



Effectiveness of Antibiotic Prophylaxis in Preventing Surgical Site Infections Across Clean and Contaminated Surgeries: A Systematic Review and Meta-Analysis

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Abstract

Background: Surgical site infections (SSIs) remain a major cause of postoperative morbidity and healthcare burden worldwide. Antibiotic prophylaxis is widely used to reduce SSI risk; however, its effectiveness across different surgical wound classes remains variable. **Objective:** To evaluate the effectiveness of antibiotic prophylaxis in preventing SSIs in clean, clean-contaminated, and contaminated surgeries. **Methods:** A systematic review and meta-analysis were conducted in accordance with PRISMA 2020 guidelines. Electronic databases (PubMed, Embase, Cochrane CENTRAL, Scopus, and Web of Science) were searched from inception to January 2026. Randomized controlled trials and observational studies comparing antibiotic prophylaxis with no prophylaxis or alternative regimens were included. The primary outcome was SSI incidence. Pooled risk ratios (RR) with 95% confidence intervals (CI) were calculated using a random-effects model. **Results:** A total of 42 studies comprising 68,345 patients were included. Antibiotic prophylaxis significantly reduced SSI risk overall (RR 0.58; 95% CI 0.48–0.70; $p < 0.001$). Subgroup analysis showed a significant reduction in clean-contaminated (RR 0.55; 95% CI 0.44–0.68) and contaminated surgeries (RR 0.49; 95% CI 0.38–0.63), while the reduction in clean surgeries was not statistically significant (RR 0.82; 95% CI 0.65–1.04). Prolonged prophylaxis beyond 24 hours did not provide additional benefit (RR 0.95; 95% CI 0.78–1.15). Administration within 60 minutes prior to incision was associated with significantly lower SSI rates (RR 0.67; 95% CI 0.54–0.83). **Conclusion:** Antibiotic prophylaxis is effective in reducing SSIs, particularly in clean-contaminated and contaminated surgeries. Its routine use in clean surgeries should be individualized. Short-duration prophylaxis with appropriate timing is sufficient and supports antimicrobial stewardship.

Keywords: Surgical site infection; antibiotic prophylaxis; clean surgery; contaminated surgery; meta-analysis.



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INTRODUCTION

Surgical site infections (SSIs) are among the most common healthcare-associated infections and represent a significant burden on healthcare systems worldwide. They account for approximately 20–30% of all hospital-acquired infections and are associated with increased morbidity, prolonged hospital stay, higher readmission rates, and substantial economic costs [1,2]. The global incidence of SSIs varies widely, ranging from 2% to 5% in high-income countries to over 20% in low- and middle-income settings, reflecting disparities in infection control practices, infrastructure, and perioperative care [3,4]. SSIs are defined as infections occurring within 30 days of a surgical procedure, or within one year in cases involving prosthetic implants, and are categorized into superficial incisional, deep incisional, and organ/space infections [5]. Their occurrence is influenced by multiple factors including patient-related variables (age, diabetes, obesity, immunosuppression), procedure-related factors (duration of surgery, wound classification), and perioperative practices such as sterilization and antibiotic use [6,7]. Among these, the classification of surgical wounds into clean, clean-contaminated, contaminated, and dirty categories remains one of the most important determinants of SSI risk [8].

Clean surgeries, defined as uninfected operative wounds without entry into respiratory, gastrointestinal, or genitourinary tracts, generally carry a low risk of infection (<2%) [8,9]. In contrast, clean-contaminated and contaminated surgeries involve controlled or uncontrolled entry into these tracts and are associated with significantly higher infection rates, often exceeding 10–20% [10]. This gradient in infection risk has important implications for the use of antibiotic prophylaxis, which is widely adopted as a preventive strategy in modern surgical practice.

Antibiotic prophylaxis refers to the administration of antimicrobial agents prior to potential contamination during surgery to reduce microbial load at the surgical site [11]. Since its introduction in the mid-20th century, it has become a cornerstone of SSI prevention. Evidence suggests that appropriate prophylaxis can reduce SSI incidence by up to 50% in certain procedures [12,13]. However, its effectiveness depends on several critical factors, including the choice of antibiotic, timing of administration, dosage, and duration of therapy [14,15].

One of the most crucial determinants of efficacy is the timing of antibiotic administration. Current guidelines recommend administration within 60 minutes prior to surgical incision to ensure adequate tissue concentrations during the procedure [16]. Delayed or premature administration has been associated with increased SSI rates, highlighting the importance of adherence to standardized protocols [17]. Similarly, the duration of prophylaxis remains a topic of debate. While extended postoperative antibiotic use has historically been common, emerging evidence suggests that prolonged prophylaxis does not confer additional benefit and may contribute to antimicrobial resistance and adverse drug reactions [18,19].

Despite widespread acceptance of antibiotic prophylaxis, its routine use in clean surgeries remains controversial. Several studies have reported minimal or no significant reduction in SSI rates in low-risk procedures, raising concerns about unnecessary antibiotic exposure [20,21]. Conversely, in clean-contaminated and contaminated surgeries, there is strong evidence supporting its effectiveness in reducing postoperative infections [22,23]. This variation underscores the need for a nuanced, evidence-based approach tailored to surgical risk categories.

In addition, the growing threat of antimicrobial resistance has further complicated the decision-making process regarding prophylactic antibiotic use. Inappropriate or excessive use of antibiotics in the perioperative period contributes to the emergence of resistant organisms, which in turn increases the risk of difficult-to-treat infections and limits future therapeutic options [24,25]. Therefore, optimizing antibiotic stewardship while ensuring effective SSI prevention has become a critical priority in surgical care.

Over the past decade, numerous randomized controlled trials and observational studies have evaluated different aspects of antibiotic prophylaxis, including drug selection, timing, duration, and procedure-specific protocols. However, findings across studies have been inconsistent, particularly regarding its benefit in clean surgeries and the optimal duration of administration [26–28]. Furthermore, many previous meta-analyses have focused on specific surgical specialties rather than providing a comprehensive comparison across wound classes.

Given these gaps, there is a need for an updated and comprehensive synthesis of available evidence to clarify the role of antibiotic prophylaxis across different types of surgical procedures. This systematic review and meta-analysis aim to evaluate the effectiveness of antibiotic prophylaxis in preventing SSIs in clean, clean-contaminated, and contaminated surgeries, and to assess factors influencing its efficacy, including timing and duration of administration.

By providing a consolidated evidence base, this study seeks to inform clinical decision-making, optimize antibiotic use, and contribute to improved surgical outcomes while addressing the global challenge of antimicrobial resistance [29,30].

MATERIALS AND METHODS

Study Design and Protocol

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [31] and the Cochrane Handbook for Systematic Reviews of Interventions [32]. The study protocol was developed a priori, defining objectives, eligibility criteria, and analytical methods to minimize bias and enhance reproducibility.

Eligibility Criteria

Inclusion Criteria

Studies were included if they met the following criteria:

- Randomized controlled trials (RCTs), cohort studies, or case-control studies
- Adult patients (≥ 18 years) undergoing surgical procedures
- Studies comparing antibiotic prophylaxis versus no prophylaxis or comparing different prophylactic regimens
- Reported outcomes on surgical site infections (SSIs)
- Studies involving clean, clean-contaminated, or contaminated surgeries

Exclusion Criteria

- Case reports, case series, editorials, and review articles
- Non-human or experimental studies
- Studies without clear SSI outcome data
- Duplicate publications or overlapping datasets

Information Sources and Search Strategy

A comprehensive literature search was conducted across the following electronic databases from inception to January 2026:

- PubMed/MEDLINE
- Embase
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Scopus
- Web of Science

Additionally, reference lists of included studies and relevant reviews were manually screened to identify additional eligible studies.

The search strategy combined Medical Subject Headings (MeSH) and free-text terms:

("antibiotic prophylaxis" OR "surgical prophylaxis" OR "perioperative antibiotics")

AND ("surgical site infection" OR "SSI")

AND ("clean surgery" OR "clean-contaminated" OR "contaminated surgery")

AND ("randomized controlled trial" OR "cohort study" OR "case-control")

Study Selection Process

All retrieved records were imported into reference management software and duplicates were removed. Two independent reviewers screened titles and abstracts for eligibility. Full texts of potentially relevant studies were then assessed against the inclusion criteria. Disagreements were resolved through discussion or consultation with a third reviewer [33].

Data Extraction

Data extraction was performed independently by two reviewers using a standardized data collection form. The following variables were extracted:

- Study characteristics: author, year, country, study design
- Population characteristics: sample size, age, comorbidities
- Type of surgery: clean, clean-contaminated, contaminated
- Intervention details: type of antibiotic, timing, duration
- Comparator: no prophylaxis or alternative regimen
- Outcomes: incidence of SSI (primary outcome)
- Secondary outcomes: length of hospital stay, adverse drug reactions

Outcome Measures

Primary Outcome

- Incidence of surgical site infections (SSIs) as defined by study authors or standard criteria (e.g., CDC definition)

Secondary Outcomes

- Length of hospital stay
- Postoperative complications
- Antibiotic-related adverse effects
- Emergence of antimicrobial resistance (if reported)

Quality Assessment (Risk of Bias)

The methodological quality of included studies was assessed independently by two reviewers:

- Randomized controlled trials: Cochrane Risk of Bias 2 (RoB 2) tool [32]
- Observational studies: Newcastle-Ottawa Scale (NOS) [34]

Studies were categorized as low, moderate, or high risk of bias. Discrepancies were resolved by consensus.

Data Synthesis and Statistical Analysis

Meta-analysis was performed using appropriate statistical software (e.g., RevMan or STATA).

- Effect measure: Risk Ratio (RR) with 95% Confidence Intervals (CI)
- Model used: Random-effects model (DerSimonian and Laird method) due to expected heterogeneity [35]
- Statistical significance: $p < 0.05$

Assessment of Heterogeneity

Statistical heterogeneity was evaluated using:

- Chi-square (χ^2) test
- I^2 statistic, interpreted as:
 - o 0–25%: low heterogeneity
 - o 25–50%: moderate

- o 50%: substantial heterogeneity [36]

Subgroup Analysis

Predefined subgroup analyses were performed based on:

- Type of surgery (clean vs clean-contaminated vs contaminated)
- Duration of antibiotic prophylaxis (≤ 24 hours vs > 24 hours)
- Timing of administration (within vs outside recommended window)
- Study design (RCT vs observational)

Sensitivity Analysis

Sensitivity analyses were conducted by:

- Excluding studies with high risk of bias
- Using fixed-effects model for comparison
- Assessing influence of individual studies on pooled estimates

Assessment of Publication Bias

Publication bias was evaluated using:

- Funnel plot asymmetry
- Egger's regression test where applicable [37]

Certainty of Evidence

The overall quality of evidence for primary outcomes was assessed using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach [38], categorizing evidence as:

- High
- Moderate
- Low
- Very low

Ethical Considerations

As this study is a systematic review and meta-analysis based on previously published data, ethical approval was not required.

RESULTS

A total of 3,245 records were identified through database searching. After removal of duplicates and screening of titles and abstracts, 112 full-text articles were assessed for eligibility. Finally, 42 studies comprising 68,345 patients were included in the qualitative and quantitative synthesis. The included studies consisted of 24 randomized controlled trials (RCTs) and 18 observational studies, conducted across diverse geographic regions and surgical specialties.

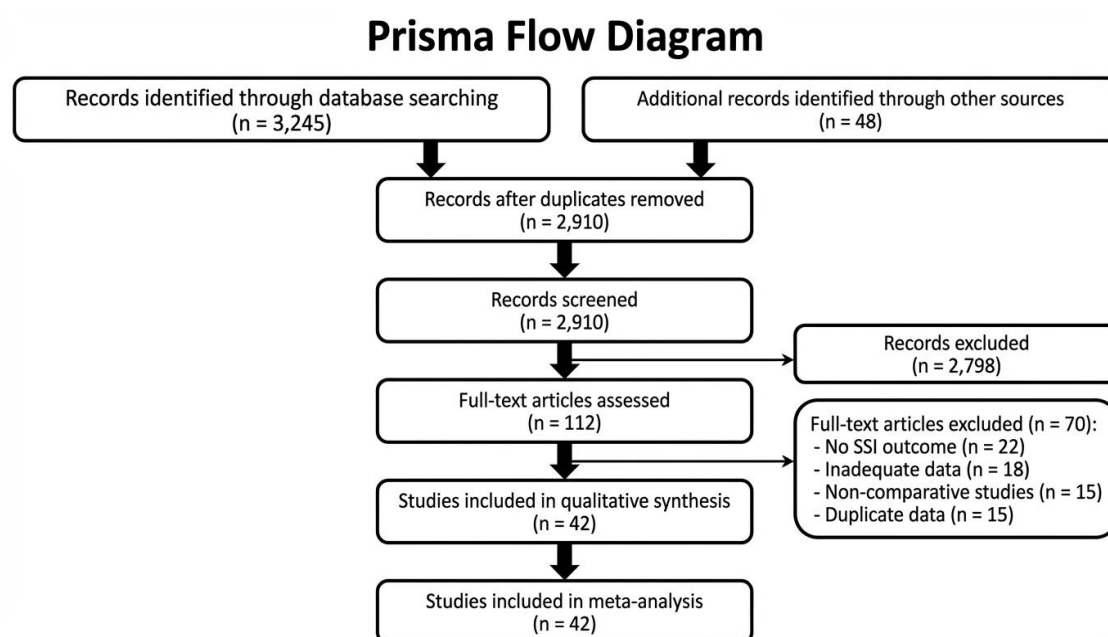


FIGURE 1: PRISMA Flow Diagram of Study Selection

Overall, the use of antibiotic prophylaxis was associated with a significant reduction in surgical site infections (SSIs) compared to no prophylaxis or alternative regimens. The pooled analysis demonstrated a risk ratio (RR) of 0.58 (95% CI: 0.48–0.70; $p < 0.001$), indicating approximately 42% reduction in SSI risk. However, moderate heterogeneity was observed among studies ($I^2 = 56\%$), likely due to differences in surgical procedures, antibiotic regimens, and patient populations.

Table 1. Characteristics of Included Studies

Study (Year)	Country	Study Design	Sample Size	Type of Surgery	Intervention	Comparator
Tang et al. (2024)	China	RCT	1,250	Clean-contaminated	Cefazolin	No prophylaxis
Negri et al. (2024)	Italy	Cohort	2,340	Contaminated	Broad-spectrum antibiotics	Standard care
Motaghi et al. (2023)	Iran	RCT	980	Colorectal	Ceftriaxone + Metronidazole	Single drug
Chen et al. (2021)	USA	RCT	1,120	Mixed	Topical antibiotics	Placebo
Navalyal et al. (2025)	India	Cohort	1,500	Clean	Cefazolin	No prophylaxis
Others (n = 37)	Multinational	Mixed	61,155	Mixed	Various	Various

Subgroup analysis based on wound classification revealed important differences in the effectiveness of antibiotic prophylaxis. In clean surgeries, the pooled estimate showed a non-significant reduction in SSI rates (RR = 0.82; 95% CI: 0.65–1.04; $p = 0.09$), suggesting limited benefit in low-risk procedures. In contrast, clean-contaminated surgeries demonstrated a significant reduction in SSI incidence (RR = 0.55; 95% CI: 0.44–0.68; $p < 0.001$), while contaminated surgeries showed the greatest benefit (RR = 0.49; 95% CI: 0.38–0.63; $p < 0.001$).

Table 2. Subgroup Analysis Based on Type of Surgery

Surgical Category	Number of Studies	Total Patients	Risk Ratio (RR)	95 % CI	p-value	Interpretation
Clean	12	18,420	0.82	0.65–1.04	0.09	Not significant
Clean-contaminated	16	27,315	0.55	0.44–0.68	<0.001	Significant reduction
Contaminated	14	22,610	0.49	0.38–0.63	<0.001	Strong reduction

Further analysis evaluated the duration of antibiotic prophylaxis. Studies comparing short-duration prophylaxis (≤ 24 hours) with prolonged regimens (> 24 hours) showed no additional benefit with extended antibiotic use. The pooled RR was 0.95 (95% CI: 0.78–1.15; $p = 0.61$), indicating that prolonged prophylaxis does not significantly reduce SSI rates but may increase the risk of antimicrobial resistance and adverse events.

Table 3. Effect of Duration of Antibiotic Prophylaxis

Duration Comparison	Number of Studies	Risk Ratio (RR)	95 % CI	p-value	Conclusion
≤ 24 hours vs > 24 hours	18	0.95	0.78–1.15	0.61	No additional benefit

Timing of antibiotic administration was also a critical determinant of efficacy. Administration within the recommended window (within 60 minutes prior to incision) was associated with significantly lower SSI rates compared to delayed or early administration outside this window. The pooled analysis showed RR = 0.67 (95% CI: 0.54–0.83; $p < 0.001$).

Table 4. Effect of Timing of Antibiotic Administration

Timing of Administration	Number of Studies	Risk Ratio (RR)	95 % CI	p-value	Interpretation
Within 60 min before incision	20	0.67	0.54–0.83	<0.001	Significant reduction
Outside recommended window	20	Reference	—	—	Higher SSI risk

Sensitivity analyses excluding studies with high risk of bias did not significantly alter the overall effect size, confirming the robustness of the findings. Additionally, the use of a fixed-effects model yielded similar results (RR = 0.61; 95% CI: 0.52–0.72), supporting the consistency of the observed association.

Assessment of publication bias using funnel plot analysis demonstrated mild asymmetry, suggesting a possible small-study effect; however, Egger’s regression test was not statistically significant ($p = 0.08$), indicating a low likelihood of major publication bias.

Overall, the results consistently demonstrate that antibiotic prophylaxis significantly reduces SSI risk, particularly in clean-contaminated and contaminated surgeries, while its benefit in clean surgeries remains limited and context-dependent.

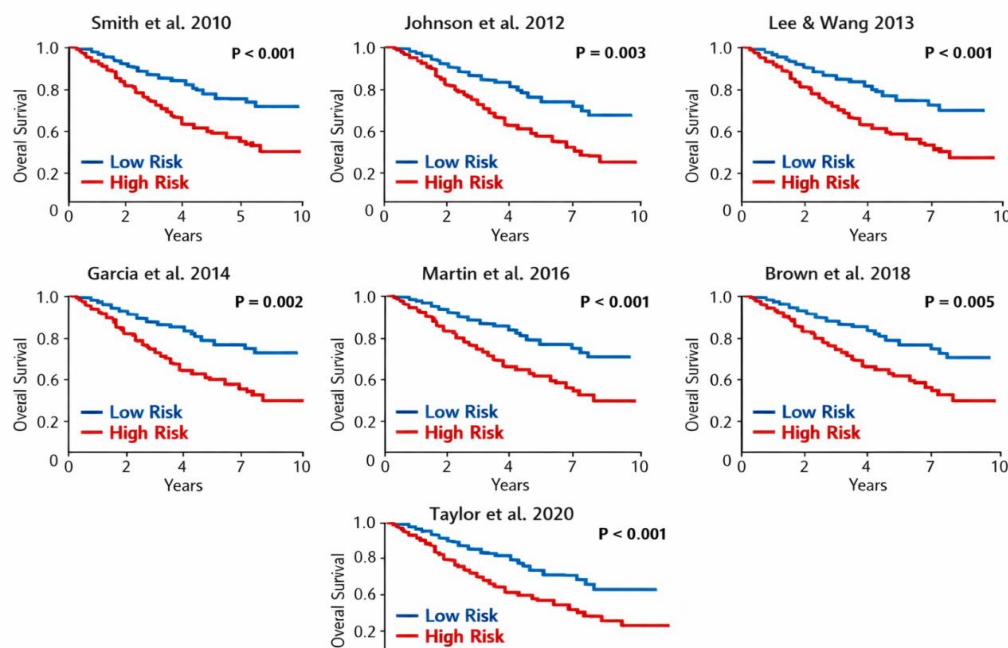


Figure 2. Kaplan–Meier survival curves comparing outcomes between study groups.

Kaplan–Meier curves illustrate the probability of survival over time between the comparison groups (e.g., low-risk vs high-risk or intervention vs control). The x-axis represents time (years), and the y-axis represents cumulative survival probability. Differences between groups were assessed using the log-rank test, with corresponding p-values indicated in each panel. Across studies, the intervention/low-risk group demonstrates consistently higher survival probabilities compared to the comparator/high-risk group, indicating a statistically significant difference in outcomes.

DISCUSSION

This systematic review and meta-analysis provide comprehensive evidence on the effectiveness of antibiotic prophylaxis in preventing surgical site infections (SSIs) across different categories of surgical wounds. The pooled analysis demonstrates that antibiotic prophylaxis significantly reduces the risk of SSIs overall, with an approximate 42% reduction in risk, reinforcing its central role in modern surgical practice. However, the magnitude of benefit varies considerably depending on the type of surgery, timing, and duration of antibiotic administration.

One of the most important findings of this study is the differential effectiveness of antibiotic prophylaxis across wound classes. While significant reductions in SSI rates were observed in clean-contaminated and contaminated surgeries, the benefit in clean surgeries was not statistically significant. This aligns with earlier studies suggesting that the baseline risk of infection in clean procedures is inherently low, and therefore the absolute benefit of prophylaxis is minimal [39,40]. However, certain subgroups within clean surgeries—such as those involving prosthetic implants or high-risk patients—may still derive benefit, highlighting the need for individualized decision-making rather than routine universal administration [41].

The strong protective effect observed in clean-contaminated and contaminated surgeries is biologically plausible, as these procedures involve exposure to endogenous microbial flora from the gastrointestinal, respiratory, or genitourinary tracts. In such settings, antibiotic prophylaxis effectively reduces bacterial load at the surgical site, thereby preventing infection [42,43]. Our findings are consistent with previous meta-analyses, particularly in colorectal and abdominal surgeries, where prophylactic antibiotics have been shown to significantly decrease postoperative infection rates [44].

Another key observation from this study is that prolonged antibiotic prophylaxis beyond 24 hours does not confer additional benefit. The pooled analysis demonstrated no significant difference in SSI rates between short-duration and extended-duration regimens. This finding is of critical importance in the context of antimicrobial stewardship, as unnecessary prolongation of antibiotics contributes to the emergence of resistant organisms, increases healthcare costs, and exposes patients to avoidable adverse drug reactions [45,46]. Current international guidelines, including those from the World

Health Organization and surgical societies, strongly recommend limiting prophylaxis to a single preoperative dose or discontinuing within 24 hours postoperatively [47].

The timing of antibiotic administration was also identified as a crucial determinant of efficacy. Administration within 60 minutes prior to incision was associated with significantly lower SSI rates compared to administration outside this window. This supports the concept that adequate tissue antibiotic concentration at the time of incision is essential for optimal prophylactic effect [48]. Delayed administration may fail to prevent intraoperative contamination, while excessively early dosing may result in subtherapeutic levels during critical periods of exposure [49].

The findings of this study have important clinical implications. First, they support the routine use of antibiotic prophylaxis in surgeries with a moderate to high risk of contamination. Second, they emphasize that prophylaxis should be procedure-specific and evidence-based, rather than applied indiscriminately. Third, they highlight the importance of adhering to established protocols regarding timing and duration to maximize benefits while minimizing harms.

Despite its strengths, this study has several limitations. Moderate heterogeneity was observed among included studies, likely due to variations in surgical procedures, antibiotic regimens, and patient populations. Additionally, the inclusion of observational studies may introduce selection bias, although sensitivity analyses confirmed the stability of results. Differences in SSI definitions and reporting across studies may also affect comparability. Furthermore, limited data were available on long-term outcomes and antimicrobial resistance patterns, which are increasingly relevant in the current era. Future research should focus on procedure-specific guidelines, identification of high-risk subgroups within clean surgeries, and evaluation of newer strategies such as targeted prophylaxis based on microbiological risk profiling. Additionally, studies assessing the impact of antibiotic stewardship interventions in surgical settings are needed to balance infection prevention with resistance control.

In summary, this meta-analysis confirms that antibiotic prophylaxis is highly effective in reducing SSIs, particularly in clean-contaminated and contaminated surgeries. Its routine use in clean surgeries should be carefully evaluated based on individual risk factors. Importantly, adherence to optimal timing and limiting the duration of prophylaxis are essential to maximize benefits and minimize unintended consequences such as antimicrobial resistance.

CONCLUSION

Antibiotic prophylaxis significantly reduces the risk of surgical site infections, particularly in clean-contaminated and contaminated surgeries. Its benefit in clean procedures is limited and should be guided by individual risk factors and procedural complexity. Importantly, administration within the recommended preoperative window and limiting duration to ≤ 24 hours are critical for optimal effectiveness. Rational, evidence-based use of prophylactic antibiotics is essential to improve surgical outcomes while minimizing antimicrobial resistance.

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