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CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

Post-Operative Prophylactic Antibiotics for Patients Undergoing Hip Fracture Repair Surgery or Hip Arthroplasty: A Review of Clinical Effectiveness and Guidelines

Service Line:	Rapid Response Service
Version:	1.0
Publication Date:	November 1, 2019
Report Length:	18 Pages

CADTH

Authors: Srabani Banerjee, Charlene Argaez

Cite As: Post-operative prophylactic antibiotics for patients undergoing surgery for hip fracture repair or hip arthroplasty: clinical effectiveness and guidelines. Ottawa: CADTH; 2019 Oct. (CADTH rapid response report: summary with critical appraisal).

ISSN: 1922-8147 (online)

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Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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Abbreviations

AMSTAR 2	A MeaSurement Tool to Assess systematic Reviews 2
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
RCTs	Randomized controlled trials
SSI	Surgical site infection

Context and Policy Issues

The incidence of hip fractures continues to increase with an increase in the aging population. Globally, by the year 2050 the annual total number of hip fractures is expected to exceed six million according to two reports.[1,2] The major risk factors for incurring hip fractures include osteoporosis and falls.[1] Surgical interventions may be needed for repairing hip fractures. Surgical interventions include internal repair of bones using screws, rods and metal plates, partial hip replacement, and total hip replacement.[3] It is estimated that a third of the fracture patients will require hip replacement (also known as hip arthroplasty).[1] Hip arthroplasty is a surgical procedure to replace a worn out or damaged hip joint and involves replacement of the joint with an artificial joint (prosthesis). Also, for individuals who are suffering from hip pain which cannot be alleviated with non-surgical interventions such as medication and physiotherapy, surgical intervention such as hip arthroplasty may be an option.[4]

Surgical procedures can be complex and there is potential for infection. Surgical site infection (SSI) after total joint arthroplasty (which includes hip arthroplasty), is one of the most severe complications and is associated with disability, morbidity, and mortality.[5] Management of such infections entails increased costs to the health care system.[5] According to one report from Northern Ireland, the risk of developing SSI after hip fracture repair surgery was 4.97%, with a third of these cases presenting a deep infection.[6] The annual incidence of SSI was reported to range between 0.4% and 2.5% for patients undergoing total hip arthroplasty.[7]

In order to prevent infections, antibiotics have been used both intraoperatively and post-operatively.[7] However there is some concern, as excessive and unnecessary use of antibiotics can lead to the development of antibiotic resistant pathogens.[8] There appears to be some uncertainty with respect to the benefits and harms of post-operative antibiotic use for patients undergoing hip fracture repair surgery or hip arthroplasty.

The purpose of this report is to review the clinical effectiveness of post-operative prophylactic antibiotics for patients undergoing hip fracture repair surgery or hip arthroplasty. Additionally, this report aims to review the evidence-based guidelines regarding the use of post-operative prophylactic antibiotics for patients undergoing hip fracture repair surgery or hip arthroplasty.

Research Questions

1. What is the clinical effectiveness of post-operative prophylactic antibiotics for patients undergoing hip fracture repair surgery or hip arthroplasty?
2. What are the evidence-based guidelines regarding the use of post-operative prophylactic antibiotics for patients undergoing hip fracture repair surgery or hip arthroplasty?

Key Findings

Two systematic reviews, with a limited number of studies that were generally of low or unclear quality, suggested that there was no statistically significant difference in infection rates with or without post-operative antibiotic prophylaxis in patients undergoing surgery for hip fracture repair or hip arthroplasty.

One non-randomized retrospective study suggested that for patients who were undergoing total hip arthroplasty and at high risk of peri-prosthetic joint infection, extended post-operative antibiotic prophylaxis resulted in a statistically significantly lower infection rate compared with no extended post-operative antibiotic prophylaxis.

Findings need to be interpreted with caution, considering the limitations (such as few identified studies specific to hip fracture repair or hip arthroplasty, and studies of low quality).

No evidence-based guideline for post-operative antibiotic prophylaxis for patients undergoing surgery for hip fracture repair or hip arthroplasty was identified.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were postoperative antibiotic prophylaxis and hip surgery. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2014 and October 3, 2019.

Selection Criteria and Methods

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

Table 1: Selection Criteria

Population	Patients undergoing hip fracture repair surgery or hip arthroplasty
Intervention	Post-operative prophylactic antibiotics (any type)
Comparator	Q1: No post-operative prophylactic antibiotics Q2: No comparator
Outcomes	Q1: Clinical effectiveness (e.g., post-operative SSI, repatriation, mortality, number of hospital days [days to discharge], safety, efficacy, harms) Q2: Guidelines
Study Designs	Health technology assessments, systematic reviews/meta-analyses, RCTs, non-randomized studies, and evidence-based guidelines.

RCTs = randomized controlled trials; SSI = surgical site infection

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2014. Studies on mixed surgical populations that did not present results separately for patients undergoing hip arthroplasty or hip fracture repair surgery were excluded. Guidelines with unclear methodology or not providing recommendations specifically for hip arthroplasty or hip fracture repair surgery were also excluded.

Critical Appraisal of Individual Studies

The included systematic reviews were critically appraised by one reviewer using the AMSTAR 2 checklist,[9] and non-randomized studies were critically appraised using the Downs and Black checklist.[10] Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 623 citations were identified in the literature search. Following screening of titles and abstracts, 600 citations were excluded and 23 potentially relevant reports from the electronic search were retrieved for full-text review. Three potentially relevant publication was retrieved from the grey literature search for full text review. Of these potentially relevant articles, 23 publications were excluded for various reasons, and three publications met the inclusion criteria and were included in this report. These comprised two systematic reviews[5,11] and one non-randomized study.[12] No relevant evidence-based guideline was identified. Appendix 1 presents the PRISMA[13] flowchart of the study selection.

Summary of Study Characteristics

Characteristics of the selected systematic reviews and non-randomized study are summarized below, and additional details are provided in Appendix 2, Table 2 and Table 3. The term hip surgery when used in the text includes both surgery for hip fracture repair and hip arthroplasty.

Study Design

Two relevant systematic reviews[5,11] with meta-analyses were selected. One systematic review[11] included three RCTs, and the second systematic review included two RCTs and one non-randomized study, that were relevant for this report. Both systematic reviews were published in 2019. The literature search period was up to March 2018 in one systematic review,[5] and was not mentioned in another systematic review.[11] There was overlap in the studies included in the systematic reviews (Appendix 5, Table 8).

One relevant non-randomized study[12] was selected. It was a retrospective cohort study and was published in 2018. The setting was a suburban academic hospital in the US.

Country of Origin

Country indicated for the first authors of the systematic reviews was the US.[5,11] Country indicated for the first author of the non-randomized study was the US.[12]

Patient Population

One systematic review[11] included 3,338 patients undergoing hip fracture repair surgery or hip arthroplasty; and another systematic review,[5] included 3,147 patients undergoing total hip arthroplasty. In both systematic reviews, the patient ages and genders were not reported.

The non-randomized study[12] involved 558 patients undergoing total hip arthroplasty. The patients were at high risk of peri-prosthetic joint infection due to specific risk factors such as diabetes, chronic kidney disease and smoking status. In the intervention group, the median age was 64 years and the proportion of females was 63%. In the control group the median age was 64.5 years and the proportion of females was 59.2%.

Interventions and Comparators

Both the systematic reviews[5,11] compared post-operative antibiotic use with no post-operative antibiotic use. The antibiotics used included cefuroxime, cefamandole, or cefazolin. Some patients received metronidazole in addition to cefazolin. Generally, the patients received antibiotics for 24 hours or less after surgery.

The non-randomized study[12] compared extended post-operative antibiotic use (i.e. oral antibiotics for seven days after discharge) with no extended post-operative antibiotic use. Peri-operative protocols were similar in both groups. Patients were generally given cefadroxil. Patients who were MRSA positive received Bactrim DS (sulfamethoxazole and trimethoprim), and those allergic to cephalosporins received clindamycin.

Outcomes

Both the systematic reviews[5,11] reported on infection rates. In one systematic review[5] the follow-up times ranged between 0.9 years and two years; and in another systematic review[11] the follow-up times were not mentioned. The non-randomized study[12] reported on infection rate, and the follow-up time was 90 days.

Summary of Critical Appraisal

The critical appraisal of the included studies is presented below and details are available in Appendix 3, Table 4 and Table 5.

In both the systematic reviews,[5,11] the objective was stated; a comprehensive literature search was conducted; article selection was described and a flow chart was presented; and list of included studies was provided; and a list of excluded studies was not presented. In one systematic review[5] article selection was done in duplicate, but it was unclear if data extraction was done in duplicate. In another systematic review,[11] data extraction was done in duplicate but it was unclear if article selection was done in duplicate. There is potential for error, if article selection or data extraction are not done in duplicate. In both systematic reviews, quality assessment of the included studies was conducted, and quality was found to be low or unclear. In both the systematic reviews the characteristics of the included studies were briefly described and lacked details. In one systematic review,[11] conflicts of interest of the authors were kept on file, but was not readily available (had to be requested) hence it is unclear if there were any issues. In another systematic review[5] conflicts of interest were presented, and one of the authors had association with industry; and the potential for bias cannot be ruled out.

In the selected non-randomized study,[12] the objective, and the inclusion and exclusion criteria were stated; and the patient characteristics, interventions and outcomes were described. The authors mentioned that there were no conflicts of interest. Sample size calculation does not appear to have been conducted however it does not seem to be an issue as the sample size used was sufficient to detect a difference between groups. As this was a non-randomized and retrospective study it has inherent biases (such as selection bias, and performance bias) and as details of baseline characteristics and any additional interventions used or not used were not presented, the extent or direction of the impact on the findings is uncertain.

Summary of Findings

Findings are summarized below, and details are available in Appendix 4, Table 6 and Table 7.

Clinical Effectiveness of post-operative prophylactic antibiotics for hip surgery

In both the systematic reviews, the pooled estimate of effect (infection rate) with post-operative antibiotic use compared with no post-operative antibiotic use was not presented separately for the patient subgroup undergoing hip surgery. However, the effect size (expressed as odds ratio) with respect to infection rates for the individual studies were presented and it was found that the numerical values for the infection rates were variable, with odds ratios in the studies relevant to this report varying between 0.11 and 1.84; also different numerical values for odds ratios were presented for one RCT included in both the systematic reviews. However, in all instances the between group differences for infection rates were not statistically significant.

One non-randomized study[12] found that for patients undergoing total hip arthroplasty and who were at high risk of peri-prosthetic joint infection, extended post-operative antibiotic prophylaxis resulted in a statistically significantly lower 90-day infection rate compared with no extended post-operative antibiotic prophylaxis. The *P* values reported for the difference in infection rates between treatment groups in patients having number of risk factors greater than or equal to one, and greater than or equal to two, were respectively $P = 0.034$ and $P = 0.0123$. For the subgroup of patients with risk factors greater than or equal to three, the *P* value was not reported. The authors mentioned that the reduction in infection rate in the extended post-operative antibiotics group was clinically meaningful, however what was considered a minimal clinically important difference was not specified.

Guidelines for post-operative prophylactic antibiotics for hip surgery

No evidence-based guidelines for post-operative antibiotic prophylaxis for patients undergoing surgery for hip fracture repair or hip arthroplasty were identified, hence a summary could not be presented.

Limitations

Pooled estimates from the meta-analyses in the selected systematic reviews[5,11] could not be used for this report as studies on various types of orthopedic surgeries were pooled and the pooled estimates for the subgroup of patients undergoing surgery for hip fracture repair, or hip arthroplasty were not presented separately. Hence the individual study results were presented in this report.

All the included publications provided findings for infection rates. However, no information regarding other outcomes such as mortality, hospital stay, and adverse effects were available.

It was unclear if sample size calculations had been conducted in the primary studies, hence it was unclear if the studies had adequate power to detect a difference.

The reason for different numerical values for the effect sizes presented for the same RCT included in both the systematic reviews was unclear, as details of the methods used were not described. However, in both instances the difference in effect size between the intervention and comparator groups were not statistically significant.

In the systematic reviews,[5,11] the patient population and interventions were described briefly, hence it was difficult to ascertain which treatment modality and patient population were likely to benefit or not benefit. Furthermore, there was limited amount of evidence available; each selected systematic review included a small number (three) of relevant studies. Also, the studies were generally described by the systematic review authors to be of low or unclear quality. The selected primary study was a non-randomized retrospective study, which has inherent biases.

The generalizability of the findings to the Canadian setting (i.e., in terms of patient population and interventions) is unclear. However, one study was conducted in Canada and the other studies were conducted in the US and Europe, where there may be some similarities with the Canadian setting.

The findings need to be interpreted with caution, considering the limitations described above.

No evidence-based guideline for post-operative antibiotic prophylaxis for patients undergoing surgery for hip fracture repair or hip arthroplasty was identified, hence a summary could not be presented.

Conclusions and Implications for Decision or Policy Making

Two systematic reviews[5,11] and one non-randomized study,[12] providing evidence on the comparative effectiveness of post-operative antibiotic prophylaxis with respect to no post-operative antibiotic prophylaxis in patients undergoing surgery for hip fracture repair or hip arthroplasty were identified. No evidence-based guideline for post-operative antibiotic prophylaxis for patients undergoing surgery for hip fracture repair or hip arthroplasty was identified.

Two systematic reviews,[5,11] with a limited number of relevant studies (three studies per systematic review, with two studies overlapping) that were generally of low or unclear quality, suggested that there was no statistically significant difference in infection rates with or without post-operative antibiotic prophylaxis in patients undergoing surgery for hip fracture repair or hip arthroplasty. One non-randomized retrospective study,[12] suggested that for patients undergoing total hip arthroplasty and who were at high risk of peri-prosthetic joint infection, extended post-operative antibiotic prophylaxis resulted in a statistically significantly lower 90-day infection rate compared with no extended post-operative antibiotic prophylaxis.

Two guideline reports,[14,15] that were evaluated for potential inclusion in this review, assessed prevention of SSIs but did not assess specifically hip fracture repair surgery or

hip arthroplasty. Hence these reports did not satisfy the inclusion criteria for this current report and were therefore not critically appraised or included in the summary of findings. However, as these reports may provide some useful insights, they are discussed here. The US Centers for Disease Control and Prevention (CDC) guideline[14] for SSI prevention recommended against the continuation of antibiotics postoperatively after the surgical incision is closed in the operating room and mentioned that the recommendation can be applied to prosthetic joint arthroplasty. The World Health Organization (WHO) guideline[15] recommended against prolonging surgical antibiotic prophylaxis administration after completion of a surgery.

Further research using well-conducted studies is needed to provide greater insights regarding the comparative effectiveness of post-operative antibiotic prophylaxis with respect to no post-operative antibiotic prophylaxis, in patients undergoing surgery for hip fracture repair or hip arthroplasty.

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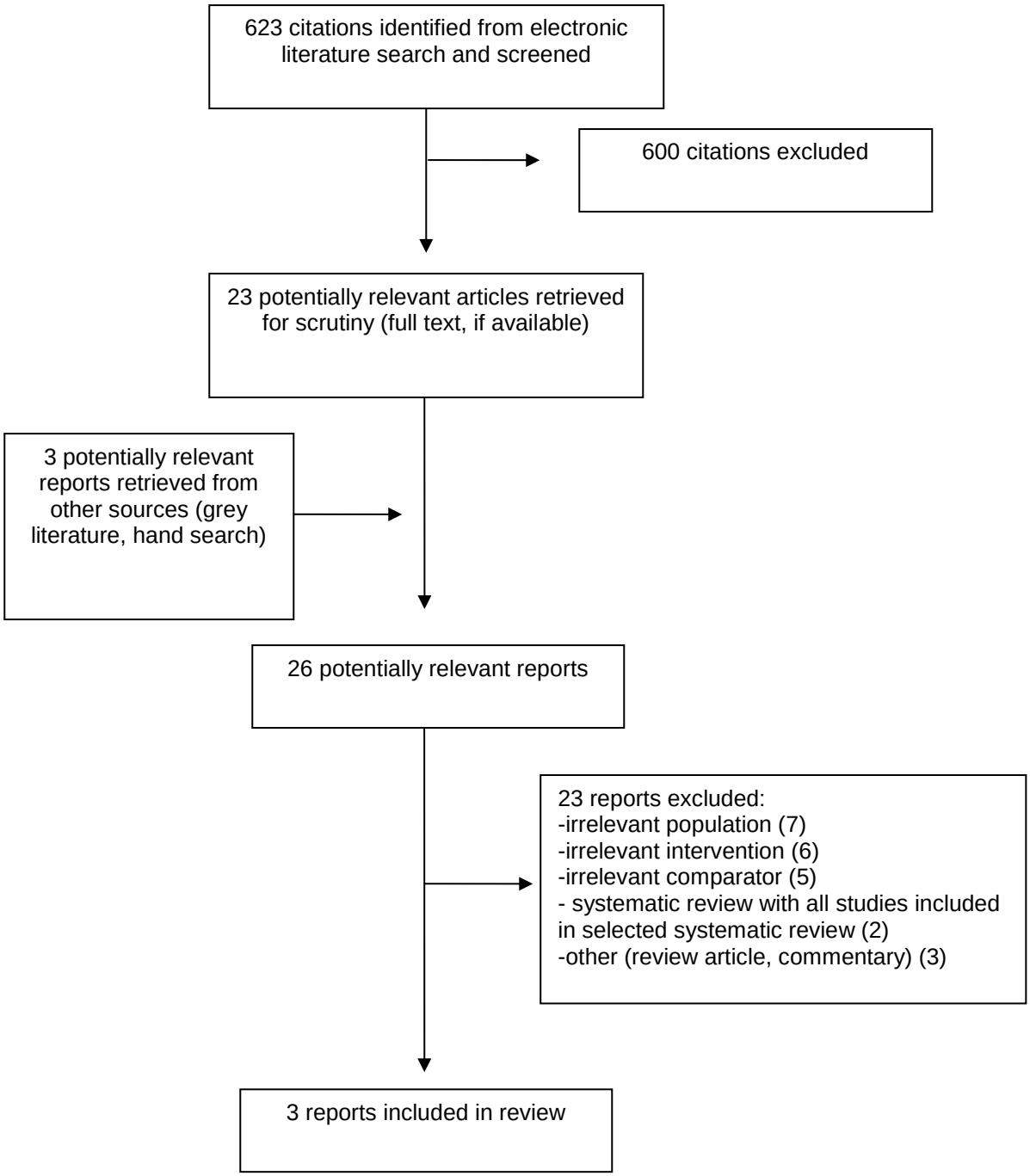
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Ryan[11] 2019, US	SR with meta-analysis, the literature search period was not stated. The SR included 3 RCTs relevant to this report. The RCTs were published between 1990 and 1994. This SR had a broad focus and only studies relevant for this report are included here. Countries where the studies were conducted were one each in Canada, Italy, and the Netherlands. Aim: To assess post-operative risk with single dose of pre-operative antibiotics compared with multiple doses of perioperative antibiotics for orthopedic procedures where implants were placed.	Patients undergoing surgery for hip fracture, or hip arthroplasty. N = 3338 (range 191 to 2651) Age: NR % Female: NR	Post-operative antibiotic (i.e, multiple doses of peri-operative antibiotics) versus no post-operative antibiotic (i.e., pre-operative dose antibiotic only) Antibiotics included cefazolin, cefuroxime, or cefamandole. Cefuroxime: 750 mg every 8 hours for 2 doses; Cefamandole: 1 g post-operatively Cefazolin: 1 g every 6 hours for 3 doses	Infection rate. Follow up: NR
Siddiqi[5] 2019, US	SR with meta-analysis, the literature search (databases: Medline, PubMed, and Embase) was up to March 2018 (for Medline (1946 to March 2018). The SR included 2 RCTs and 1 non-randomized study relevant to this report. The 2 RCTs and the non-randomized study were published in 1992, 1994, and 2006 respectively. Countries where the studies were conducted were not specified. Aim: To assess the efficacy and duration of surgical antibiotic prophylaxis in total joint arthroplasty	Patients undergoing total hip arthroplasty. N = 3147 (range 496 to 2651) Age: NR % Female: NR	Post-operative antibiotic versus no post-operative antibiotic (both groups received pre-operative antibiotic) Antibiotics included cefuroxime, cefamandole, cefazolin, and metronidazole Cefuroxime: 3 doses in ≤24 hours; Cefamandole: 3 doses in ≤24 hours; Cefazolin ± metronidazole: multiple doses in 24 hours.	Infection rate. Follow up: 0.9 years to 2 years

NR = not reported; SR = systematic review.

Table 3: Characteristics of Included Primary Clinical Study

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Inabathula[12] 2018, US	Retrospective cohort study. Setting: a suburban academic hospital in the US. Surgery was conducted by 4 fellowship trained surgeons using the same perioperative protocols. Patients undergoing TJAs between December 2011 and December 2016 were considered. A modified infection prevention was used from January 2015 onwards and the modified protocol also included prophylactic antibiotics for a minimum of 7 days after discharge for patients at high risk of PJI This study had a broad objective and only the subgroup (hip arthroplasty) of patients relevant for this report are presented here Aim: To assess whether extended oral antibiotic use minimized PJI after primary TJA (hip or knee) in high-risk patients	Patients undergoing total hip arthroplasty, who were at high risk of PJI based on specific risk factors (such as diabetes, chronic kidney disease, active smoker, autoimmune disease, and nasal colonization with MRSA and/ or MSSA) N = 558 (276 in group 1, and 282 in group 2) Age (median) (years: 64 in group 1, and 64.5 in group 2. % Female: 63% in group 1, and 59.2% in group 2.	Extended post-operative antibiotic (group 1, i.e., intervention group) versus without extended post-operative antibiotic (group 2, i.e., control group). The same peri-operative protocol was followed in both groups. After discharge Group 1 received oral antibiotic for 7 days whereas Group 2 did not. Extended antibiotic protocol: 500 mg cefadroxil twice daily for 7 days. Patients who were MRSA positive received Bactrim DS (sulfamethoxazole and trimethoprim) twice daily for 7 days or if they were allergic to cephalosporins with documented anaphylaxis, 300 mg clindamycin thrice daily for 7 days.	Infection rate. Follow up: 90 days

MRSA = methicillin-resistant staphylococcus aureus; MSSA = methicillin-sensitive staphylococcus aureus; PJI = peri-prosthetic joint infection; TJA = total joint arthroplasty.

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR[9]

Strengths	Limitations
Ryan[11] 2019, US	
• The objective was clearly stated • Multiple databases (MEDLINE, Embase, Cochrane library, and Google Scholar) were searched. • Study selection was described, and a flow chart was presented. • A list of included studies was provided • Data extraction was done independently by two reviewers • Quality assessment of the studies was done independently by two reviewers using the Cochrane risk of bias tool. The quality of the studies was low or unclear. The quality of evidence was determined using GRADE and was generally low. • Characteristics of the included studies were presented, however, details were lacking • Meta-analysis was conducted. • Publication bias was explored using Funnel plot and the potential for bias was low. However, it should be noted that publication bias was determined using all the studies on orthopedic surgeries and not just the studies relevant for this report (i.e., those on surgery for hip fracture or hip arthroplasty) • Conflicts of interest were not presented in the publication. However, it was mentioned that conflicts of interest were on file and could be viewed on request.	• The literature search period was not specified • A list of excluded studies was not provided • Unclear if article selection was done in duplicate • Study characteristics were not presented in detail
Siddiqi[5] 2019, US	
• The objective was clearly stated • Multiple databases (MEDLINE, PubMed, and Embase,) were searched. The authors mentioned that for the literature search no time frame was specified with respect to publication dates. • Study selection was described, and a flow chart was presented. • A list of included studies was provided • Article selection was done independently by two reviewers • Quality was done independently by two reviewers using the Cochrane risk of bias tool. The quality of the studies was low or unclear. The quality of evidence was determined using GRADE and was generally low. • Characteristics of the included studies were presented, however, details were lacking • Meta-analysis was conducted. • Conflicts of interest were declared. Of the six authors, one author had association with industry	• A list of excluded studies was not provided • Unclear if data extraction was done in duplicate • Study characteristics were not presented in detail • Method of assessment of publication bias was not described, however the authors mentioned that potential for publication bias was high

GRADE = Grading of Recommendations Assessment, Development, and Evaluation

Table 5: Strengths and Limitations of Clinical Study using Downs and Blacks checklist[10]

Strengths	Limitations
Inabathula[12] 2018, US	
• The objective was clearly stated • The inclusion and exclusion criteria were stated • Patient characteristics, intervention and outcomes were described. • *P* values were reported • The authors mentioned that there were no conflicts of interest	• Not a randomized study. A retrospective cohort study • Sample size calculation does not appear to have been conducted. • It was unclear if there were any withdrawals. • Unclear if ITT was conducted

ITT = intention-to-treat

Appendix 4: Main Study Findings and Authors' Conclusions

Table 6: Summary of Findings Included Systematic Reviews and Meta-Analyses

<table>
<tr><th>Main Study Findings</th><th>Authors' Conclusion</th></tr>
<tr><td colspan="2">Ryan[11] 2019, US</td></tr>
<tr><td>Patients undergoing surgery for hip fracture, or hip arthroplasty.

Infection rate with single dose pre-operative antibiotic versus multiple doses of peri-operative antibiotics (from 3 RCTs)
<table><tr><th>Study</th><th>No. of patients</th><th>Effect size: OR (95% CI)</th></tr><tr><td>RCT</td><td>191</td><td>1.31 (0.18 to 9.49)</td></tr><tr><td>RCT[a]</td><td>496</td><td>0.11 (0.01 to 2.01)</td></tr><tr><td>RCT[a,b]</td><td>2651</td><td>0.97 (0.61 to 1.54)</td></tr></table>[a]Studies that overlapped between systematic reviews.
[b]Same study with different effect sizes reported in the two systematic reviews

Note: This systematic review had a broad focus and included studies on hip and knee arthroplasty; only the relevant studies with respect to hip arthroplasty are presented here.</td><td>"Currently, the best available data suggest that a single preoperative dose of antibiotics offers equivalent infection prophylaxis when compared with multiple perioperative doses for orthopaedic procedures where implants are placed. However, the quality of evidence is low, and a randomized study with a sufficient sample size is needed to examine the issue before universal adoption." (p.1588)

Note: the authors conclusions apply to hip and knee arthroplasty.</td></tr>
<tr><td colspan="2">Siddiqi[5] 2019, US</td></tr>
<tr><td>Patients undergoing total hip arthroplasty.

Infection rate with pre-operative antibiotic versus pre-operative and postoperative antibiotics (from 2 RCTs, and 1 non-randomized study)
<table><tr><th>Study</th><th>No. of patients</th><th>Effect size: OR (95% CI)</th></tr><tr><td>RCT[a]</td><td>496</td><td>0.11 (0.01 to 2.01)</td></tr><tr><td>RCT[a,b]</td><td>2651</td><td>1.84 (0.68 to 4.98)</td></tr><tr><td>Cohort</td><td>2000</td><td>0.87 (0.52 to 1.47)</td></tr></table>[a]Studies that overlapped between systematic reviews.
[b]Same study with different effect sizes reported in the two systematic reviews

Note: This systematic review had a broad focus and included studies on all types of total joint arthroplasty; only the relevant studies with respect to total hip arthroplasty are presented here.</td><td>"Our review confirms the benefit of SAP utilization in total joint arthroplasty. The available evidence does not show added benefit of postoperative SAP or continuation beyond 24 hours. However, the overall GRADE (Grading of Recommendations Assessment, Development and Evaluation) of evidence of the available literature was low (high risk of bias, high risk of publication bias, and low precision). The findings of this study demonstrate the need for Level-I studies with adequate power to evaluate the safety of shortened SAP duration after total joint arthroplasty and its effect on SSI/PJI prior to widespread implementation." (p.828)

Note: the authors conclusions apply to total joint arthroplasty.</td></tr>
</table>

CI = confidence interval; OR = odds ratio; PJI = periprosthetic joint infection; SAP = surgical antibiotic prophylaxis; SSI = surgical site infection

Table 7: Summary of Findings of Included Primary Clinical Study

Main Study Findings	Authors' Conclusion
Inabathula[12] 2018, US	
Patients undergoing total hip arthroplasty who were at high risk of periprosthetic joint infection Comparison of 90-day infection rates in patients receiving extended post-operative antibiotics (group 1) with patients not receiving extended post-operative antibiotics (group 2) according to risk level:	"Extended postoperative antibiotic prophylaxis led to a statistically significant and clinically meaningful reduction in the 90-day infection rate of selected patients at high risk for infection. We encourage further study and

Main Study Findings	Authors' Conclusion
Infection rate in patients with ≥1 risk factor: 1.1% in group 1 (N = 268), and 4.3% in group 2 (N = 282); *P* = 0.034. Infection rate in patients with ≥2 risk factors: 0.8% in group 1 (N = 130), and 7.6% in group 2 (N = 79); *P* = 0.013. Infection rate in patients with ≥3 risk factors: 3.3% in group 1 (N = 30), and 5.6% in group 2 (N = 18); *P* = NR. (N indicates the number in each group with a particular number of risk factors)	deliberation prior to adoption of a protocol involving extended oral antibiotic prophylaxis after high-risk TJA, with the benefits weighed appropriately against potential adverse consequences such as increasing the development of antimicrobial resistance." (p.2103) (Note TJA includes both total hip arthroplasty and total knee arthroplasty. These conclusions also appear to be consistent with the results obtained for the subgroup hip arthroplasty patients)

NR = not reported; TJA = total joint arthroplasty

Appendix 5: Overlap between Included Systematic Reviews

Table 8: Primary Study Overlap between Included Systematic Reviews[a]

Primary Study Citation	Systematic Review Citation	
	Ryan[11] 2019, US	Siddiqi[5] 2019, US
Buckley, 1990	x	
Mannien, 2006		x
Suter, 1994	x	x
Wymenga, 1992	x	x

[a]Overlap of primary studies relevant to this report