

A Systematic Review With Narrative Synthesis of Antibiotic Prophylaxis in Orthopaedic Surgery: Clinical, Microbiological, Histopathological, and Antimicrobial Resistance Outcomes

Received 10/03/2026
Review began 10/06/2026
Review ended 10/19/2026
Published 10/22/2026

© Copyright 2026

Jayant et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.118421

Santosh Jayant ^{1,2,3}, Asim Israr Khan ⁴, Mamta Gupta ¹, S Zeeshan A. Hashmi ⁵, Tushar Malik ⁶, Abhiraj Ramchandani ¹, Rajesh Kumar ⁷, Kuldeep Singh ⁸, Rajdeep Paul ⁸

1. Pathology and Laboratory Medicine, Amaltas Institute of Medical Sciences, Amaltas University, Dewas, IND 2. Pathology and Laboratory Medicine, Gajra Raja Medical College, Gwalior, IND 3. Pathology, Sunderlal Patwa Government Medical College, Mandsaur, IND 4. Pathology, Shri Siddhi Vinayak Medical College, Sambhal, IND 5. Clinical Microbiology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, IND 6. Internal Medicine, Fortis Hospital Manesar, Gurugram, IND 7. Orthopaedics, Maa Vindhyavasini Autonomous State Medical College, Mirzapur, IND 8. Clinical Microbiology, Mahaveer Institute of Medical Sciences and Research, Bhopal, IND

Corresponding author: Rajdeep Paul, rimo.micro@gmail.com

Abstract

Orthopaedic surgical procedures involving prostheses, fracture-fixation devices, spinal instrumentation, and tumour endoprostheses are particularly vulnerable to surgical site infections (SSIs). Systemic perioperative antibiotic prophylaxis is widely used to reduce postoperative infection; however, considerable variation remains in antibiotic selection, dose, timing, redosing, and duration. This systematic review with narrative synthesis evaluated the clinical effectiveness, microbiological findings, histopathological outcomes, antimicrobial resistance, and adverse events associated with antibiotic prophylaxis in orthopaedic surgery. MEDLINE/PubMed, Embase, Scopus, Web of Science Core Collection, and the Cochrane Central Register of Controlled Trials were searched from database inception through June 30, 2026. Randomised and non-randomised clinical studies evaluating systemic perioperative prophylaxis were eligible, with observational studies additionally considered for microbiological, resistance, and histopathological outcomes. A total of 1,879 records were identified, of which 1,459 underwent title and abstract screening. After assessment of 172 full-text reports, 32 reports representing 30 unique underlying studies were included. The evidence was synthesised narratively because of substantial clinical and methodological heterogeneity across procedures, prophylactic regimens, study designs, and outcome definitions. Appropriate perioperative prophylaxis was generally associated with favourable infection outcomes in higher-risk settings, whereas prolonged postoperative administration did not consistently provide additional benefit over shorter perioperative regimens. *Staphylococci* remained the predominant pathogens, while Gram-negative and antimicrobial-resistant organisms also contributed to breakthrough infection. Histopathological outcomes were reported less consistently than clinical and microbiological outcomes. The findings support procedure-appropriate prophylaxis, correct dosing and timing, local microbiological surveillance, and antimicrobial stewardship rather than indiscriminate extension of postoperative antibiotics.

Categories: General Surgery, Orthopedics, Infectious Disease

Keywords: antibiotic prophylaxis, antimicrobial resistance, histopathology, microbiology, orthopaedic surgery, periprosthetic joint infection, surgical site infection

Introduction And Background

A surgical site infection (SSI) is one of the most serious complications of orthopaedic surgery. Infection following joint arthroplasty, fracture fixation, spinal instrumentation, or tumour endoprosthetic reconstruction may result in prolonged antimicrobial treatment, recurrent debridement, implant removal, revision surgery, impaired function, and substantial healthcare costs. Perioperative systemic antibiotic prophylaxis is therefore an established infection-prevention measure in many orthopaedic procedures [1].

The effectiveness of antimicrobial prophylaxis depends on several perioperative factors, including agent selection, dose, timing of administration, intraoperative redosing, blood loss, patient body mass, renal function, and local susceptibility patterns. A double-blind multicentre arthroplasty study demonstrated comparable efficacy between one day of cefuroxime and three days of cefazolin [2]. Observational arthroplasty evidence has also suggested that inadequately dosed vancomycin may be associated with increased rates of periprosthetic joint infection (PJI) compared with cefazolin when there is no specific indication for vancomycin use [3].

There is also no clear benefit from routinely broadening the prophylactic spectrum. In a large multicentre randomised study, the routine addition of vancomycin to cefazolin in patients without known methicillin-resistant *Staphylococcus aureus* (MRSA) colonisation did not reduce the rate of SSI after arthroplasty [4].

How to cite this article

Jayant S, Khan A, Gupta M, et al. (October 22, 2026) A Systematic Review With Narrative Synthesis of Antibiotic Prophylaxis in Orthopaedic Surgery: Clinical, Microbiological, Histopathological, and Antimicrobial Resistance Outcomes. Cureus 18(10): e118421. DOI 10.7759/cureus.118421

These findings support a patient-specific and indication-based approach rather than routine escalation of prophylactic coverage.

Open fractures represent a different clinical setting because contamination and infection risk may be present before definitive surgical treatment. Randomised evidence supports early systemic antibiotic prophylaxis, while prolonged antibiotic courses have not been consistently superior to shorter regimens [5]. Orthopaedic oncology represents another high-risk setting. The Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) trial found no reduction in SSI with five days of intravenous cephalosporin prophylaxis compared with one day following lower-extremity tumour endoprosthesis reconstruction [6]. A microbiological secondary analysis of the same trial identified a substantial burden of prophylaxis-resistant pathogens among breakthrough infections [7].

Procedure-specific evidence further highlights the heterogeneity of antibiotic prophylaxis across orthopaedic surgery. Routine perioperative antibiotic prophylaxis has not demonstrated a clear reduction in infection in clean K-wire fixation studies [8], while a systematic review of spinal surgery found no significant benefit from prolonged postoperative prophylaxis compared with shorter perioperative regimens [9]. Evidence from arthroplasty likewise challenges routine continuation of antibiotics beyond the perioperative period [10].

Antimicrobial resistance adds further complexity. *Staphylococci* remain the predominant organisms in orthopaedic SSI, although resistant Gram-positive organisms and Gram-negative pathogens also contribute to breakthrough infections [11]. Standardisation of prophylaxis may be particularly challenging in orthopaedic oncology because of heterogeneity in patient characteristics, reconstruction complexity, procedural risk, and microbial susceptibility [12]. A comprehensive review should therefore consider not only clinical infection outcomes but also microbiological findings, antimicrobial resistance, histopathological findings, and antibiotic-related adverse events.

Existing systematic reviews have generally focused on individual orthopaedic procedures or specific prophylactic comparisons. However, less attention has been given to integrating clinical infection outcomes with microbiological findings, antimicrobial resistance, histopathological findings, and antibiotic-related adverse events across different orthopaedic settings. The present systematic review with narrative synthesis therefore aimed to evaluate perioperative antibiotic prophylaxis across orthopaedic procedures, with particular attention to surgical site infection, microbiological isolates, antimicrobial resistance, histopathological findings, reoperation or revision, and antibiotic-related adverse events.

Review

Materials and methods

Reporting Framework

This systematic review with narrative synthesis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [13] and PRISMA 2020 explanation and elaboration guidance [14]. Prospective PROSPERO registration was not conducted, and there was no separate review protocol published.

Eligibility Criteria

Studies were selected according to predefined inclusion and exclusion criteria, as summarised in Table 1.

Criterion	Inclusion criteria	Exclusion criteria
Population	Patients of any age undergoing elective or emergency orthopaedic surgery	Animal studies, in-vitro studies, and non-orthopaedic populations
Procedures	Primary or revision arthroplasty, spinal surgery, fracture fixation, open-fracture management, percutaneous K-wire fixation, implant-related procedures, and orthopaedic oncological reconstruction	Procedures unrelated to orthopaedic surgery
Intervention	Systemic antibiotics administered prophylactically before, during, or immediately after surgery	Antibiotics used solely for treatment of established infection
Comparator	Placebo, no prophylaxis, standard prophylaxis, alternative antibiotic regimens, different doses or timing, and shorter versus prolonged prophylaxis	Studies without an appropriate comparator where comparative effectiveness was required
Study design	Randomised controlled trials, quasi-randomised studies, prospective cohorts, retrospective comparative cohorts, and case-control studies	Case reports, editorials, guidelines, protocols, narrative reviews, and purely laboratory studies
Outcomes	Surgical site infection, deep infection, reoperation, revision, microbiology, antimicrobial resistance, histopathology, adverse events, and mortality	Studies not reporting outcomes relevant to antibiotic prophylaxis
Publication period	No publication-year restriction	None based solely on publication year
Language/full-text availability	Reports with sufficient information for eligibility assessment and data extraction	Unavailable or insufficient full-text information

TABLE 1: Inclusion and exclusion criteria for study selection

Information Sources and Search Strategy

MEDLINE/PubMed, Embase, Scopus, Web of Science Core Collection, and the Cochrane Central Register of Controlled Trials were searched from database inception through 30 June 2026. Reference lists of included studies and relevant reviews were manually screened, and citation searching was used to identify additional records. No publication-year restriction was applied. Complete database-specific search strategies are presented in the Appendix.

Study Selection and Data Collection

Two reviewers independently screened titles and abstracts, and full reports were independently assessed if they were potentially eligible. Disagreements were settled through discussion and/or by having a third reviewer adjudicate, when needed. The following data was obtained from the standardised form: study design, country, sample size, participant characteristics, surgical procedure, antibiotic agent, dose, route, timing, redosing, duration of antibiotic prophylaxis, comparator group, microbiological isolates, antimicrobial susceptibility, study design, adverse events, funding, and conflicts of interests. Multiple reports arising from the same underlying study were linked to avoid double counting. Primary trial reports were used for participant and clinical-outcome data, while secondary analyses were used only for additional outcomes not available in the primary report and were not counted as independent studies.

Outcomes

The primary outcome was SSI, including superficial incisional, deep incisional, organ/space, implant-associated, and periprosthetic infection as defined by individual studies. Secondary outcomes included deep infection, therapeutic antibiotic requirement, debridement, reoperation, revision surgery, implant removal, readmission, hospital stay, microbiological isolates, antimicrobial resistance, histopathological evidence of acute or chronic infection, antibiotic-related adverse events, and mortality where reported.

Risk of Bias and Synthesis Methods

Randomised controlled trials were assessed using the Cochrane Risk of Bias 2 (RoB 2) tool [15], while non-randomised comparative studies were evaluated using ROBINS-I [16]. Two reviewers performed the assessments independently, and disagreements were resolved through discussion or consultation with a

third reviewer.

Because quantitative pooling was not considered appropriate, a structured narrative synthesis was undertaken. The synthesis was organised according to orthopaedic procedure, prophylactic comparison, study design, clinical outcomes, microbiological findings, antimicrobial resistance, histopathological findings, and antibiotic-related adverse events. Randomised and non-randomised studies were considered separately when interpreting the strength and consistency of the evidence.

Randomised and non-randomised evidence were considered separately when interpreting the strength of the findings. Greater emphasis was placed on consistency of direction of effect, methodological quality, clinical applicability, and agreement across studies rather than on generating a single pooled estimate across heterogeneous procedures.

Results

Study Selection

In total, 1,879 records were identified: 1,824 from electronic databases and 55 through citation searching. After removal of 420 duplicates, 1,459 records underwent title and abstract screening, of which 1,278 were excluded. A total of 181 reports were sought for retrieval; nine could not be retrieved, leaving 172 full-text reports for eligibility assessment. Of these, 140 were excluded for predefined reasons. Ultimately, 32 reports representing 30 unique underlying studies were included in the synthesis. The study-selection process is presented in Figure 1.

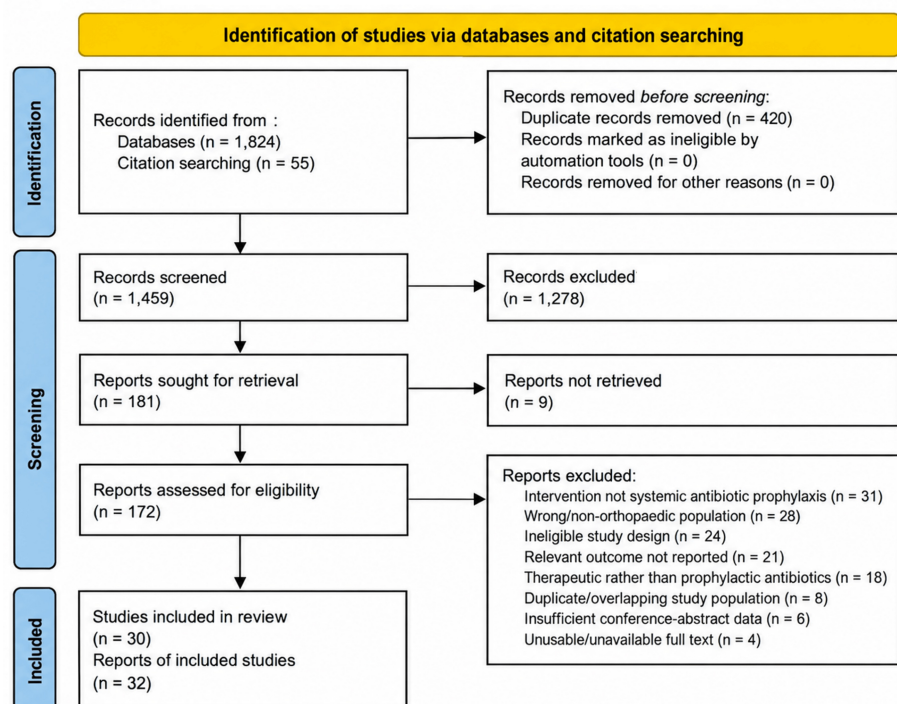


FIGURE 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 flow diagram for study selection

Characteristics of the Included Studies

The range of evidence covered arthroplasty, spine surgery, open fracture and trauma surgery, K-wire fixation, implant removal, and orthopaedic oncology. The key clinical studies and reports were used to demonstrate the review framework, as summarised in Table 2.

Study	Year	Design	Setting/procedure	Participants	Comparison	Key finding
Mauerhan et al. [2]	1994	Multicentre double-blind randomised trial	Hip and knee arthroplasty	1,354	One-day cefuroxime vs three-day cefazolin	Comparable infection prevention

McQueen et al. [17]	1990	Randomised trial	Total joint arthroplasty	401	Systemic cefuroxime vs cefuroxime in bone cement	No meaningful early deep-infection difference
Tyllianakis et al. [18]	2010	Prospective randomised study	Primary total hip arthroplasty and total knee arthroplasty	Not reported	Cefuroxime vs antistaphylococcal alternatives	Procedure-specific prophylactic efficacy assessed
Sewick et al. [19]	2012	Retrospective cohort	Primary total hip arthroplasty and total knee arthroplasty	1,828	Cefazolin vs cefazolin plus vancomycin	Dual regimen did not reduce overall surgical site infection
Kheir et al. [3]	2017	Retrospective cohort	Primary total joint arthroplasty	7,638	Vancomycin vs cefazolin; dose assessment	Vancomycin cohort had higher periprosthetic joint infection rates; underdosing was frequent
Honkanen et al. [20]	2023	Retrospective cohort	Primary hip and knee replacement	27,220 procedures	Cefuroxime vs clindamycin or vancomycin	No significant adjusted difference in periprosthetic joint infection
Peel et al. [4]	2023	Multicentre double-blind randomised controlled trial	Arthroplasty	4,113 analysed	Cefazolin plus vancomycin vs cefazolin plus placebo	Addition of vancomycin was not superior overall
Carender et al. [21]	2021	Retrospective cohort	Primary total hip or total knee arthroplasty in patients with body mass index ≥ 40 kg/m ²	650	Extended oral postoperative prophylaxis vs no extended prophylaxis	No significant reduction in early wound complications or periprosthetic joint infection
Lopez et al. [22]	2019	Retrospective pre-post cohort	Instrumented spinal fusion	Large cohort	Cefazolin vs cefazolin plus vancomycin protocol	Revision for surgical site infection decreased after protocol change
Lambrechts et al. [23]	2022	Retrospective cohort	Cervical or lumbar fusion	2,643	Adequate vs inadequate cefazolin dosing	Inadequate dosing was associated with higher surgical site infection risk
Kim et al. [24]	2026	Propensity-matched cohort	Elective spine surgery	12,996	Cefazolin vs vancomycin	Cefazolin was associated with lower or comparable surgical site infection risk
Kazarian et al. [25]	2024	Retrospective cohort	Primary spine surgery	10,122	Cefazolin vs vancomycin	Vancomycin was associated with higher risk of deep surgical site infection
Marimuthu et al. [26]	2016	Prospective comparative study	Instrumented spinal fusion	326	24-hour vs 72-hour cefazolin	Surgical site infection rates were comparable
Dellinger et al. [5]	1988	Double-blind randomised controlled trial	Open extremity fractures	248	One-day vs five-day cephalosporin regimens	Longer duration was not superior
Vasenius et al. [27]	1998	Prospective randomised study	Open fractures	227 patients / 240 fractures	Clindamycin vs cloxacillin	Efficacy varied according to fracture severity
Stevenson et al. [28]	2003	Double-blind placebo-controlled randomised controlled trial	Open distal phalanx fractures	193	Flucloxacillin vs placebo	No significant benefit after meticulous wound care
Saveli et al. [29]	2013	Randomised pilot trial	Open fractures	130	Cefazolin vs cefazolin plus vancomycin	No significant overall difference in surgical site infection
Redfern et al. [30]	2016	Retrospective cohort	Gustilo type III open fractures	72	Cefazolin plus gentamicin vs piperacillin/tazobactam	Similar one-year surgical site infection rates
Patanwala et al. [31]	2021	Multicentre retrospective cohort	Type III open fractures	134	Cefazolin alone vs cefazolin plus aminoglycoside	Similar infection rates

Heras et al. [32]	2005	Retrospective study	Paediatric K-wire fixation	77	Cefazolin prophylaxis vs no prophylaxis	Comparative K-wire evidence
Lobst et al. [33]	2007	Retrospective study	Paediatric K-wire fixation	304	Perioperative cefazolin vs no prophylaxis	No clear reduction in infection
Bashyal et al. [34]	2009	Retrospective cohort	Supracondylar humerus pinning	622	Preoperative antibiotic vs no prophylaxis	Low surgical site infection rates; effect uncertain
van Leeuwen et al. [35]	2016	Retrospective study	Hand and wrist percutaneous pinning	1,213	Prophylaxis vs no prophylaxis	No convincing reduction in pin-site infection
Mangwani et al. [36]	2017	Randomised controlled trial	Lesser-toe fusion with K-wire	100	Flucloxacillin or teicoplanin vs no antibiotic	No significant difference in surgical site infection
PARITY Investigators [6]	2022	International blinded randomised controlled trial	Orthopaedic oncology and endoprosthetic reconstruction	604 analysed	One-day vs five-day cephalosporin prophylaxis	Five days did not reduce surgical site infection and produced more antibiotic-related complications
Milhem et al. [37]	2015	Pilot multicentre randomised controlled trial	Bone-tumour endoprosthetic reconstruction	60	24-hour vs five-day prophylaxis	Demonstrated feasibility of the definitive PARITY trial
Byers et al. [38]	2022	Retrospective cohort	Megaprosthesis reconstruction	184	Short vs prolonged postoperative prophylaxis	Prolonged antibiotics did not reduce infection
Kiran et al. [39]	2022	Prospective cohort	Megaendoprosthetic replacement for metastatic bone disease	51	Single preoperative antibiotic dose	Deep infection rate was 1.9%; single-dose prophylaxis appeared effective
Tahir et al. [40]	2026	Retrospective cohort	K-wire fixation	264	Prophylaxis vs no prophylaxis	No convincing evidence that routine prophylaxis reduced K-wire-associated infection
Rumalla et al. [41]	2026	Retrospective database cohort	Primary total knee arthroplasty	528,250	Cefazolin vs non-cefazolin prophylaxis	Non-cefazolin prophylaxis was associated with increased periprosthetic joint infection risk

TABLE 2: Characteristics of the included studies

Clinical Outcomes

The direction and magnitude of benefit varied according to the surgical setting. Systemic antibiotic prophylaxis was generally beneficial in higher-risk procedures, particularly contaminated trauma and open-fracture surgery [5]. By contrast, studies comparing shorter and prolonged prophylactic regimens generally did not demonstrate additional infection prevention from extending postoperative antibiotic exposure [2,6,26].

In open-fracture surgery, randomised and comparative evidence supports early systemic antibiotic prophylaxis, while longer courses have not consistently demonstrated additional benefit over shorter regimens. Dellinger et al. reported infection rates of approximately 12-13% across one-day and five-day cephalosporin regimens, illustrating the absence of a clear duration-response relationship once effective prophylaxis had been administered [5]. Additional studies have evaluated alternative agents and combinations according to fracture severity and contamination risk [27-31].

Spinal surgery showed a similar pattern. A systematic review found no significant advantage of extended postoperative antimicrobial prophylaxis over shorter perioperative administration [9]. The individual comparative studies summarised in Table 2 likewise suggest that dose adequacy and agent selection may be more important than routine postoperative continuation [22-26].

Arthroplasty

Arthroplasty studies generally indicated that routine broadening or prolongation of prophylaxis did not improve infection outcomes. Cefazolin remained an effective standard regimen in patients without a specific indication for alternative prophylaxis, while several observational studies raised concerns regarding inappropriate vancomycin use, underdosing, and non-cephalosporin regimens [3,4,19-21,41].

Spinal Surgery

Evidence from spinal surgery similarly suggested that agent selection and dose adequacy may be more important than prolonged postoperative administration. Observational studies reported higher infection risk with inappropriate or non-cefazolin prophylaxis, while comparative duration studies did not consistently demonstrate benefit from extending prophylaxis beyond 24 hours [22-26].

Open Fractures and Trauma

In open fractures and trauma, early systemic prophylaxis remains clinically important because of the higher contamination risk. Studies evaluated cephalosporins, antistaphylococcal agents, aminoglycoside combinations, and broader-spectrum regimens, but longer prophylactic courses were not consistently superior once appropriate early treatment had been administered [5,27-31].

K-wire Fixation and Implant Removal

Routine systemic prophylaxis is less clearly beneficial in clean K-wire procedures. A procedure-specific systematic review found no statistically significant reduction in infection with perioperative antibiotics [8], and the underlying comparative evidence included paediatric, hand/wrist, and toe-fusion studies [32-36]. A recent retrospective cohort provides additional contemporary evidence [40]. Implant-removal surgery has also produced mixed findings [42].

Orthopaedic Oncology

Orthopaedic tumour reconstruction carries a substantially higher infection risk than routine clean elective orthopaedic surgery. The PARITY trial found no reduction in surgical site infection when postoperative cephalosporin prophylaxis was extended from one day to five days, while antibiotic-related complications were more frequent with prolonged exposure [6]. Microbiological analyses also demonstrated a considerable burden of pathogens resistant to standard prophylaxis [7]. Other oncology cohorts similarly suggest that drug selection and appropriate dosing may be more important than prolonged duration [38,39]. Broader prophylactic strategies are also being investigated in selected high-risk orthopaedic populations, but their routine use requires further clinical and microbiological evidence [43].

Microbiological and Antimicrobial-Resistance Findings

Staphylococci remained the predominant Gram-positive organisms, while Gram-negative bacilli and resistant pathogens were also clinically relevant, particularly in trauma, complex reconstruction, and orthopaedic oncology. Methicillin-resistant and cefazolin-resistant organisms have been reported among orthopaedic surgical site infections [11]. In the PARITY microbiological analysis, resistant breakthrough pathogens occurred frequently, and extending the duration of prophylaxis did not eliminate these organisms [7].

Histopathological Outcomes

Histopathological outcomes were reported infrequently and inconsistently. Acute neutrophilic inflammation and chronic inflammatory changes were used as supportive diagnostic findings in some studies; however, differences in tissue sampling, definitions, and reporting prevented meaningful quantitative comparison. Histopathology was therefore considered a complementary diagnostic outcome rather than a primary measure of prophylactic effectiveness.

Narrative Synthesis

A structured narrative synthesis was undertaken because considerable clinical and methodological heterogeneity was observed across the included studies. Procedures ranged from primary arthroplasty and spinal surgery to open fractures, K-wire fixation, implant removal, and orthopaedic oncology. Prophylactic strategies also differed in antimicrobial agent, dose, timing, route, and duration. In addition, definitions and follow-up periods for surgical site infection varied across studies.

For these reasons, the findings were synthesised narratively rather than combined into a single pooled effect estimate. Randomised trials were given greater weight when available, while observational studies were used to provide complementary evidence regarding real-world prescribing, dose adequacy, microbiological findings, resistance patterns, and uncommon outcomes.

Across settings, the evidence generally supported timely and appropriately dosed perioperative prophylaxis. By contrast, routine extension of prophylaxis for several postoperative days did not consistently demonstrate additional clinical benefit. The magnitude and certainty of these findings varied according to procedure type, study design, and baseline infection risk.

Risk of Bias

Two separate reviewers checked for potential bias. The RoB 2 tool was used to evaluate randomised controlled trials, while the ROBINS-I tool was used to assess non-randomised comparative studies. Both tools were developed by the Cochrane Collaboration to ensure the highest level of objectivity in their respective assessments. Argumentation and, if required, the involvement of a third reviewer helped settle any disagreements that arose. Domains examined for randomised trials included selection of the reported result, missing outcome data, variations from planned interventions, assessment of the outcome, and bias resulting from the randomisation procedure. The categories that were examined for non-randomised studies included participant selection, intervention categorisation, missing data, outcome measurement, confounding, and the selection of the reported result.

Overall, randomised studies generally demonstrated stronger internal validity than observational studies. The most frequent concerns among randomised studies involved incomplete reporting of allocation concealment, small sample sizes, and limited numbers of infection events. Among non-randomised studies, the principal concerns were confounding by indication, retrospective treatment allocation, baseline differences in infection risk, differences in operative complexity, and incomplete adjustment for patient comorbidities.

Study-level RoB assessments using RoB 2 and ROBINS-I are presented in Table 3.

Study	Design	Tool	Main risk-of-bias considerations	Overall judgment
Mauerhan et al. [2]	Multicentre double-blind randomised trial	RoB 2	Randomised and blinded design; older reporting standards with limited detail on allocation methods	Low
McQueen et al. [17]	Randomised trial	RoB 2	Limited reporting of sequence generation and allocation concealment	Some concerns
Tyllianakis et al. [18]	Prospective randomised study	RoB 2	Randomisation reported; blinding and selective-reporting safeguards incompletely described	Some concerns
Peel et al. [4]	Multicentre double-blind randomised controlled trial	RoB 2	Large blinded trial, prespecified outcomes, and low attrition	Low
Dellinger et al. [5]	Double-blind randomised trial	RoB 2	Appropriate randomised design; older study with some limitations in contemporary reporting detail	Low
Vasenius et al. [27]	Prospective randomised study	RoB 2	Limited information on allocation concealment and blinding	Some concerns
Stevenson et al. [28]	Double-blind placebo-controlled randomised controlled trial	RoB 2	Appropriate randomisation, placebo control, and blinding	Low
Saveli et al. [29]	Randomised pilot trial	RoB 2	Pilot nature, small sample size, few infection events, and imprecision	Some concerns
Mangwani et al. [36]	Prospective randomised controlled trial	RoB 2	Small sample size and limited infection-event numbers	Some concerns
PARITY Investigators [6]	International blinded randomised controlled trial	RoB 2	Robust multicentre randomisation, blinded outcome assessment, and prespecified outcomes	Low
Milhem et al. [37]	Pilot multicentre randomised controlled trial	RoB 2	Pilot study with limited power despite appropriate randomised methodology	Some concerns
Sewick et al. [19]	Retrospective cohort	ROBINS-I	Confounding by indication and non-random selection of dual prophylaxis	Moderate
Kheir et al. [3]	Retrospective cohort	ROBINS-I	Antibiotic selection and dosing related to patient characteristics; residual confounding	Moderate
Honkanen et		ROBINS-	Non-random prophylaxis selection; residual confounding	

al. [20]	Retrospective cohort	I	despite statistical adjustment	Moderate
Carender et al. [21]	Retrospective cohort	ROBINS-I	Selection for extended oral prophylaxis and obesity-related baseline infection-risk differences	Moderate
Lopez et al. [22]	Retrospective pre-post cohort	ROBINS-I	Temporal confounding and possible concurrent changes in perioperative infection-control practices	Serious
Lambrechts et al. [23]	Retrospective cohort	ROBINS-I	Association between body weight, cefazolin dosing, operative complexity, and surgical site infection risk	Moderate
Kim et al. [24]	Propensity-matched cohort	ROBINS-I	Propensity matching reduces but does not eliminate confounding by indication	Moderate
Kazarian et al. [25]	Retrospective cohort	ROBINS-I	Vancomycin use influenced by allergy, colonisation, and other baseline risk factors	Serious
Marimuthu et al. [26]	Prospective comparative study	ROBINS-I	Non-randomised assignment of antibiotic duration and potential clinical confounding	Moderate
Redfern et al. [30]	Retrospective cohort	ROBINS-I	Small sample size, differences in injury severity, and antibiotic-selection confounding	Serious
Patanwala et al. [31]	Multicentre retrospective cohort	ROBINS-I	Confounding from fracture severity, institutional practice, and treatment selection	Moderate
Heras et al. [32]	Retrospective study	ROBINS-I	Limited control for fracture severity, operative factors, and indication for prophylaxis	Serious
Lobst et al. [33]	Retrospective study	ROBINS-I	Selection bias and incomplete adjustment for baseline infection risk	Serious
Bashyal et al. [34]	Retrospective cohort	ROBINS-I	Low event rate, retrospective exposure ascertainment, and residual confounding	Moderate
van Leeuwen et al. [35]	Retrospective study	ROBINS-I	Confounding by procedure type, duration of pinning, and prophylaxis indication	Moderate
Byers et al. [38]	Retrospective cohort	ROBINS-I	Duration of antibiotics influenced by clinical complexity and oncology-related risk factors	Moderate
Tahir et al. [40]	Retrospective cohort	ROBINS-I	Confounding by indication and incomplete adjustment for procedural infection risk	Moderate
Rumalla et al. [41]	Retrospective cohort	ROBINS-I	Choice of non-cephalosporin prophylaxis likely related to allergy, comorbidity, and baseline infection risk	Moderate
Kiran et al. [39]	Prospective cohort	ROBINS-I	No randomised comparator; potential confounding by case selection and operative complexity	Moderate

TABLE 3: Study-by-study risk-of-bias assessment of the 30 included primary studies

RoB 2: Risk of Bias 2; ROBINS-I: Risk of Bias in Non-randomized Studies of Interventions

Summary of the Overall Risk of Bias

Among the 11 randomised controlled trials, five were judged to have low risk of bias, and six had some concerns (Table 4). No randomised trial was judged to have high overall risk of bias. Among the 19 non-randomised studies, 14 were judged to have moderate risk of bias, and five were considered to have serious risk of bias; none was judged to have critical risk. The principal concerns were confounding by indication, retrospective treatment allocation, temporal changes in institutional practice, and incomplete adjustment for differences in patient and procedural risk.

Study design	Low	Some concerns	Moderate	Serious	Critical
Randomised studies (n = 11)	5 (45.5%)	6 (54.5%)	-	-	-
Non-randomised studies (n = 19)	-	-	14 (73.7%)	5 (26.3%)	0
Total (n = 30)	5	6	14	5	0

TABLE 4: Summary of risk-of-bias assessment

Risk of Bias and Interpretation of Findings

The RoB assessment informed the interpretation of the review findings. Evidence from randomised trials was considered methodologically stronger than evidence derived from retrospective observational cohorts, particularly for comparisons of prophylaxis duration.

Observational studies provided important information on antibiotic selection, dose adequacy, microbiological outcomes, antimicrobial resistance, and real-world practice, but were more susceptible to confounding by indication and differences in baseline infection risk. Findings from these studies were therefore interpreted cautiously and considered alongside study design, procedural context, and methodological limitations.

Discussion

The findings support an important distinction between appropriate perioperative prophylaxis and unnecessary prolongation of antibiotic exposure. Early systemic prophylaxis remains important in contaminated and higher-risk surgery, particularly open fractures [5,11]. By contrast, evidence across arthroplasty, spinal surgery, and orthopaedic tumour reconstruction does not consistently support extending prophylaxis for several postoperative days once adequate perioperative coverage has been provided [2,6,9,10,26].

The choice of prophylactic agent is equally important. Cefazolin remains a key option because of its activity against methicillin-susceptible *Staphylococci* and favourable pharmacokinetic profile. Routine substitution with or addition of vancomycin is not supported for all patients. Arthroplasty evidence has not demonstrated overall benefit from routine vancomycin addition in patients without known MRSA colonisation [4], while observational arthroplasty and spine studies suggest that non-cephalosporin prophylaxis without a clear indication may be associated with higher infection risk [3,24,41].

Dose adequacy may be more important than prolonged duration. Orthopaedic studies suggest that underdosing can compromise prophylactic exposure, particularly in patients with higher body mass or during complex procedures [3,22]. Weight-appropriate dosing and intraoperative redosing should therefore be considered when pharmacokinetic or operative factors warrant them.

Local microbiological surveillance remains important. *Staphylococci* predominate, but resistant Gram-positive organisms and Gram-negative pathogens also contribute to breakthrough infection [7,11]. Extending the same prophylactic agent is unlikely to prevent infection caused by organisms resistant to that agent. More individualised prophylaxis may be appropriate in selected high-risk populations, but broader regimens should be supported by microbiological and clinical evidence rather than adopted routinely.

Antimicrobial stewardship is particularly relevant because prophylaxis is administered to large numbers of patients without established infection. Unnecessary extension increases antimicrobial exposure and may contribute to adverse drug reactions, nephrotoxicity, *Clostridioides difficile* infection, ecological selection pressure, and additional healthcare costs. The goal should therefore be the minimum effective prophylactic exposure rather than the longest possible duration.

This review has several limitations. The included studies were clinically heterogeneous with respect to procedure type, baseline contamination risk, implant burden, patient characteristics, prophylactic regimen, follow-up duration, and outcome definitions. These differences limited direct comparability across studies and were the principal reason a quantitative meta-analysis was not considered appropriate. Much of the evidence concerning antibiotic selection was observational and therefore susceptible to confounding, while antimicrobial-resistance, adverse-event, and histopathological outcomes were inconsistently reported. The absence of prospective protocol registration should also be considered when interpreting the review findings.

Future studies should use standardised definitions of surgical site infection, distinguish superficial from

deep and implant-associated infection, report the susceptibility of breakthrough organisms to the prophylactic antimicrobial used, and prospectively capture antibiotic-related harms. Greater consistency in reporting microbiological, antimicrobial resistance, and histopathological outcomes would also improve comparability across studies.

Conclusions

Effective orthopaedic prophylaxis requires the right antimicrobial, dose, route, timing, frequency, and duration, with redosing when indicated. Routine prolongation beyond the perioperative period has not shown consistent additional benefit, although combination prophylaxis may be appropriate in selected high-risk situations.

Agent selection should consider pharmacokinetics, procedure-specific risk, local susceptibility patterns, and institutional antibiotic policy. Better standardisation of microbiological, antimicrobial-resistance, adverse-event, and histopathological reporting is needed in future orthopaedic prophylaxis studies.

Appendices

Database search strategies

All searches were conducted from database inception through 30 June 2026. No publication-year restriction was applied. Search syntax was adapted to the indexing and field structure of each database. The principal strategy combined orthopaedic procedure terms with antibiotic-prophylaxis terms; additional sensitivity terms relating to surgical site infection, implant infection, microbiology, histopathology, and antimicrobial resistance were used to maximise retrieval.

Database	Search strategy
MEDLINE/PubMed	("Orthopedic Procedures"[MeSH] OR orthopaedic*[Title/Abstract] OR orthopedic*[Title/Abstract] OR arthroplast*[Title/Abstract] OR "joint replacement"[Title/Abstract] OR "fracture fixation"[Title/Abstract] OR "spinal surgery"[Title/Abstract] OR "spinal instrumentation"[Title/Abstract] OR "orthopedic oncology"[Title/Abstract] OR "orthopaedic oncology"[Title/Abstract]) AND ("Antibiotic Prophylaxis"[MeSH] OR "antibiotic prophylaxis"[Title/Abstract] OR "antimicrobial prophylaxis"[Title/Abstract] OR "perioperative antibiotic**"[Title/Abstract] OR "prophylactic antibiotic**"[Title/Abstract])
Embase	('orthopedic surgery'/exp OR orthopaedic*:ti,ab OR orthopedic*:ti,ab OR arthroplast*:ti,ab OR 'joint replacement':ti,ab OR 'fracture fixation':ti,ab OR 'spinal surgery':ti,ab OR 'spinal instrumentation':ti,ab OR 'orthopedic oncology':ti,ab OR 'orthopaedic oncology':ti,ab) AND ('antibiotic prophylaxis'/exp OR 'antibiotic prophylaxis':ti,ab OR 'antimicrobial prophylaxis':ti,ab OR 'perioperative antibiotic**':ti,ab OR 'prophylactic antibiotic**':ti,ab)
Scopus	TITLE-ABS-KEY (orthopaedic* OR orthopedic* OR arthroplast* OR "joint replacement" OR "fracture fixation" OR "spinal surgery" OR "spinal instrumentation" OR "orthopedic oncology" OR "orthopaedic oncology") AND TITLE-ABS-KEY ("antibiotic prophylaxis" OR "antimicrobial prophylaxis" OR "perioperative antibiotic**" OR "prophylactic antibiotic**")
Web of Science Core Collection	TS=(orthopaedic* OR orthopedic* OR arthroplast* OR "joint replacement" OR "fracture fixation" OR "spinal surgery" OR "spinal instrumentation" OR "orthopedic oncology" OR "orthopaedic oncology") AND TS=("antibiotic prophylaxis" OR "antimicrobial prophylaxis" OR "perioperative antibiotic**" OR "prophylactic antibiotic**")
Cochrane CENTRAL	#1 MeSH descriptor: [Orthopedic Procedures] explode all trees; #2 orthopaedic/orthopedic/procedure terms; #3 MeSH descriptor: [Antibiotic Prophylaxis] explode all trees; #4 prophylaxis terms; #5 (#1 OR #2) AND (#3 OR #4)
Sensitivity concepts	"surgical site infection", SSI, "implant infection", "periprosthetic joint infection", microbiolog*, histopatholog*, "antimicrobial resistance", "antibiotic resistance", MRSA, and "Gram-negative"

TABLE 5: Database-specific search strategies

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Rajdeep Paul, Asim Israr Khan, Mamta Gupta, Tushar Malik, Abhiraj Ramchandani, Rajesh Kumar, Kuldeep Singh

Acquisition, analysis, or interpretation of data: Rajdeep Paul, Santosh Jayant, Mamta Gupta, S Zeeshan A. Hashmi, Rajesh Kumar, Kuldeep Singh

Drafting of the manuscript: Rajdeep Paul, Santosh Jayant, Asim Israr Khan, S Zeeshan A. Hashmi, Abhiraj Ramchandani

Critical review of the manuscript for important intellectual content: Rajdeep Paul, Mamta Gupta, S Zeeshan A. Hashmi, Tushar Malik, Rajesh Kumar, Kuldeep Singh

Supervision: Rajdeep Paul

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

ChatGPT (GPT-5.6 Sol, OpenAI, California, USA) and Grammarly (Grammarly, Inc., California, USA) were used only to help with language editing, grammar, formatting, and improving the readability of the manuscript. They were not used to generate or alter research data, statistical analyses, or scientific findings. All content was reviewed and approved by the authors, who take full responsibility for the final manuscript. The authors are from different institutions and worked together independently on the conception, review, interpretation, and preparation of this manuscript.

References

- Bratzler DW, Dellinger EP, Olsen KM, et al.: Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm*. 2013, 70:195-283. [10.2146/ajhp120568](#)
- Mauerhan DR, Nelson CL, Smith DL, et al.: Prophylaxis against infection in total joint arthroplasty. One day of cefuroxime compared with three days of cefazolin. *J Bone Joint Surg Am*. 1994, 76:39-45. [10.2106/00004623-199401000-00006](#)
- Kheir MM, Tan TL, Azboy I, Tan DD, Parvizi J: Vancomycin prophylaxis for total joint arthroplasty: incorrectly dosed and has a higher rate of periprosthetic infection than cefazolin. *Clin Orthop Relat Res*. 2017, 475:1767-74. [10.1007/s11999-017-5302-0](#)
- Peel TN, Astbury S, Cheng AC, et al.: Trial of vancomycin and cefazolin as surgical prophylaxis in arthroplasty. *N Engl J Med*. 2023, 389:1488-98. [10.1056/NEJMoa2301401](#)
- Dellinger EP, Caplan ES, Weaver LD, et al.: Duration of preventive antibiotic administration for open extremity fractures. *Arch Surg*. 1988, 123:333-9. [10.1001/archsurg.1988.01400270067010](#)
- Ghert M, Schneider P, Guyatt G, et al.: Comparison of prophylactic intravenous antibiotic regimens after endoprosthetic reconstruction for lower extremity bone tumors: a randomized clinical trial. *JAMA Oncol*. 2022, 8:345-53. [10.1001/jamaoncol.2021.6628](#)
- Kuster S, Gottlich C, O'Shea T, Ghert M, Mertz D: The burden of surgical site infections with pathogens presumably resistant to perioperative prophylaxis in orthopedic tumor surgery: secondary analysis of the Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) Trial. *J Infect Dis*. 2026, 233:e174-82. [10.1093/infdis/jiaf513](#)
- Abul A, Karam M, Al-Shammari S, Giannoudis P, Pandit H, Nisar S: Peri-operative antibiotic prophylaxis in K-wire fixation: a systematic review and meta-analysis. *Indian J Orthop*. 2023, 57:1000-7. [10.1007/s43465-023-00879-6](#)
- Phillips BT, Sheldon ES, Orhurhu V, et al.: Preoperative versus extended postoperative antimicrobial prophylaxis of surgical site infection during spinal surgery: a comprehensive systematic review and meta-analysis. *Adv Ther*. 2020, 37:2710-33. [10.1007/s12325-020-01371-5](#)
- Thornley P, Evaniew N, Riediger M, Winemaker M, Bhandari M, Ghert M: Postoperative antibiotic prophylaxis in total hip and knee arthroplasty: a systematic review and meta-analysis of randomized controlled trials. *CMAJ Open*. 2015, 3:E338-43. [10.9778/cmajo.20150012](#)
- Norton TD, Skeete F, Dubrovskaya Y, Phillips MS, Bosco JD 3rd, Mehta SA: Orthopedic surgical site infections: analysis of causative bacteria and implications for antibiotic stewardship. *Am J Orthop (Belle Mead NJ)*. 2014, 43:E89-92.
- Müller D, Kaiser D, Sairanen K, Studhalter T, Uçkay İ: Antimicrobial prophylaxis for the prevention of surgical site infections in orthopaedic oncology: a narrative review of current concepts. *J Bone Jt Infect*. 2019, 4:254-63. [10.7150/jbji.39050](#)
- Page MJ, McKenzie JE, Bossuyt PM, et al.: The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021, 372:n71. [10.1136/bmj.n71](#)
- Page MJ, Moher D, Bossuyt PM, et al.: PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ*. 2021, 372:n160. [10.1136/bmj.n160](#)
- Sterne JA, Savović J, Page MJ, et al.: RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019, 366:l4898. [10.1136/bmj.l4898](#)
- Sterne JA, Hernán MA, Reeves BC, et al.: ROBINS-I: a tool for assessing risk of bias in non-randomised

- studies of interventions. *BMJ*. 2016, 355:i4919. [10.1136/bmj.i4919](https://doi.org/10.1136/bmj.i4919)
17. McQueen MM, Hughes SP, May P, Verity L: Cefuroxime in total joint arthroplasty. Intravenous or in bone cement. *J Arthroplasty*. 1990, 5:169-72. [10.1016/S0883-5403\(06\)80236-6](https://doi.org/10.1016/S0883-5403(06)80236-6)
18. Tyllianakis ME, Karageorgos ACh, Marangos MN, Saridis AG, Lambiris EE: Antibiotic prophylaxis in primary hip and knee arthroplasty: comparison between cefuroxime and two specific antistaphylococcal agents. *J Arthroplasty*. 2010, 25:1078-82. [10.1016/j.arth.2010.01.105](https://doi.org/10.1016/j.arth.2010.01.105)
19. Sewick A, Makani A, Wu C, O'Donnell J, Baldwin KD, Lee GC: Does dual antibiotic prophylaxis better prevent surgical site infections in total joint arthroplasty?. *Clin Orthop Relat Res*. 2012, 470:2702-7. [10.1007/s11999-012-2255-1](https://doi.org/10.1007/s11999-012-2255-1)
20. Honkanen M, Sirkeoja S, Karpelin M, Eskelinen A, Syrjänen J: Effect of non-cephalosporin antibiotic prophylaxis on the risk of periprosthetic joint infection after total joint replacement surgery: a retrospective study with a 1-year follow-up. *Infect Prev Pract*. 2023, 5:100285. [10.1016/j.infpip.2023.100285](https://doi.org/10.1016/j.infpip.2023.100285)
21. Carender CN, DeMik DE, Glass NA, Noiseux NO, Brown TS, Bedard NA: Do extended oral postoperative antibiotics prevent early periprosthetic joint infection in morbidly obese patients undergoing primary total joint arthroplasty?. *J Arthroplasty*. 2021, 36:2716-21. [10.1016/j.arth.2021.03.018](https://doi.org/10.1016/j.arth.2021.03.018)
22. Lopez WY, Rider SM, Nwosu K, et al.: The impact of vancomycin and cefazolin as standard preoperative antibiotic prophylaxis on surgical site infections following instrumented spinal fusion. *Spine (Phila Pa 1976)*. 2019, 44:E366-71. [10.1097/BRS.0000000000002839](https://doi.org/10.1097/BRS.0000000000002839)
23. Karamian BA, Toci GR, Lambrechts MJ, et al.: Cefazolin prophylaxis in spine surgery: patients are frequently underdosed and at increased risk for infection. *Spine J*. 2022, 22:1442-50. [10.1016/j.spinee.2022.05.018](https://doi.org/10.1016/j.spinee.2022.05.018)
24. Kim MS, Romoff MR, Beyer R, et al.: Cefazolin prophylaxis is associated with lower surgical site infection risk than vancomycin following elective spine surgery. *N Am Spine Soc J*. 2026, 25:100857. [10.1016/j.xnsj.2026.100857](https://doi.org/10.1016/j.xnsj.2026.100857)
25. Kazarian GS, Mok JK, Johnson M, et al.: Perioperative infection prophylaxis with vancomycin is a significant risk factor for deep surgical site infection in spine surgery. *Spine (Phila Pa 1976)*. 2024, 49:1583-90. [10.1097/BRS.0000000000005081](https://doi.org/10.1097/BRS.0000000000005081)
26. Marimuthu C, Abraham VT, Ravichandran M, Achimuthu R: Antimicrobial prophylaxis in instrumented spinal fusion surgery: a comparative analysis of 24-hour and 72-hour dosages. *Asian Spine J*. 2016, 10:1018-22. [10.4184/asj.2016.10.6.1018](https://doi.org/10.4184/asj.2016.10.6.1018)
27. Vasenius J, Tulikoura I, Vainionpää S, Rokkanen P: Clindamycin versus cloxacillin in the treatment of 240 open fractures. A randomized prospective study. *Ann Chir Gynaecol*. 1998, 87:224-8.
28. Stevenson J, McNaughton G, Riley J: The use of prophylactic flucloxacillin in treatment of open fractures of the distal phalanx within an accident and emergency department: a double-blind randomized placebo-controlled trial. *J Hand Surg Br*. 2003, 28:388-94. [10.1016/S0266-7681\(03\)00175-X](https://doi.org/10.1016/S0266-7681(03)00175-X)
29. Saveli CC, Morgan SJ, Belknap RW, et al.: Prophylactic antibiotics in open fractures: a pilot randomized clinical safety study. *J Orthop Trauma*. 2013, 27:552-7. [10.1097/BOT.0b013e31828d92ee](https://doi.org/10.1097/BOT.0b013e31828d92ee)
30. Redfern J, Wasilko SM, Groth ME, McMillian WD, Bartlett CS 3rd: Surgical site infections in patients with type 3 open fractures: comparing antibiotic prophylaxis with cefazolin plus gentamicin versus piperacillin/tazobactam. *J Orthop Trauma*. 2016, 30:415-9. [10.1097/BOT.0000000000000554](https://doi.org/10.1097/BOT.0000000000000554)
31. Patanwala AE, Radosevich JJ, Meshay I, et al.: Cefazolin monotherapy versus cefazolin plus aminoglycosides for antimicrobial prophylaxis of type III open fractures. *Am J Ther*. 2019, 28:e284-91. [10.1097/MJT.0000000000001121](https://doi.org/10.1097/MJT.0000000000001121)
32. de las Heras J, Durán D, de la Cerda J, Romanillos O, Martínez-Miranda J, Rodríguez-Merchán EC: Supracondylar fractures of the humerus in children. *Clin Orthop Relat Res*. 2005, 57-64. [10.1097/01.blo.0000155373.03565.78](https://doi.org/10.1097/01.blo.0000155373.03565.78)
33. Iobst CA, Spurdle C, King WF, Lopez M: Percutaneous pinning of pediatric supracondylar humerus fractures with the semistere technique: the Miami experience. *J Pediatr Orthop*. 2007, 27:17-22. [10.1097/bpo.0b013e31802b68dc](https://doi.org/10.1097/bpo.0b013e31802b68dc)
34. Bashyal RK, Chu JY, Schoenecker PL, Dobbs MB, Luhmann SJ, Gordon JE: Complications after pinning of supracondylar distal humerus fractures. *J Pediatr Orthop*. 2009, 29:704-8. [10.1097/BPO.0b013e3181b768ac](https://doi.org/10.1097/BPO.0b013e3181b768ac)
35. van Leeuwen WF, van Hoorn BT, Chen N, Ring D: Kirschner wire pin site infection in hand and wrist fractures: incidence rate and risk factors. *J Hand Surg Eur Vol*. 2016, 41:990-4. [10.1177/1755193416661280](https://doi.org/10.1177/1755193416661280)
36. Mangwani J, Gulati A, Benson R, Cichero M, Williamson DM: Role of prophylactic antibiotics in lesser toe fusion surgery: a prospective randomised controlled trial. *Foot Ankle Surg*. 2017, 23:50-2. [10.1016/j.fas.2016.02.004](https://doi.org/10.1016/j.fas.2016.02.004)
37. Prophylactic antibiotic regimens in tumour surgery (PARITY): a pilot multicentre randomised controlled trial. *Bone Joint Res*. 2015, 4:154-62. [10.1302/2046-3758.49.2000482](https://doi.org/10.1302/2046-3758.49.2000482)
38. Byers IS, Turner NA, Levine NL, et al.: Antibiotic prophylaxis for megaprosthesis reconstructions: drug and dosing may matter more than duration. *Antimicrob Agents Chemother*. 2022, 66:e0014022. [10.1128/aac.00140-22](https://doi.org/10.1128/aac.00140-22)
39. Kiran M, Alsousou J, Dalal N, Ralte P, Kumar G, Kapoor B: Is a single dose of preoperative antibiotic therapy effective for patients treated with megaendoprosthesis after metastatic bone tumour resection?. *Musculoskelet Surg*. 2022, 106:187-93. [10.1007/s12306-020-00692-6](https://doi.org/10.1007/s12306-020-00692-6)
40. Tahir MA, Malik HZ, Nisar S: Effect of prophylactic antibiotics on K-wire-associated infection: a retrospective cohort study. *Cureus*. 2026, 18:e101334. [10.7759/cureus.101334](https://doi.org/10.7759/cureus.101334)
41. Rumalla KC, Sontag-Milobsky IL, Chen AR, Selph TJ, Compton TM, Edelstein AI: Noncefazolin antibiotic prophylaxis is associated with increased periprosthetic joint infection risk following total knee arthroplasty. *J Arthroplasty*. 2026, 41:601-7. [10.1016/j.arth.2025.06.057](https://doi.org/10.1016/j.arth.2025.06.057)
42. Rather II, Shafiq N, Pandey AK, Bhandari RK, Malhotra S, Chouhan DK: Antibiotic prophylaxis for orthopaedic implant removal: what does the evidence say?. *Curr Drug Saf*. 2023, 18:116-20. [10.2174/1574886317666220429081207](https://doi.org/10.2174/1574886317666220429081207)
43. Uçkay I, Bomberg H, Risch M, Müller D, Betz M, Farshad M: Broad-spectrum antibiotic prophylaxis in tumor and infected orthopedic surgery-the prospective-randomized, microbiologist-blinded, stratified, superiority trials: BAPTIST Trials. *Trials*. 2024, 25:69. [10.1186/s13063-023-07605-5](https://doi.org/10.1186/s13063-023-07605-5)