JHWCR JOURNAL OF HEALTH, WELLNESS AND COMMUNITY RESEARCH 3007-0570

https://doi.org/10.61919/3hjn9x18

Review Article

In Sepsis: Procalcitonin-Guided Antibiotic Stewardship in Surgical Patients: A Systematic Review

Rohit Kumar[1], Yougesh Kumar[2], Bhoomika Manglani[2], Deesha Panjwani[2], Menahel Muneer[3], Nazish Marvi[4], Dr. Saoud Javed[5]

[1] SMBBIT, Karachi, Pakistan
[2] MBBS 2nd year, Jinnah Medical and Dental College, Karachi, Pakistan
[3] Dow University of Health Sciences - Dow Medical College, Karachi, Pakistan
[4] University of Sindh, Jamshoro, Pakistan
[5] Dr. Ziauddin Hospital Clifton, Karachi, Pakistan

*Corresponding author: Rohit Kumar, keswanirkk69@gmail.com

"Cite this Article" **Received**: 28 February 2026; **Accepted**: 20 May 2026; **Published**: 04 June 2026
Author Contributions: Concept: RK; Design: RK and SJ; Data Collection: YK, BM, DP, MM, and NM; Analysis: RK and SJ; Drafting: RK, YK, BM, DP, MM, NM, and SJ.
Ethical Approval: Ayub Medical College, Abbottabad, KPK, Pakistan. **Informed Consent**: Written informed consent was obtained from all participants; **Conflict of Interest**: The authors declare no conflict of interest. **Funding**: No external funding; **Data Availability**: Available from the corresponding author on reasonable request; **Acknowledgments**: N/A.

ABSTRACT

Background: Surgical patients with sepsis frequently require early empirical antimicrobial therapy, but prolonged or unnecessary antibiotic exposure contributes to antimicrobial resistance, adverse drug events, secondary infections, and increased healthcare costs. Differentiating persistent bacterial infection from sterile postoperative inflammation remains difficult because conventional inflammatory markers often lack specificity in surgical and critical care settings. Procalcitonin-guided antibiotic stewardship has been proposed as a biomarker-supported strategy to optimize antibiotic discontinuation and de-escalation. Objective: This systematic review aimed to evaluate whether procalcitonin-guided antibiotic stewardship reduces unnecessary antimicrobial exposure without compromising clinical safety among adult surgical or surgically relevant critically ill patients with sepsis. Methods: A systematic literature search was conducted across PubMed/MEDLINE, Scopus, Web of Science, CINAHL, Cochrane Library, Embase, and additional sources for literature published from 2022 to 2026. Eligible records evaluated procalcitonin-guided antibiotic discontinuation, de-escalation, or stewardship in adult sepsis, surgical sepsis, postoperative infection, intra-abdominal infection, acute pancreatitis, cancer-associated sepsis, or critically ill populations relevant to surgical decision-making. Findings were synthesized narratively because of heterogeneity in study design, populations, thresholds, algorithms, and outcome reporting. Results: Fourteen records were included, comprising randomized controlled trials, a pre–post implementation study, systematic reviews/meta-analyses, narrative and stewardship reviews, consensus guidance, and cost-effectiveness evidence. The most consistent finding was reduced antibiotic duration or antimicrobial exposure with procalcitonin-guided strategies. Mortality and clinical safety findings were generally reassuring, but direct surgical-specific evidence remained limited. Evidence for ICU or hospital length of stay, antimicrobial resistance, and cost-effectiveness was less consistent and largely indirect. Conclusion: Procalcitonin-guided stewardship may support earlier antibiotic discontinuation and reduce unnecessary antimicrobial exposure in sepsis care, but in surgical patients it should be used as an adjunct to clinical judgment, source-control assessment, microbiology, imaging, and serial clinical evaluation. Surgical-specific randomized trials are needed to define optimal thresholds, timing, safety outcomes, resistance effects, and economic value. Keywords: Procalcitonin; Sepsis; Surgical Sepsis; Antibiotic Stewardship; Antimicrobial Stewardship; Critical Care; Biomarkers; Antibiotic De-escalation.

INTRODUCTION

Sepsis remains a leading cause of morbidity, mortality, prolonged intensive care admission, and healthcare expenditure among critically ill patients, and surgical patients represent a clinically distinct high-risk population because operative trauma, invasive procedures, tissue contamination, source-control challenges, immunological stress, and prolonged hospitalization increase susceptibility to severe bacterial infection. In surgical practice, early empirical antimicrobial therapy is often necessary because delayed treatment in sepsis may accelerate organ dysfunction and worsen survival; however, prolonged or unnecessary antibiotic exposure contributes to antimicrobial resistance, adverse drug reactions,

ISSN 3007-0570

nephrotoxicity, hepatotoxicity, Clostridioides difficile infection, secondary fungal infection, microbiome disruption, and avoidable healthcare costs (1). This balance between urgent treatment and timely discontinuation is particularly difficult in postoperative and surgical intensive care settings, where fever, leukocytosis, tachycardia, elevated C-reactive protein, and systemic inflammatory responses may reflect either true bacterial sepsis or sterile postoperative inflammation.

Conventional inflammatory markers have limited specificity in surgical patients because tissue injury, anesthesia, blood loss, ischemia-reperfusion injury, drains, catheters, and wound healing responses may produce biochemical and clinical changes that resemble infection. As a result, clinicians may continue broad-spectrum antimicrobials despite negative cultures or clinical improvement, especially when source control is uncertain or the risk of deterioration is perceived to be high. Antibiotic stewardship in surgical sepsis therefore requires decision-support strategies that can help identify when ongoing bacterial infection is unlikely while preserving clinician judgment, microbiological interpretation, imaging findings, hemodynamic assessment, and adequacy of source control as central elements of care (2).

Procalcitonin, the precursor peptide of calcitonin, has gained attention as a biomarker that may support antimicrobial stewardship because serum concentrations generally rise during systemic bacterial infection and tend to decline when infection is controlled or effective antimicrobial therapy is established. Unlike non-specific inflammatory markers, serial procalcitonin trends may provide clinically useful information about the probability of persistent bacterial infection and the appropriateness of antibiotic discontinuation or de-escalation. Many stewardship protocols use absolute thresholds or percentage declines from baseline to guide antimicrobial decisions, particularly when procalcitonin values fall below defined cutoffs or decrease substantially from peak levels (3). Nevertheless, interpretation is more complex in surgical patients because major operations, trauma, pancreatitis, postoperative complications, and incomplete source control may influence procalcitonin kinetics and may reduce the reliability of isolated measurements.

The available literature suggests that procalcitonin-guided antibiotic strategies may reduce antimicrobial exposure in critically ill patients with sepsis without consistently worsening mortality or treatment failure, but the direct applicability of this evidence to surgical populations remains uncertain. Several randomized trials, systematic reviews, implementation studies, and consensus-based algorithms have reported shorter antibiotic duration or improved discontinuation practices when procalcitonin was incorporated into antibiotic stewardship decisions (4–8). However, much of this evidence derives from mixed intensive care units, general sepsis cohorts, cancer-associated sepsis, acute pancreatitis, or heterogeneous critically ill populations rather than exclusively postoperative or surgical sepsis cohorts. This distinction is important because surgical sepsis is strongly influenced by infection source, operative timing, anatomical contamination, drainage adequacy, wound status, microbiological confirmation, and procedural source control.

A focused synthesis is therefore needed to clarify whether procalcitonin-guided stewardship can meaningfully support antibiotic optimization in surgical or surgically relevant sepsis populations. Existing evidence remains heterogeneous in terms of patient selection, procalcitonin thresholds, timing and frequency of measurement, criteria for antibiotic discontinuation, comparator care, outcome definitions, and reporting of clinical safety. Although reduced antibiotic duration is frequently described, evidence regarding mortality, intensive care unit length of stay, hospital length of stay, antimicrobial resistance, adverse events, recurrence of infection, and cost-effectiveness is less consistently reported and often indirectly applicable to surgical practice. This uncertainty limits the translation of procalcitonin algorithms into routine surgical antimicrobial stewardship and highlights the need for a structured review that separates direct surgical evidence from broader critically ill sepsis evidence.

This systematic review was therefore designed around the following PICO framework: the population comprised adult surgical or surgically relevant critically ill patients with sepsis, septic shock, postoperative infection, intra-abdominal infection, pancreatitis-associated infection, or suspected bacterial infection requiring antimicrobial therapy; the intervention was procalcitonin-guided antibiotic stewardship using serial procalcitonin measurement to support antibiotic discontinuation, de-escalation, continuation, or optimization; the comparator was standard care, clinician-directed antimicrobial management, usual stewardship without procalcitonin guidance, or alternative biomarker-guided care; and the outcomes were antibiotic duration, antimicrobial de-escalation, mortality, treatment failure or recurrent infection, intensive care unit length of stay, hospital length of stay, adverse events, antimicrobial resistance-related outcomes, and healthcare-resource utilization. The objective of this review was to evaluate whether procalcitonin-guided antibiotic stewardship reduces unnecessary antimicrobial exposure without compromising clinical safety among adult surgical or surgically relevant patients with sepsis.

This systematic review was conducted as a structured evidence synthesis without meta-analysis and was prepared in accordance with PRISMA 2020 principles for systematic reviews. A narrative synthesis approach was selected because the anticipated evidence base included heterogeneous study designs, patient populations, surgical relevance, procalcitonin thresholds, testing schedules, antibiotic algorithms, comparator practices, and outcome definitions, making statistical pooling inappropriate without sufficient clinical and methodological homogeneity. The review focused on contemporary evidence addressing procalcitonin-guided antibiotic stewardship among adult surgical or surgically relevant critically ill patients with sepsis, with particular emphasis on antibiotic duration, antimicrobial de-escalation, mortality, clinical safety, intensive care utilization, hospital stay, antimicrobial resistance-related outcomes, and cost-related findings.

The eligibility criteria were defined according to the PICO framework. Eligible populations included adults with sepsis, septic shock, postoperative infection, intra-abdominal infection, pancreatitis-associated infection, surgical intensive care admission, or critically ill conditions with clear relevance to surgical antimicrobial decision-making. Eligible interventions included serial procalcitonin monitoring or procalcitonin-guided algorithms used to support antibiotic discontinuation, de-escalation, continuation, or optimization. Eligible comparators included standard care, usual clinician-directed antibiotic management, antimicrobial stewardship without procalcitonin guidance, or alternative biomarker-guided strategies. Eligible study designs included randomized controlled trials, prospective and retrospective cohort studies, before-and-after implementation studies, observational comparative studies, and systematic reviews or meta-analyses used for contextual synthesis where they directly addressed procalcitonin-guided stewardship in sepsis or critically ill populations. Primary clinical studies were prioritized for interpretation of outcomes, while secondary reviews were used cautiously to contextualize the direction and consistency of evidence and to avoid overstating duplicated findings.

Studies were excluded if they were limited exclusively to pediatric populations, involved noninfectious or non-septic conditions without antibiotic-stewardship outcomes, evaluated procalcitonin only as a diagnostic marker without antimicrobial decision-making, lacked measurable stewardship or clinical outcomes, were editorials or opinion papers without analyzable clinical evidence, were conference abstracts without sufficient methodological detail, were duplicate reports, were inaccessible in full text, or were published in languages other than English. Studies involving mixed intensive care populations were retained only when their findings were clinically relevant to surgical sepsis, postoperative infection, intra-abdominal infection, or critically ill antimicrobial stewardship. During synthesis, these studies were interpreted as indirect evidence when surgical-specific subgroup data were not available.

A systematic literature search was conducted using PubMed/MEDLINE, Scopus, Web of Science, Cochrane Library, Google Scholar, SpringerLink, Wiley Online Library, Oxford Academic, and PubMed Central. The search covered literature published from January 2022 to 2026 to capture recent evidence relevant to contemporary procalcitonin-guided stewardship practice. The search strategy combined controlled vocabulary and free-text terms related to sepsis, surgical populations, procalcitonin, and antimicrobial stewardship. Core terms included "sepsis," "septic shock," "surgical sepsis," "postoperative infection," "intra-abdominal infection," "surgical intensive care," "critically ill," "procalcitonin," "PCT," "procalcitonin-guided therapy," "antibiotic stewardship," "antimicrobial stewardship," "antibiotic discontinuation," "antibiotic de-escalation," and "biomarker-guided therapy." The PubMed search strategy was structured as follows: ("sepsis" OR "septic shock" OR "surgical sepsis" OR "postoperative infection" OR "intra-abdominal infection") AND ("procalcitonin" OR "PCT") AND ("antibiotic stewardship" OR "antimicrobial stewardship" OR "antibiotic discontinuation" OR "antibiotic de-escalation" OR "biomarker-guided therapy") AND ("surgical patients" OR "surgical ICU" OR "critically ill" OR "postoperative"). Search terms were adapted for other databases according to their indexing systems and search interfaces. Reference lists of relevant articles were hand-searched to identify additional eligible studies.

Retrieved records were screened in sequential stages. Duplicate records were removed before screening. Titles and abstracts were assessed for relevance to procalcitonin, sepsis, surgical or critically ill populations, and antibiotic stewardship. Full texts of potentially eligible articles were then reviewed against the predefined inclusion and exclusion criteria. Studies were categorized by design, population, clinical setting, surgical relevance, procalcitonin algorithm, comparator care, and outcome domain. When populations were mixed, the degree of applicability to surgical sepsis was assessed according to whether the study included surgical intensive care patients, postoperative infection, intra-abdominal sepsis, pancreatitis-related infection, source-control considerations, or critically ill cohorts in which surgical antimicrobial decisions were clinically relevant.

Data extraction focused on variables required for reproducibility, applicability, and clinical interpretation. Extracted information included author name, publication year, study design, population, setting, sample size where reported, infection type, surgical relevance, procalcitonin measurement schedule, threshold or percentage-decline rule, antibiotic decision algorithm, comparator strategy, antibiotic duration, de-escalation or discontinuation outcomes, mortality, treatment failure, recurrent infection, intensive care unit length of stay, hospital length of stay, adverse events, antimicrobial resistance-related outcomes, cost or resource-use findings, and main study conclusions. Where available, numerical data including absolute values, between-group differences, confidence intervals, p-values, and effect estimates were extracted. Where studies reported only qualitative or directional conclusions, results were summarized descriptively without generating unreported statistics.

Methodological quality and risk of bias were evaluated according to study design. Randomized controlled trials were assessed with attention to randomization process, allocation concealment, baseline comparability, adherence to the procalcitonin algorithm, deviations from intended intervention, completeness of outcome data, outcome measurement, and selective reporting. Observational and before-and-after studies were assessed for participant selection, comparability of groups, confounding, intervention fidelity, outcome measurement, missing data, and temporal bias. Systematic reviews and meta-analyses used for contextual interpretation were assessed for search transparency, eligibility criteria, risk-of-bias appraisal, appropriateness of synthesis, and strength of conclusions. Greater interpretive weight was assigned to studies with direct surgical relevance, clearly described procalcitonin algorithms, comparative outcome reporting, and extractable stewardship or safety outcomes.

Potential sources of bias and confounding were considered during synthesis. At the clinical level, important confounders included illness severity, infection source, adequacy and timing of source control, postoperative day, antimicrobial spectrum, microbiological confirmation, immune status, organ dysfunction, surgical complexity, and institutional stewardship practices. At the review level, heterogeneity was anticipated because studies differed in procalcitonin thresholds, testing intervals, discontinuation rules, patient populations, comparator care, and definitions of antibiotic exposure or treatment failure. Findings were therefore interpreted according to directness of evidence, consistency of effect direction, methodological quality, and clinical applicability rather than study count alone.

Evidence from mixed ICU populations was treated as supportive but indirect when surgical-specific findings were not separately reported.

The synthesis was organized narratively by outcome domain. The primary outcome was antibiotic duration or total antimicrobial exposure. Secondary outcomes included antibiotic discontinuation or de-escalation, mortality, clinical safety, treatment failure or recurrent infection, intensive care unit length of stay, hospital length of stay, adverse events, antimicrobial resistance-related outcomes, and cost-effectiveness or resource utilization. Study characteristics and outcome findings were planned for presentation in structured tables to distinguish primary studies from secondary reviews, direct surgical evidence from indirect critically ill evidence, and quantitative findings from descriptive conclusions. Meta-analysis was not performed because of heterogeneity in study design, patient population, procalcitonin algorithm, threshold definition, comparator care, and outcome reporting.

Ethical approval was not required because the review used previously published literature and did not involve direct contact with human participants, identifiable patient data, or individual-level clinical records. Data integrity was supported by applying predefined eligibility criteria, maintaining consistent extraction domains, distinguishing direct from indirect surgical evidence, and avoiding the creation of unreported numerical estimates. The final review should report the complete study-selection flow, study-characteristics table, outcome-extraction table, and risk-of-bias summary to improve transparency, reproducibility, and interpretability.

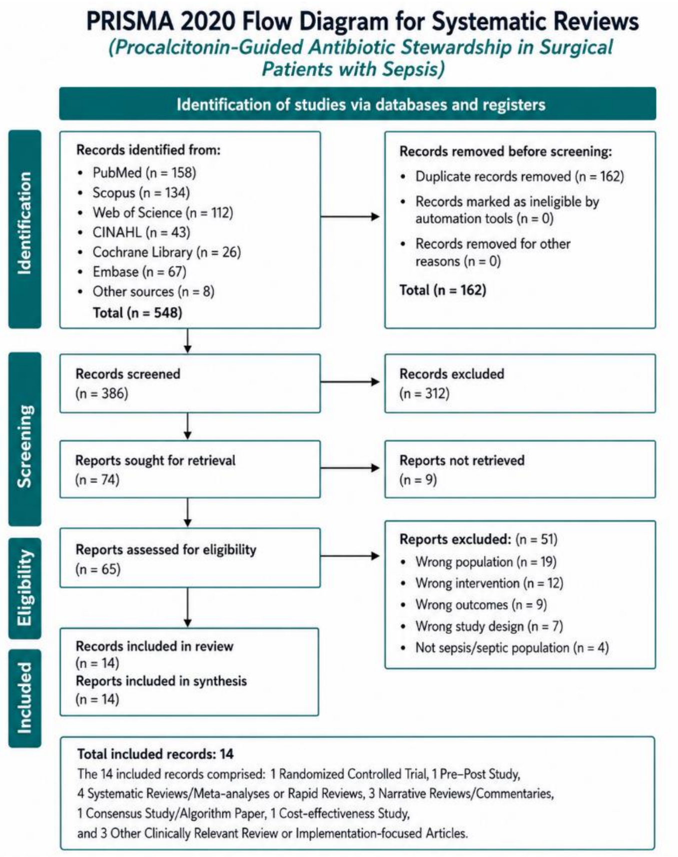

Figure 1 PRISMA Flowchart

RESULTS

The database and supplementary search identified 548 records, including records from PubMed, Scopus, Web of Science, CINAHL, Cochrane Library, Embase, and other sources. After removal of 162 duplicate records, 386 records were screened by title and abstract. Of these, 312 records were excluded because they did not meet the review scope or eligibility criteria. Seventy-four reports were sought for retrieval, of which 9 could not be retrieved. The remaining 65 reports were assessed in full text for eligibility. Fiftyone reports were excluded after full-text assessment, most commonly because of wrong population, wrong intervention, wrong outcome, wrong study design, or absence of a sepsis or septic population. Fourteen records were finally included in the review and narrative synthesis.

The 14 included records represented a heterogeneous evidence base consisting of randomized controlled trials, pre–post implementation evidence, systematic reviews, meta-analyses, narrative reviews, clinical commentaries, consensus guidance, stewardship-focused reviews, network meta-analysis, and cost-effectiveness evidence. Two records were randomized controlled trials, one was a pre–post interventional study, five were systematic reviews, meta-analyses, rapid reviews, or network meta-analyses, four were narrative reviews, clinical commentaries, or stewardship-focused reviews, one was a consensus algorithm paper, and one was a cost-effectiveness study. Because the included evidence varied substantially in design, study population, clinical setting, procalcitonin threshold, comparator care, and outcome definition, the findings were synthesized narratively rather than statistically pooled.

Table 1. Characteristics of Included Records

Study	Design / Evidence Type	Population / Setting	Surgical Relevance	Main Focus	Principal Finding
Kiya et al. (2024) (1)	Review	Sepsis and surgical/critically ill patients	Indirect to moderate	Procalcitonin-guided stewardship	Reported reduced antibiotic exposure and improved de-escalation when PCT was integrated into stewardship decisions
Gupta et al. (2026) (2)	Clinical commentary	Critically ill patients with sepsis	Indirect	Lessons from ADAPT-Sepsis	Emphasized cautious implementation and use of PCT as an adjunct rather than a replacement for clinical judgment
Kim (2022) (3)	Narrative review	Patients with sepsis and infection	Indirect	Clinical utility of PCT	Supported PCT as a useful stewardship biomarker, particularly for discontinuation decisions
Raja et al. (2026) (4)	Systematic review and meta-analysis	Patients with sepsis	Indirect	Efficacy and safety of PCT-guided therapy	Reported reduced antibiotic duration without clear evidence of increased mortality
Nazer et al. (2024) (5)	Randomized controlled trial	Critically ill cancer patients with sepsis	Indirect to surgical oncology relevance	PCT-guided antibiotic duration	Reported shorter antibiotic treatment duration with PCT-guided management
Papp et al. (2023) (6)	Systematic review and meta-analysis	Critically ill ICU patients	Indirect	Antibiotic duration and survival	Reported shorter treatment duration and possible survival benefit in selected critically ill populations
Mathew et al. (2024) (7)	Pre–post interventional study	Septic ICU patients	Indirect	PCT-guided stewardship implementation	Reported improved antimicrobial discontinuation and reduced exposure after stewardship implementation
Park et al. (2022) (8)	Consensus algorithm paper	Clinical practice population	Indirect	PCT algorithm implementation	Proposed standardized decision pathways for PCT-guided antibiotic use
Fugit and McCoury (2023) (9)	Stewardship review	ICU sepsis management	Indirect	PCT within antimicrobial stewardship programs	Highlighted stewardship implementation benefits and the need for protocolized use
Siriwardena et al. (2022) (10)	Randomized controlled trial	Acute pancreatitis patients	Surgically relevant gastrointestinal/inflammatory context	PCT-based antibiotic algorithm	Reported reduced unnecessary antibiotic use in acute pancreatitis
Rafiq et al. (2026) (11)	Rapid systematic review	Critically ill adults with sepsis	Indirect	PCT- or CRP-guided discontinuation	Supported biomarker-guided discontinuation strategies in critical illness
Gregoriano et al. (2024) (12)	Patient-level meta-analysis	Patients with cancer	Indirect to surgical oncology relevance	PCT-guided antibiotic treatment	Reported reduced overtreatment in cancer populations
Kubo et al. (2024) (13)	Systematic review and network meta-analysis	Critically ill adults with sepsis	Indirect	Benefits and harms of biomarker-guided discontinuation	Supported PCT-guided discontinuation as a favorable strategy among critically ill adults
Stevenson et al. (2025) (14)	Cost-effectiveness study	Hospitalized patients with sepsis	Indirect	Economic outcomes of PCT-guided duration	Suggested cost-saving potential through reduced antibiotic duration and resource use

Across the included records, the most consistent finding was that procalcitonin-guided stewardship was associated with reduced antibiotic exposure or shorter antibiotic duration compared with usual care or clinician-directed management. This finding was reported across systematic reviews, meta-analyses, randomized trials, and stewardship implementation evidence. The strongest clinical relevance was observed in studies where serial procalcitonin measurement was used to support antibiotic discontinuation or de-escalation once bacterial infection appeared controlled. In surgical or surgically relevant contexts, this finding is important because postoperative inflammation often complicates decisions about whether antibiotics can be safely stopped.

Table 2. Narrative Synthesis of Main Outcome Domains

Outcome Domain	Evidence Base	Direction of Finding	Interpretation for Surgical or Surgically Relevant Sepsis
Antibiotic duration / antimicrobial exposure	RCTs, pre–post study, systematic reviews, meta-analyses, stewardship reviews	Generally reduced with PCT-guided strategies	PCT may help shorten unnecessary antibiotic courses when used with clinical assessment and source-control evaluation
Antibiotic de-escalation / discontinuation	Consensus algorithm, implementation study, reviews, meta-analyses	Generally improved or supported	Serial PCT trends may provide practical support for earlier discontinuation or de-escalation decisions
Mortality and clinical safety	Systematic reviews, meta-analyses, RCT evidence	No consistent evidence of increased mortality reported in the included synthesis	Available evidence suggests antibiotic reduction can be achieved without obvious safety compromise, but direct surgical-specific certainty remains limited
ICU and hospital length of stay	Meta-analyses, cost-effectiveness study, ICU-focused evidence	Mixed or variably reported	Shorter antibiotic exposure may reduce resource use, but length-of-stay effects are likely influenced by surgical complexity, comorbidity, and source control
Antimicrobial resistance and stewardship impact	Stewardship reviews, implementation evidence, consensus guidance	Directionally favorable but not consistently measured as a direct outcome	PCT-guided reduction in antibiotic exposure may reduce selection pressure, but direct AMR outcome evidence in surgical sepsis remains limited
Cost-effectiveness / resource utilization	Cost-effectiveness study and stewardship literature	Potentially favorable	Reduced antibiotic duration and avoidance of unnecessary treatment may offset testing costs, but setting-specific economic evaluation is needed
Surgical-specific applicability	Mixed ICU, pancreatitis, cancer ICU, and general sepsis evidence	Indirect and heterogeneous	Evidence supports potential usefulness, but pure surgical sepsis trials remain limited

The evidence on antibiotic duration was the clearest and most reproducible outcome. Raja et al. and Papp et al. reported that procalcitonin-guided therapy reduced antibiotic duration among sepsis or critically ill populations, while Nazer et al. showed shorter antibiotic treatment in critically ill cancer patients with sepsis. Mathew et al. similarly reported improved antimicrobial discontinuation after implementing a procalcitonin-guided stewardship approach in septic ICU patients. Siriwardena et al. demonstrated reduced unnecessary antibiotic use in acute pancreatitis, a surgically relevant gastrointestinal condition in which inflammatory markers can be difficult to interpret. Collectively, these findings suggest that procalcitonin may be most useful as a discontinuation and de-escalation support tool rather than as a stand-alone diagnostic test.

Mortality and clinical safety outcomes were generally reassuring, although the evidence should be interpreted cautiously. Meta-analytic and network meta-analytic evidence reported no consistent increase in mortality with procalcitonin-guided discontinuation strategies despite reduced antibiotic exposure. However, surgical-specific certainty remains limited because many included studies were conducted in mixed ICU, cancer, pancreatitis, or general sepsis populations rather than exclusively in postoperative surgical patients. This distinction is clinically important because antibiotic decisions in surgical sepsis are strongly influenced by source control, anatomical site of infection, operative timing, drainage adequacy, and ongoing contamination risk.

The effect of procalcitonin-guided stewardship on ICU length of stay, hospital length of stay, and healthcare-resource utilization was less consistent than its effect on antibiotic exposure. Some studies and economic evaluations suggested potential reductions in resource use through shorter antibiotic courses and fewer treatment-related complications, but these outcomes were not uniformly reported and were likely influenced by baseline illness severity, comorbidities, surgical complexity, organ dysfunction, and institutional stewardship practices. Therefore, length-of-stay and cost findings should be considered supportive but not definitive for surgical sepsis populations.

Evidence regarding antimicrobial resistance was clinically relevant but indirect. Several included reviews and stewardship-focused articles emphasized that reducing unnecessary broad-spectrum antibiotic exposure may reduce resistance selection pressure and improve antimicrobial stewardship.

However, few included records directly measured antimicrobial resistance emergence, resistant organism acquisition, or long-term microbiological outcomes as primary endpoints. Consequently, the available evidence supports the stewardship rationale for procalcitonin-guided discontinuation, but does not provide definitive surgical-specific proof that PCT-guided protocols reduce antimicrobial resistance.

Overall, the synthesis indicates that procalcitonin-guided antibiotic stewardship may reduce antibiotic exposure and support earlier antimicrobial discontinuation in sepsis and critically ill populations without clear evidence of worsened mortality or clinical safety outcomes. The evidence is strongest for antibiotic duration and weakest for direct antimicrobial resistance outcomes, cost-effectiveness in surgical settings, and outcomes specific to postoperative surgical sepsis. Because much of the evidence is indirect, procalcitonin should be interpreted as an adjunct to clinical judgment, source-control assessment, microbiological results, radiological findings, and patient trajectory rather than as an independent rule for stopping antibiotics.

DISCUSSION

This systematic review synthesized contemporary evidence on procalcitonin-guided antibiotic stewardship in surgical or surgically relevant patients with sepsis and found that the most consistent benefit of procalcitonin-guided strategies was reduction in antibiotic exposure or shorter duration of antimicrobial therapy. Across the included randomized trials, implementation evidence, systematic reviews, meta-analyses, narrative reviews, stewardship-focused articles, consensus guidance, and economic evaluation, serial procalcitonin monitoring most frequently supported earlier antibiotic discontinuation or de-escalation when used alongside clinical assessment. This finding is clinically important in surgical sepsis because postoperative inflammation often produces fever, leukocytosis, raised inflammatory markers, and systemic physiological responses that may resemble persistent infection even when bacterial activity is resolving. In this context, procalcitonin appears most useful as a decision-support biomarker for antibiotic discontinuation rather than as an isolated diagnostic or prescribing determinant (1–14).

The principal finding of reduced antibiotic exposure is consistent with previous evidence indicating that procalcitonin-guided antimicrobial algorithms can shorten treatment duration in critically ill and septic populations without clearly worsening patient safety outcomes. Meta-analytic and review-level evidence included in this synthesis generally supported reduced duration of therapy when procalcitonin thresholds or percentage-decline rules were incorporated into antibiotic decision-making (4,6,11,13). The randomized trial evidence also supported this direction, with procalcitonin-guided strategies contributing to shorter antibiotic treatment in critically ill cancer patients with sepsis and reduced unnecessary antibiotic use in acute pancreatitis (5,10). Although these populations are not identical to postoperative surgical sepsis, they are clinically relevant because surgical oncology, pancreatitis, intra-abdominal infection, and critical care settings often present similar challenges of inflammatory overlap, diagnostic uncertainty, and concern about premature antimicrobial discontinuation.

Despite this encouraging direction of evidence, the findings should be interpreted with appropriate caution. The strongest evidence in the review relates to antibiotic duration, whereas evidence for mortality, intensive care unit length of stay, hospital stay, antimicrobial resistance, recurrent infection, adverse events, and cost-effectiveness is less consistent and often indirectly applicable to surgical populations. Available review-level and network meta-analytic evidence did not suggest a consistent increase in mortality with procalcitonin-guided discontinuation, but many included records involved mixed intensive care cohorts rather than exclusively surgical patients (4,6,13). Therefore, the conclusion that procalcitonin-guided stewardship is safe in all surgical sepsis contexts would be premature. A more defensible interpretation is that procalcitonin-guided strategies may reduce antibiotic exposure without an obvious signal of increased mortality in available critically ill sepsis evidence, provided that biomarker results are interpreted in conjunction with source control, hemodynamic stability, microbiological data, imaging findings, and the patient's overall clinical trajectory.

The surgical applicability of procalcitonin-guided stewardship deserves particular attention. Surgical sepsis differs from medical sepsis because antimicrobial decisions are strongly influenced by anatomical source, operative findings, adequacy of drainage or debridement, timing after surgery, wound status, presence of prosthetic material, and risk of ongoing contamination. In a patient with adequate source control and improving clinical parameters, a declining procalcitonin trend may strengthen confidence in antibiotic discontinuation. Conversely, in a patient with persistent organ dysfunction, unresolved abscess, anastomotic leak, infected necrosis, or inadequate source control, a low or falling procalcitonin level should not be used as the sole justification for stopping therapy. This distinction aligns with stewardship-focused and consensus literature emphasizing that procalcitonin should complement clinical judgment rather than replace it (2,8,9).

The heterogeneity of procalcitonin thresholds and algorithms remains a major implementation challenge. Included evidence described variable approaches, including absolute concentration thresholds, percentage declines from baseline or peak values, and serial monitoring patterns. This variability limits direct comparison across studies and reduces confidence in a single universal threshold for surgical patients. Postoperative inflammatory responses may transiently elevate procalcitonin, particularly after major abdominal surgery, trauma, pancreatitis, or procedures associated with extensive tissue injury. Therefore, isolated procalcitonin values may be less informative than serial trends interpreted against operative timing and clinical status. Future surgical stewardship protocols should define procedure-specific timing, threshold rules, and escalation safeguards to prevent inappropriate antibiotic cessation in patients with unresolved infection.

The review also highlights a gap between the biological rationale for stewardship and direct evidence for antimicrobial resistance outcomes. Reducing unnecessary antibiotic exposure is a core antimicrobial stewardship goal and is expected to reduce selection pressure for resistant organisms, drug toxicity, and secondary infections. However, the included evidence did not consistently measure antimicrobial resistance emergence, resistant organism acquisition, microbiological recurrence, or long-term ecological outcomes as primary endpoints. As a result, the evidence supports the rationale that procalcitonin-guided stewardship may contribute to better antimicrobial optimization, but it does not prove that these protocols reduce antimicrobial resistance in surgical sepsis populations. This distinction is important because antimicrobial resistance is a population-level and institution-level outcome that requires longer follow-up, microbiological surveillance, and adjustment for antibiotic class, local resistance patterns, infection-control practices, and baseline colonization risk.

The findings on resource utilization and cost-effectiveness were also promising but not definitive. Reduced antibiotic duration may lower pharmacy costs, monitoring burden, adverse drug events, and unnecessary hospital resource use, and the included cost-effectiveness evidence suggested potential economic benefit in hospitalized sepsis populations (14). However, surgical patients often remain hospitalized because of operative recovery, wound care, drains, nutritional support, rehabilitation needs, or management of complications rather than antibiotic duration alone. Therefore, even when procalcitonin reduces antimicrobial exposure, its effect on hospital length of stay or total cost may be diluted by noninfectious surgical factors. Economic evaluation in surgical sepsis should therefore incorporate not only procalcitonin testing costs and antibiotic days, but also source-control procedures, readmissions, treatment failure, resistant infections, and adverse drug-related complications.

The present synthesis has several methodological and evidence-level limitations. First, the included records were heterogeneous in design, ranging from randomized trials and pre–post implementation evidence to systematic reviews, meta-analyses, narrative reviews, clinical commentaries, consensus guidance, and economic evaluation. This heterogeneity limited the appropriateness of statistical pooling and required narrative synthesis. Second, direct surgical sepsis evidence was limited, and several included records were only indirectly applicable through mixed intensive care, cancer, pancreatitis, or general sepsis populations. Third, outcome reporting was inconsistent, particularly for antimicrobial resistance, recurrent infection, adverse events, and cost outcomes. Fourth, variation in procalcitonin thresholds, timing of measurement, comparator care, and stewardship implementation reduced comparability across records. Finally, inclusion of secondary evidence such as reviews and commentaries may broaden contextual interpretation but also requires caution because primary study findings may overlap across reviews.

From a clinical perspective, the findings support cautious integration of procalcitonin into surgical antimicrobial stewardship programs as an adjunctive tool for antibiotic discontinuation and de-escalation. The most appropriate use appears to be in clinically improving patients where infection control is likely, cultures and imaging do not suggest ongoing uncontrolled infection, and serial procalcitonin values show a declining trend. Procalcitonin should not be used independently to withhold or discontinue antibiotics in unstable postoperative patients, those with incomplete source control, persistent organ dysfunction, immunosuppression, infected necrosis, or high-risk intra-abdominal complications. Implementation should therefore be protocolized, multidisciplinary, and embedded within antimicrobial stewardship rounds involving surgeons, intensivists, infectious disease specialists, microbiologists, pharmacists, and critical care teams.

Future research should prioritize multicenter randomized trials focused specifically on postoperative and surgical intensive care sepsis populations. These studies should stratify patients by source of infection, operative category, adequacy of source control, postoperative timing, and baseline illness severity. They should compare standardized procalcitonin algorithms with usual care and report antibiotic-free days, antibiotic duration, mortality, treatment failure, recurrent infection, adverse events, ICU and hospital length of stay, readmission, antimicrobial resistance acquisition, and cost-effectiveness. Future trials should also evaluate whether combining procalcitonin with clinical scoring systems, microbiological results, imaging findings, C-reactive protein trends, or artificial intelligence-supported stewardship tools improves decision accuracy. Until such surgical-specific evidence is available, procalcitonin-guided stewardship should be regarded as a promising but adjunctive strategy rather than a standalone standard for antibiotic decision-making in surgical sepsis.

CONCLUSION

Procalcitonin-guided antibiotic stewardship may help reduce unnecessary antimicrobial exposure and support earlier antibiotic discontinuation or de-escalation in patients with sepsis, including surgical or surgically relevant critically ill populations. The available evidence is most consistent for reducing antibiotic duration, while findings related to mortality, intensive care unit stay, hospital stay, antimicrobial resistance, adverse events, and cost-effectiveness remain less definitive and are often derived from mixed or indirect populations. In surgical sepsis, procalcitonin should therefore be used as an adjunct to clinical judgment rather than as a standalone decision rule, with interpretation guided by source control, operative context, microbiological data, imaging findings, hemodynamic status, and serial biomarker trends. Further well-designed, surgical-specific randomized trials are needed to define optimal thresholds, timing of measurement, discontinuation algorithms, safety outcomes, antimicrobial resistance effects, and economic value before procalcitonin-guided protocols can be recommended as a uniform standard across surgical sepsis practice.

REFERENCES

1. Kiya GT, Asefa ET, Abebe G, et al. Procalcitonin guided antibiotic stewardship. Biomark Insights. 2024.

2. Gupta S, Klompas M, Rhee C. Reassessing procalcitonin-guided antibiotic therapy in critically ill patients with sepsis: lessons from the ADAPT-Sepsis trial. Clin Infect Dis. 2026.

3. Kim JH. Clinical utility of procalcitonin on antibiotic stewardship: a narrative review. Infect Chemother. 2022.

4. Raja HAA, Afridi MJ, Asad F, et al. Efficacy and safety of procalcitonin-guided antibiotic therapy versus standard of care for sepsis: a systematic review and meta-analysis. Med Princ Pract. 2026.

5. Nazer LH, Awad W, Thawabieh H, et al. Procalcitonin-guided management and duration of antibiotic therapy in critically ill cancer patients with sepsis (Pro-Can Study): a randomized controlled trial. Crit Care Explor. 2024.

6. Papp M, Kiss N, Baka M, et al. Procalcitonin-guided antibiotic therapy may shorten length of treatment and may improve survival: a systematic review and meta-analysis. Crit Care. 2023.

7. Mathew P, Vargese SS, Mathew LM. Procalcitonin-guided antimicrobial stewardship in critically ill patients with sepsis: a pre-post interventional study. J Clin Res. 2024.

8. Park DW, Choi JY, Kim CJ, et al. Implementation of procalcitonin in antibiotic stewardship: derivation of a consensus algorithm for procalcitonin use in clinical practice. Infect Chemother. 2022.

9. Fugit RV, McCoury JB. Procalcitonin for sepsis management: implementation within an antimicrobial stewardship program. Am J Health Syst Pharm. 2023.

10. Siriwardena AK, Jegatheeswaran S, et al. A procalcitonin-based algorithm to guide antibiotic use in patients with acute pancreatitis (PROCAP): a randomised controlled trial. Lancet Gastroenterol Hepatol. 2022.

11. Rafiq S, Shi C, Ghosal S, et al. Effectiveness of procalcitonin- or C-reactive protein-guided antibiotic discontinuation protocols for adult patients who are critically ill with sepsis: a rapid systematic review. Wiley Online Library. 2026.

12. Gregoriano C, Wirz Y, Heinsalo A, et al. Procalcitonin-guided antibiotic treatment in patients with cancer: a patient-level meta-analysis from randomized controlled trials. BMC Cancer. 2024.

13. Kubo K, Sakuraya M, Sugimoto H, et al. Benefits and harms of procalcitonin- or C-reactive protein-guided antimicrobial discontinuation in critically ill adults with sepsis: a systematic review and network meta-analysis. Crit Care Med. 2024.

14. Stevenson M, Forsyth JE, Hossain A, et al. Cost-effectiveness of procalcitonin-guided antibiotic duration for hospitalized patients with sepsis. Crit Care. 2025.