of deep infection between patients who received tobramycin-laden bone cement and those who received plain bone cement ($P = 0.27$). The use of ALBC was not found to be predictive of infection at 1 year in an adjusted analysis ($P = 0.84$). The GRADE for this body of evidence was assessed as very low (See Appendix 2, Tables A2 and A3). (13)

Conclusions

- Based on very low quality evidence, 2 randomized controlled trials identified significantly lower infection rates with antibiotic-laden bone cement (ALBC) versus plain bone cement among patients with and without diabetes receiving primary total knee arthroplasty.
- Based on very low quality of evidence, 1 observational study found no significant difference between patients receiving ALBC versus plain bone cement for primary knee arthroplasty.

Acknowledgements

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Expert Panel for Health Quality Ontario: Episode 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 Houwelling	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

Panel Member	Affiliation(s)	Appointment(s)
Internal Medicine		
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Anesthesiology		
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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

Literature Search—Hip and Knee Arthroplasty QBP Rapid Review—Knee Bone Cement

Search date: April 22, 2013

Databases searched: Ovid MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, Embase; Cochrane Library; Centre for Reviews and Dissemination

Limits: 2005-current; English

Filters: none

Database: Embase 1980 to 2013 Week 16, Ovid MEDLINE(R) 1946 to April Week 2 2013, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations April 19, 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/	32542
3	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prothes?s) or TKR).mp.	47575
4	or/1-3	51222
5	exp Bone Cements/ use mesz	16497
6	exp Bone Cement/ use emez	10145
7	((bone* or orthop?edic*) adj2 (paste* or glue* or cement*)).ti,ab.	11267
8	or/5-7	30789
9	exp Anti-Bacterial Agents/ use mesz or exp Anti-Infective Agents/ use mesz	1195043
10	exp antibiotic agent/ use emez or exp antiinfective agent/ use emez	2005786
11	(anti?biotic* or anti?infect* or anti?bacteria? or Gentamycin or Clindamycin or Cefalotin or Tobramycin or Erythromycin or Oxacillin or Cefuroxime or Colistin or Methicillin or Tetracycline or Lincomycin or Dicloxacillin or vancomycin or trimetoprim).ti,ab.	654735
12	exp antibiotic bone cement/ use emez	17
13	or/9-12	3383241
14	4 and 8 and 13	461
15	limit 14 to english language	416
16	limit 15 to yr="2005 -Current"	255
17	remove duplicates from 16	190

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: [Bone Cements] explode all trees	274
#7	((bone* or orthop?edic*) near/2 (paste* or glue* or cement*)):ti (Word variations have been searched)	70
#8	((bone* or orthop?edic*) near/2 (paste* or glue* or cement*)):ab (Word variations have been searched)	150
#9	#6 or #7 or #8	348
#10	MeSH descriptor: [Anti-Bacterial Agents] explode all trees	8281
#11	MeSH descriptor: [Anti-Infective Agents] explode all trees	21040
#12	(anti?biotic* or anti?infect* or anti?bacteria? or Gentamycin or Clindamycin or Cefalotin or Tobramycin or Erythromycin or Oxacillin or Cefuroxime or Colistin or Methicillin or Tetracycline or Lincomycin or Dicloxacillin or vancomycin or trimetoprim):ti (Word variations have been searched)	3806
#13	(anti?biotic* or anti?infect* or anti?bacteria? or Gentamycin or Clindamycin or Cefalotin or Tobramycin or Erythromycin or Oxacillin or Cefuroxime or Colistin or Methicillin or Tetracycline or Lincomycin or Dicloxacillin or vancomycin or trimetoprim):ab (Word variations have been searched)	4450
#14	#10 or #11 or #12 or #13	25162
#15	#5 and #9 and #14 from 2005 to 2013	5

Centre for Reviews and Dissemination

Line	Search	Hits
1	MeSH DESCRIPTOR Arthroplasty, Replacement, Knee EXPLODE ALL TREES	242
2	MeSH DESCRIPTOR Arthroplasty, Replacement	46
3	MeSH DESCRIPTOR Knee Prosthesis EXPLODE ALL TREES	60
4	((knee* adj2 (replacement* or arthroplast*)) or (knee* adj2 prosthes?s) or TKR)	431
5	#1 OR #2 OR #3 OR #4	489
6	MeSH DESCRIPTOR Bone Cements EXPLODE ALL TREES	45
7	((bone* or orthop?edic*) adj2 (paste* or glue* or cement*))	69
8	#6 OR #7	69
9	MeSH DESCRIPTOR Anti-Bacterial Agents EXPLODE ALL TREES	1016
10	MeSH DESCRIPTOR Anti-Infective Agents EXPLODE ALL TREES	2229
11	(anti?biotic* or anti?infect* or anti?bacteria? or Gentamycin or Clindamycin or Cefalotin or Tobramycin or Erythromycin or Oxacillin or Cefuroxime or Colistin or Methicillin or Tetracycline or Lincomycin or Dicloxacillin or vancomycin or trimetoprim)	583
12	#9 OR #10 OR #11	2522
13	#5 AND #8 AND #12	3
14	(#13) FROM 2005 TO 2013	2

Appendix 2: Quality Assessment Tables

Table A1: Assessment of Multiple Systematic Reviews (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
CADTH, 2008 (1)	5			✓	✓	✓	✓					✓
Block and Stubbs, 2005 (8)	4	✓						✓	✓			✓

Abbreviations: AMSTAR, assessment of multiple systematic reviews; CADTH, Canadian Agency for Drugs and Technologies in Health.

^aDetails of AMSTAR method are described in Shea et al. (6)

Table A2: GRADE Evidence Profile for Comparison of Antibiotic-Laden Bone Cement and Plain Bone Cement

No. of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Infections							
2 (RCTs)	Very serious limitations (-2) ^a	No serious limitations	Serious limitations (-1) ^b	No serious limitations ^c	Undetected	None	⊕ Very low
1 (observational)	Very serious limitations (-2) ^d	No serious limitations	No serious limitations	No serious limitations	Undetected	None	⊕ Very low

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

^aSee Appendix 2, Table A3 for Risk of Bias table.

^bOperating room standards in both studies might not reflect practices in Ontario. Authors described their operating room environments as poor and their patients as in a poor state of hygiene. Operations were performed in operating theatres without routine ultraviolet lights for disinfection, laminar flow, special air handling, or isolation suits.

^cNo power calculation was provided by the authors. Similarly, no effect estimate or confidence intervals were provided by the authors.

^dSee Appendix 2, Table A4 for Risk of Bias table.

Table A3: Risk of Bias Among Randomized Controlled Trials for the Comparison of Antibiotic-Laden Bone Cement and Plain Bone Cement

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Chiu et al, 2002 (11)	Serious limitations ^a	Serious limitations ^b	Serious limitations ^c	No limitations	Serious limitations ^d
Chiu et al, 2001 (12)	Serous limitations ^a	Serious limitations ^b	Serious limitations ^c	No limitations	Serious limitations ^d

^aQuasi-randomized study design, patients randomized by odd and even chart numbers.

^bPhysicians were not blinded, and it was not stated if the patient or outcome assessors were blinded.

^cIt was not stated how long patients were followed up, or who was lost to follow-up. Average duration of follow-up ranged from 26 to 80 months.

^dBilateral total knee replacements were randomized by patient leg.

Table A4: Risk of Bias Among Observational Trials for the Comparison of Antibiotic-Laden Bone Cement and Plain Bone Cement

Author, Year	Appropriate Eligibility Criteria	Appropriate Measurement of Exposure	Appropriate Measurement of Outcome	Adequate Control for Confounding	Complete Follow-Up
Gandhi et al, 2009 (13)	Serious limitations ^a	No limitations	No limitations	Serious limitations ^b	No limitations

^aHow patients were assigned to the surgeon, and how selection of procedure was determined by the surgeon was unclear.

^bThere was no assessment of individual comorbidities that can increase risk of infection; only Carlson Index was included in adjusted analysis.

References

- (1) Murphy G, Spry C, Canadian Agency for Drugs and Technologies in Health, Health Technology Inquiry Service. Antibiotic infused bone cement for orthopedic surgeries: a review of the clinical benefit and harm [Internet]. Canada; 2008. Available from: <http://www.cadth.ca/media/pdf/htis/L0040%20Antibiotic%20Infused%20Bone%20Cement%20for%20Orthopedic%20Surgeries%20final.pdf>.
- (2) British Orthopaedic Association. Primary total hip replacement: a guide to good practice. London, England: 2012 38p. Available from: <http://www.britishhipociety.com/uploaded/Blue%20Book%202012%20fsh%20nov%202012.pdf>.
- (3) British Orthopaedic Association. Knee replacement: a guide to good practice [Internet]. London, England; 1999. 24p. Available from: http://www.boa.ac.uk/Publications/Documents/tkr_good_practice.pdf.
- (4) Scottish Intercollegiate Guidelines Network (SIGN). Antibiotic prophylaxis in surgery: a national clinical guideline [Internet]. London, England; 2008. 71p. Available from: <http://www.sign.ac.uk/pdf/sign104.pdf>.
- (5) Jiranek WA, Hanssen AD, Greenwald AS. Antibiotic-loaded bone cement for infection prophylaxis in total joint replacement. *J Bone Joint Surg*. 2006;88(11):2487-500.
- (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):1-7.
- (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) Block JE, Stubbs HA. Reducing the risk of deep wound infection in primary joint arthroplasty with antibiotic bone cement. *Orthopedics*. 2005;28(11):1334-45.
- (9) Canadian Agency for Drugs and Technologies in Health, Health Technology Inquiry Service. Antibiotic infused bone cement for orthopedic surgeries: clinical and cost-effectiveness. [Internet]. 2010 5p. Available from: http://www.cadth.ca/media/pdf/K0146_Antibiotic-Infused_Bone_Cement_final.pdf.
- (10) Namba RS, Chen Y, Paxton EW, Slipchenko T, Fithian DC. Outcomes of routine use of antibiotic-loaded cement in primary total knee arthroplasty. *J Arthroplast*. 2009;24(6 Suppl):44-7.
- (11) Chiu FY, Chen CM, Lin CFJ, Lo WH. Cefuroxime-impregnated cement in primary total knee arthroplasty: a prospective, randomized study of three hundred and forty knees. *J Bone Joint Surg*. 2002;84-A(5):759-62.
- (12) Chiu FY, Lin CFJ, Chen CM, Lo WH, Chung TY. Cefuroxime-impregnated cement at primary total knee arthroplasty in diabetes mellitus. *J Bone Joint Surg (Br)*. 2001;83-B(5):691-5.

- (13) Gandhi R, Razak F, Pathy R, Davey JR, Syed K, Mahomed NN. Antibiotic bone cement and the incidence of deep infection after total knee arthroplasty. *J Arthroplast.* 2009;24(7):1015-8.

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