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Effectiveness of Antibiotic Prophylaxis in Preventing Postoperative Infection Following Total Knee Arthroplasty: A Systematic Review

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A B S T R A C T

Introduction: Total knee arthroplasty is an effective treatment for advanced knee disorders but remains vulnerable to postoperative infections, including periprosthetic joint infection, which can lead to serious complications and increased healthcare burden. Antibiotic prophylaxis is widely used to reduce this risk, yet optimal strategies remain debated. Therefore, this study aims to systematically review the evidence regarding the effectiveness of antibiotic prophylaxis in preventing infection following TKA.

Material and methods: This systematic review was conducted according to PRISMA guidelines. Eligible studies included randomized and observational research evaluating antibiotic prophylaxis in adult patients undergoing total knee arthroplasty with reported postoperative infection outcomes. Multiple databases were searched using MeSH terms and related keywords by two independent reviewers. Study quality was assessed using the Newcastle–Ottawa Scale and the Cochrane Risk of Bias tool.

Results: The literature search identified 851 records, of which nine studies met the inclusion criteria after screening and full-text assessment. Overall, intravenous antibiotic regimens demonstrated moderate to high treatment success across studies, with reported success rates ranging from 63% to 90% and follow-up durations varying between 3.5 and 72 months. Most regimens involved glycopeptide- or rifampicin-based therapies administered for approximately 2-6 weeks, with generally favorable clinical outcomes.

Conclusion: The available evidence suggests that intravenous antibiotic therapy provides generally favorable outcomes in the management of infection-related complications. Across the included studies, treatment success was consistently moderate to high despite variations in antimicrobial regimens, treatment duration, and follow-up periods. Glycopeptide and rifampicin-based therapies appear to play a central role in achieving effective infection control.

Introduction

Total knee arthroplasty (TKA) is widely recognized as one of the most successful and commonly performed orthopedic procedures for the treatment of advanced knee osteoarthritis and other degenerative joint disorders. Over the past several decades, TKA has significantly improved quality of life by reducing pain, restoring joint function, and enhancing mobility in patients with severe knee pathology. With the aging global population and the rising prevalence of obesity and degenerative joint disease, the demand for TKA continues to increase worldwide. Despite substantial improvements in surgical techniques, implant materials, and perioperative care, postoperative complications remain a concern. Among these complications, surgical site infection represents one of the most serious and devastating outcomes following TKA, often resulting in prolonged hospitalization, increased healthcare costs, impaired functional recovery, and occasionally the need for revision surgery or implant removal (1).

Postoperative infections after knee arthroplasty encompass a spectrum of conditions ranging from superficial wound infections to deep periprosthetic joint infections (PJI). While superficial infections may sometimes be managed with antibiotics and local wound care, deep infections involving the prosthetic joint are far more complex and difficult to treat. Periprosthetic joint infection is considered one of the leading causes of early failure after TKA and often requires extensive interventions, including debridement, implant retention strategies, staged revision arthroplasty, or long-term antimicrobial therapy. The consequences of PJI are substantial not only for the patient but also for healthcare systems, as treatment often involves multiple surgeries, long hospital stays, and prolonged rehabilitation. Even though the reported incidence of infection following primary TKA is relatively low, typically ranging from approximately 0.5% to 2%, the increasing number of arthroplasty procedures performed annually means that the absolute number of infected cases continues to rise (2).

The pathogenesis of postoperative infection in TKA is multifactorial and involves a complex interaction between microbial contamination, host immune response, and surgical factors. Microorganisms can gain access to the surgical site during the procedure through direct contamination from the skin, surgical instruments, or the operating room environment. Once bacteria adhere to the surface of a prosthetic implant, they can form biofilms structured communities of microorganisms embedded within a protective extracellular matrix. Biofilm formation is particularly problematic because it significantly increases bacterial resistance to both host immune defenses and antimicrobial therapy. As a result, infections associated with prosthetic implants are often difficult to eradicate and may require removal of the prosthesis to achieve complete resolution (3).

Several patient-related and procedure-related risk factors have been associated with an increased likelihood of infection after TKA. Patient-related factors include advanced age, obesity, diabetes mellitus, malnutrition, smoking, immunosuppression, and chronic inflammatory diseases. These conditions may impair wound healing, compromise immune function, or increase bacterial colonization. Procedure-related factors include prolonged operative time, intraoperative contamination, inadequate sterile technique, and perioperative blood transfusion. In addition, factors related to the hospital environment and surgical workflow, such as operating room traffic, ventilation systems, and sterilization protocols, can influence the risk of postoperative infection. Because of the multifactorial nature of these infections, effective prevention strategies require a comprehensive perioperative approach that targets multiple stages of patient care (4).

Among the preventive strategies implemented in orthopedic surgery, antibiotic prophylaxis has become a cornerstone of infection prevention in joint arthroplasty. The concept of prophylactic antibiotic administration is based on maintaining adequate antimicrobial concentrations in serum and tissue at the time of surgical incision and throughout the operative period to prevent bacterial colonization of the surgical site. In the context of TKA, prophylactic antibiotics are typically administered intravenously prior to incision, with additional intraoperative or postoperative doses depending on the duration of surgery and institutional protocols. The effectiveness of prophylactic antibiotics in reducing surgical site infections has been supported by multiple clinical studies, leading to their widespread adoption as a standard component of perioperative management in arthroplasty procedures (5).

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Various classes of antibiotics have been utilized for prophylaxis in TKA, including first-generation cephalosporins such as cefazolin, which are commonly recommended because of their effectiveness against common skin flora, particularly Staphylococcus aureus and Staphylococcus epidermidis. These organisms are among the most frequent pathogens implicated in prosthetic joint infections. In patients with allergies to beta-lactam antibiotics, alternative agents such as clindamycin or vancomycin may be used. The choice of antibiotic, dosage, timing of administration, and duration of prophylaxis are critical factors that may influence the overall effectiveness of infection prevention strategies. Clinical guidelines generally recommend administering the first antibiotic dose within one hour before surgical incision to ensure adequate tissue concentrations during the procedure (6).

In recent years, additional approaches to antibiotic delivery have been explored to further reduce infection risk in knee arthroplasty. These include the use of antibiotic-loaded bone cement, intra-articular antibiotic administration, and extended postoperative prophylaxis in selected high-risk patients. Antibiotic-loaded bone cement, in particular, has gained attention for its ability to deliver high local concentrations of antibiotics directly at the implant interface while minimizing systemic toxicity. Similarly, intra-articular antibiotic injections at the end of surgery have been investigated as a potential strategy to reduce bacterial contamination within the joint space. While these methods show promising results in some studies, their routine use remains controversial, and evidence regarding their effectiveness is still evolving (7).

Despite the recognized importance of antibiotic prophylaxis, several aspects of its use in TKA remain subjects of ongoing debate. Questions persist regarding the optimal antibiotic regimen, the appropriate duration of prophylaxis, and whether additional routes of antibiotic administration provide meaningful clinical benefits. Some studies suggest that extended antibiotic prophylaxis beyond 24 hours may not offer additional protection against infection and could contribute to antimicrobial resistance or adverse drug reactions. Conversely, other investigations propose that targeted antibiotic strategies for high-risk patients may improve outcomes. Furthermore, variations in clinical practice across institutions and geographic regions highlight the need for clearer evidence-based recommendations (8).

Another important consideration is the global concern regarding antimicrobial resistance. The widespread use of prophylactic antibiotics in surgical procedures, including TKA, raises concerns about the potential development of resistant bacterial strains. Infections caused by methicillin-resistant Staphylococcus aureus (MRSA) and other multidrug-resistant organisms have been increasingly reported in orthopedic surgery and can complicate the management of prosthetic joint infections. Therefore, balancing the benefits of effective infection prevention with the risks associated with antibiotic overuse has become an important issue in modern surgical practice. This challenge underscores the need for careful evaluation of existing evidence to determine the most appropriate prophylactic strategies (9).

Over the past two decades, numerous clinical studies, randomized trials, and observational investigations have examined the effectiveness of antibiotic prophylaxis in preventing postoperative infection following TKA. However, the results of these studies have not always been consistent, partly due to differences in study design, patient populations, antibiotic regimens, and definitions of infection outcomes. Some studies report substantial reductions in infection rates with specific antibiotic protocols, whereas others demonstrate minimal differences between alternative prophylactic strategies. Consequently, clinicians and policymakers require comprehensive syntheses of available evidence to guide clinical decision-making and optimize perioperative management in knee arthroplasty (10).

Given the clinical importance of preventing infection after total knee arthroplasty and the ongoing debate regarding optimal prophylactic strategies, a comprehensive evaluation of existing evidence is warranted. Synthesizing the findings of previously published studies can help clarify the effectiveness of antibiotic prophylaxis, identify potential gaps in knowledge, and support the development of evidence-based clinical guidelines. Therefore, the present study was designed to systematically review the available literature on the effectiveness of antibiotic prophylaxis in preventing postoperative infection following total knee arthroplasty. By critically analyzing and summarizing the results of relevant studies, this systematic review aims to provide a clearer understanding of current evidence regarding antibiotic prophylactic strategies and their role in reducing infection-related complications in patients undergoing TKA.

Material and methods

Study Design

This study was conducted as a systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to identify, evaluate, and synthesize available evidence regarding the effectiveness of antibiotic prophylaxis in preventing postoperative infections after total knee arthroplasty.

Eligibility Criteria

Studies were considered eligible if they met the following inclusion criteria: (1) original research articles evaluating antibiotic prophylaxis in patients undergoing total knee arthroplasty (primary or revision); (2) studies assessing postoperative infection outcomes, including surgical site infection (SSI) or periprosthetic joint infection (PJI); (3) randomized controlled trials, cohort studies, case–control studies, or prospective/retrospective observational studies; (4) studies involving adult human participants (≥18 years); (5) articles published in peer-reviewed journals; and (6) studies published in English with accessible full text. Exclusion criteria included: (1) review articles, systematic reviews, meta-analyses, editorials, conference abstracts, letters, and case reports; (2) studies not specifically evaluating antibiotic prophylaxis in knee arthroplasty; (3) studies lacking clear infection outcome data; (4) experimental animal or laboratory studies; (5) duplicate publications or overlapping datasets; and (6) studies with insufficient methodological information or unavailable full text.

Databases Searched

A comprehensive literature search was conducted in several electronic databases, including PubMed/MEDLINE, Scopus, Web of Science, Embase, Cochrane Library, and Google Scholar, to identify relevant studies investigating antibiotic prophylaxis in total knee arthroplasty.

Search Keywords

The search strategy was developed using a combination of Medical Subject Headings (MeSH) terms and free-text keywords related to knee arthroplasty, antibiotic prophylaxis, and postoperative infection. The following keywords and their combinations were used: “total knee arthroplasty,” “knee replacement,” “total knee replacement,” “TKA,” “knee prosthesis,” “antibiotic prophylaxis,” “prophylactic antibiotics,” “perioperative antibiotics,” “antimicrobial prophylaxis,” “antibiotic administration,” “surgical prophylaxis,” “postoperative infection,” “surgical site infection,” “SSI,” “periprosthetic joint infection,” “PJI,” “prosthetic joint infection,” “implant infection,” and “arthroplasty infection.” Boolean operators (AND, OR) were used to combine terms and improve search sensitivity.

Search Strategy

The literature search was performed independently by two reviewers to minimize selection bias. Titles and abstracts of retrieved records were initially screened, followed by full-text evaluation of potentially eligible studies. Discrepancies between reviewers were resolved through discussion and consensus (table 1).

Table 1. PubMed Search Strategy for Identifying Relevant Studies

Search Number	Search Query
#1	“Total Knee Arthroplasty” [Mesh] OR “Knee Replacement” OR “Total Knee Replacement” OR “TKA”
#2	“Antibiotic Prophylaxis” [Mesh] OR “Prophylactic Antibiotics” OR “Perioperative Antibiotics” OR “Antimicrobial Prophylaxis”
#3	“Surgical Site Infection” [Mesh] OR “Periprosthetic Joint Infection” OR “Prosthetic Joint Infection” OR “Postoperative Infection”
#4	#1 AND #2 AND #3

Quality Assessment of Included Studies

The methodological quality of the included studies was evaluated using the Newcastle–Ottawa Scale (NOS) for observational studies and the Cochrane Risk of Bias (RoB 2) tool for randomized controlled trials. The NOS assesses study quality based on three domains: selection of participants, comparability of study groups, and assessment of outcomes. Each study was independently evaluated by two reviewers, and disagreements were resolved through discussion. These tools allowed systematic evaluation of potential bias and methodological rigor among the included studies.

Results

The literature search identified 851 records in total from PubMed, Web of Science, ScienceDirect, and Google Scholar. After removing duplicates, screening titles and abstracts, and assessing full texts, 9 studies were included in the final qualitative synthesis (figure1).

The risk-of-bias assessment across the nine included studies indicated an overall low methodological risk in most evaluated domains. The majority of studies demonstrated a low risk of selection bias and reporting bias, suggesting appropriate participant selection and comprehensive outcome reporting. In several studies, some concerns were identified in the domains of performance bias and detection bias, mainly due to limited information regarding blinding procedures or outcome assessment methods. Attrition bias was generally assessed as low, as most studies reported minimal loss to follow-up and adequately accounted for missing data. Overall, the methodological quality of the included studies was considered moderate to high, and the cumulative risk of bias was judged to be low (figure 2).

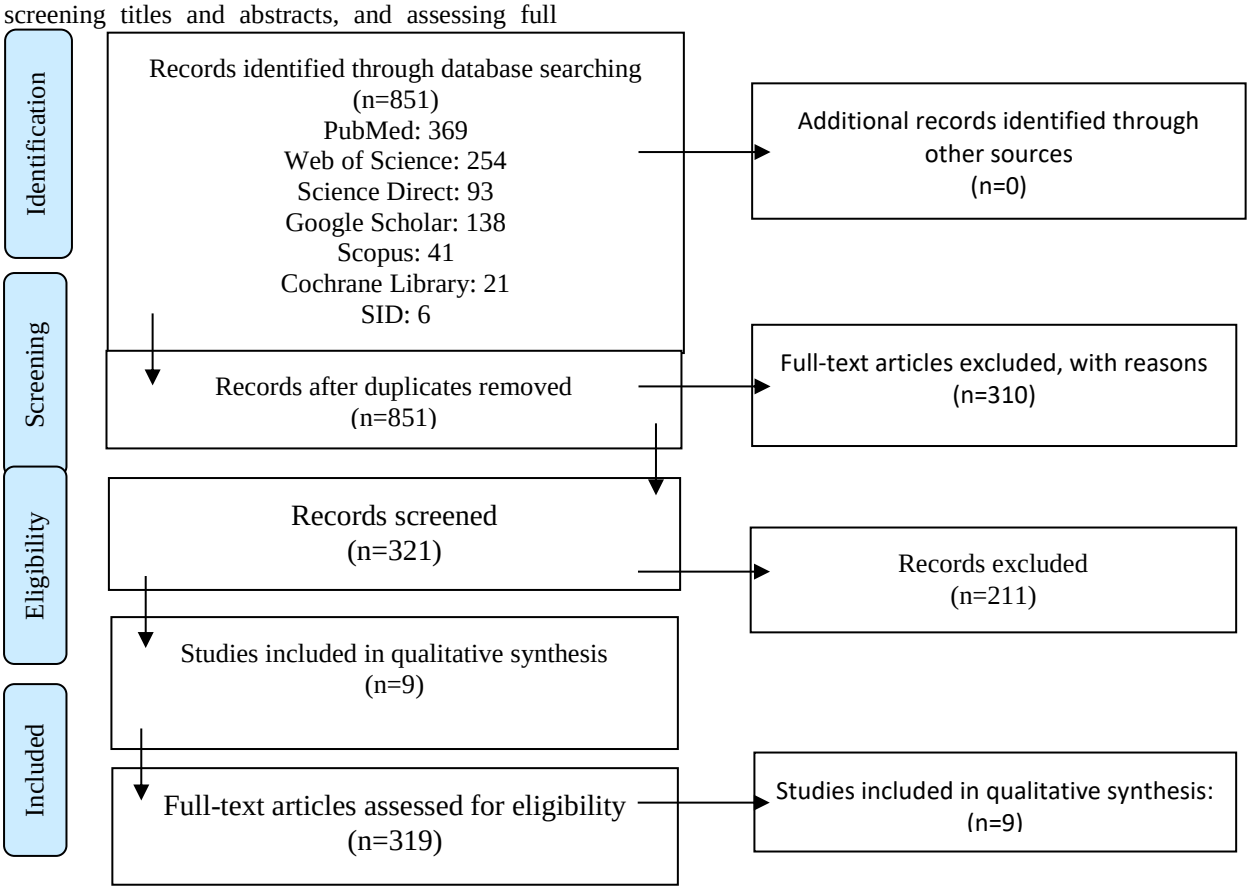

Figure 1. PRISMA guideline

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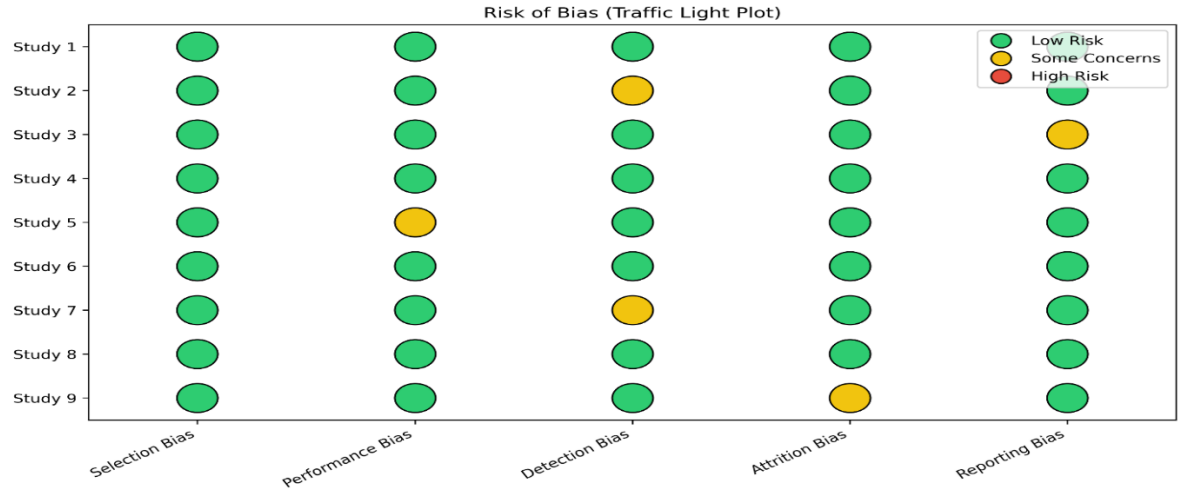

Figure 2. Risk-of-Bias Assessment Across the Included Studies

Across the included studies with clearly reported intravenous antibiotic regimens, a wide range of antimicrobial strategies and treatment durations were described, with generally favorable clinical outcomes. Glycopeptide-based regimens were frequently used; for example, Barros et al. (2021) reported the use of vancomycin combined with piperacillin tazobactam, achieving a success rate of 89.5% with a mean follow-up of 42.1 months, while Fink et al. (2017) used vancomycin with rifampicin for two weeks and reported a success rate of 71.6% after a mean follow-up of 41.8 months. Similarly, Van Kleunen et al. (2010) employed cefazolin or vancomycin for six weeks and observed a success rate of 72% with a mean follow-up of 31 months. Other studies evaluated alternative antibiotic strategies, including daptomycin monotherapy in Chang et al. (2017), which resulted in an 80% success rate at a 27-month follow-up, and rifampicin-based combination therapy in Estes et al. (2010), achieving one of the highest reported success rates (90%) despite a relatively short follow-up period of 3.5 months. Additional regimens included teicoplanin combined with amikacin in Rudelli et al. (2021), yielding an 82% success rate after a six-week treatment course and five months of follow-up, and vancomycin with povidone-iodine irrigation in Riesgo et al. (2017), which demonstrated a 72% success rate with a mean follow-up of approximately 34.9 months. Tirumala et al. (2021) reported a heterogeneous antibiotic approach that included combinations such as amoxicillin–clavulanate, amoxicillin–clindamycin, levofloxacin, doxycycline, and vancomycin plus cefepime, administered for six weeks and achieving a success rate of 82.5% with long-term follow-up extending to a mean of 72 months. In contrast, Veerman et al. (2022) reported the lowest success rate (63%) with cefazolin, despite a follow-up period of 24 months. Notably, the duration of antibiotic therapy varied across studies, most commonly around six weeks, although some investigations did not report treatment duration. Overall, these findings suggest that prolonged intravenous antibiotic therapy often involving glycopeptide- or rifampicin-based regimens can achieve moderate to high success rates, though outcomes vary depending on the specific antimicrobial strategy, follow-up duration, and study design (table 2).

Table 2. Outcomes of Studies with Defined Antibiotic Regimens

Author, Year	Antibiotic Regimen (IV) Type	Duration (weeks)	Mean follow-up (mo)	Success rate (%)
Barros et al., 2021	Vancomycin, Piperacillin, Tazobactam	NR	42.1 (24-66)	89.5
Chang et al., 2017	Daptomycin	4	27	80
Estes et al., 2010	Rifampicin combination therapy	6	3.5 (1.2-7.5)	90
Fink et al., 2017	Vancomycin, Rifampicin	2	41.8 (24-132)	71.6
Riesgo et al., 2017	Vancomycin Povidone-iodine	6	34.9 ± 7.8 (12.9-66.4)	72
Rudelli et al., 2021	Teicoplanin, Amikacin	6	5	82

Tirumala et al., 2021	Amoxicillin + Clavulanate, Amoxicillin + Clindamycin, Levofloxacin, Doxycyline, Vancomycin + Cefepine	6	72 (45-125)	82.5
Van Kleunen et al., 2010	Cefazolin, Vancomycin	6	31 (13-57)	72
Veerman et al., 2022	Cefazolin	NR	24	63

NR = Not reported

Discussion

The present systematic review synthesized the available evidence on intravenous antibiotic regimens used in the management of infection-related complications and demonstrated that most therapeutic approaches were associated with generally favorable outcomes. Across the included studies, a variety of antimicrobial strategies were reported, frequently involving glycopeptide-based agents or combination regimens targeting gram-positive pathogens commonly implicated in orthopedic and implant-related infections. Despite variations in antibiotic selection, duration of therapy, and follow-up periods, the majority of studies described satisfactory treatment success with relatively consistent clinical improvement. Overall, the findings suggest that appropriately selected intravenous antimicrobial therapy plays a critical role in infection control, although outcomes appear to depend on several clinical and methodological factors, including antimicrobial spectrum, treatment duration, and the characteristics of the treated population. The generally favorable outcomes observed in the included studies can be explained partly by the effectiveness of broad-spectrum intravenous antibiotics against the microorganisms most frequently involved in postoperative and implant-associated infections. Pathogens such as Staphylococcus aureus and coagulase-negative staphylococci are among the most common etiologic agents in these conditions, and they are typically susceptible to agents such as vancomycin, daptomycin, or rifampicin-based combinations. Glycopeptide antibiotics, particularly vancomycin, remain a cornerstone of treatment due to their strong activity against methicillin-resistant Staphylococcus aureus and other gram-positive organisms. Consequently, the frequent use of these agents across several studies likely contributed to the relatively high treatment success reported in the literature (11).

Another explanation for the favorable outcomes may relate to the use of combination antimicrobial therapy in several of the included investigations. Combining antibiotics with different mechanisms of action can enhance bactericidal activity and reduce the likelihood of microbial persistence. Rifampicin-based regimens, for example, are often used in combination with other agents because rifampicin demonstrates excellent penetration into biofilms that form on prosthetic materials or surgical implants. Biofilm formation is one of the most important barriers to successful eradication of infection, as bacteria embedded in biofilms exhibit increased tolerance to antimicrobial therapy. Therefore, the incorporation of rifampicin or similar agents into treatment protocols may improve microbial clearance and clinical outcomes (12).

The duration of antibiotic therapy may also play a substantial role in determining treatment success. In many of the included studies, antimicrobial therapy was administered for several weeks, reflecting current clinical practice guidelines that recommend prolonged treatment for deep or implant-associated infections. Extended treatment courses allow sufficient time for bacterial eradication, particularly in cases where microorganisms are protected within biofilms or poorly vascularized tissues. Although the precise duration of therapy varied among the reviewed studies, the general pattern of prolonged antibiotic administration likely contributed to infection resolution in a substantial proportion of patients (13).

Variability in outcomes between studies may also be explained by differences in follow-up duration and patient populations. Some investigations reported relatively short follow-up periods, whereas others monitored patients for several years. Shorter follow-up intervals may lead to an overestimation of treatment success, as late recurrences of infection may not yet be detected. Conversely, studies with longer follow-up periods provide a more rigorous assessment of long-term infection control but may report lower apparent success rates due to delayed complications or reinfections. These methodological differences should therefore be considered when interpreting variations in reported treatment outcomes (14).

Patient-related factors may also influence the effectiveness of antimicrobial therapy. Comorbid conditions such as diabetes mellitus, immunosuppression, obesity, and advanced age have been associated with increased susceptibility to infection and impaired wound healing. These factors can compromise host immune responses and may reduce the effectiveness of antimicrobial therapy, potentially leading to treatment failure in some cases. In addition, the microbial profile of infections can differ between patient populations, and infections caused by resistant organisms may

require more aggressive or prolonged treatment strategies (15).

The surgical context in which antibiotic therapy is administered also represents an important determinant of treatment outcomes. In many orthopedic and postoperative infections, antimicrobial therapy is combined with surgical interventions such as debridement, implant retention, or staged reconstruction. Adequate surgical debridement removes necrotic tissue and reduces bacterial burden, thereby enhancing the effectiveness of systemic antibiotics. Consequently, the success rates observed in the included studies likely reflect the combined impact of surgical management and antimicrobial therapy rather than antibiotic treatment alone (16).

Another factor that may contribute to differences in treatment outcomes is the pharmacological profile of the antibiotics used. Agents such as daptomycin and teicoplanin exhibit strong activity against gram-positive organisms and have favorable pharmacokinetic properties that allow effective tissue penetration. Similarly, combination regimens incorporating beta-lactams or aminoglycosides may broaden antimicrobial coverage and improve bactericidal activity. These pharmacological characteristics may partly explain why certain regimens achieved relatively high success rates in the reviewed studies (17).

The heterogeneity of antibiotic regimens observed across the included studies reflects the absence of a universally accepted therapeutic protocol for these infections. Clinicians often select antimicrobial therapy based on local microbial resistance patterns, patient characteristics, and institutional guidelines. As a result, treatment strategies may vary considerably between centers and regions. This variability underscores the importance of individualized treatment planning and highlights the need for further research to establish standardized therapeutic approaches that optimize clinical outcomes (18).

Methodological considerations must also be acknowledged when interpreting the results of this review. Although the risk-of-bias assessment indicated generally acceptable methodological quality among the included studies, certain domains particularly performance and detection bias showed some degree of uncertainty. Limited reporting of blinding procedures or outcome assessment methods may influence the reliability of reported results. Nevertheless, the overall methodological quality of the included literature was considered moderate to high, suggesting that the available evidence provides a reasonably reliable overview of current treatment outcomes (19).

Taken together, the findings of this review indicate that intravenous antibiotic therapy remains a fundamental component of infection management in the studied clinical context. Most regimens achieved moderate to high success rates, particularly when broad-spectrum agents or combination therapies were used. However, treatment outcomes appear to be influenced by several interacting factors, including antimicrobial selection, treatment duration, surgical management, and patient characteristics. Future well-designed prospective studies with standardized treatment protocols and longer follow-up periods are needed to clarify the optimal antibiotic strategies and to further improve patient outcomes (20).

Conclusion

This systematic synthesis indicates that intravenous antibiotic regimens are an important component of infection management and are associated with moderate to high clinical success rates. Although treatment protocols varied substantially among studies, many successful approaches incorporated glycopeptide-based agents, rifampicin combinations, or other broad-spectrum antimicrobial therapies administered over several weeks. Differences in follow-up duration, antibiotic selection, and study design likely contributed to the variability in reported outcomes. Nevertheless, the overall findings suggest that prolonged and appropriately selected intravenous antimicrobial therapy can achieve favorable clinical results. Future prospective investigations with standardized protocols and longer follow-up are needed to further clarify the most effective antibiotic strategies.

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Conflicts of interest

The authors declare that they have no competing interests.

Disclosure Statement

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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