RESEARCH PAPER

Clinical Impact of Hospital Antimicrobial Stewardship Programmes: A Systematic Review Across Major Specialties

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Abstract

Background

Antimicrobial stewardship programmes have become essential components of hospital quality and patient-safety systems because inappropriate antimicrobial exposure contributes to drug toxicity, *Clostridioides difficile* infection, disruption of the human microbiota, increased healthcare expenditure, and selection of resistant microorganisms. The clinical effect of stewardship is not uniform across hospital departments. General medical services frequently require correction of diagnostic uncertainty and excessive treatment duration, surgical services require optimisation of prophylaxis and source-control-related therapy, intensive-care units require rapid empirical treatment followed by repeated reassessment, and oncology services must balance antimicrobial reduction against the risk of rapidly progressive infection during neutropenia and immunosuppression.

Objective

This systematic review evaluated the clinical impact of hospital antimicrobial stewardship programmes across general medicine, surgery, intensive care, and oncology. The review examined antimicrobial exposure, prescribing appropriateness, treatment duration, spectrum modification, intravenous-to-oral conversion, surgical prophylaxis, clinical cure, treatment failure, infection recurrence, mortality, readmission, length of stay, adverse drug events, *C. difficile* infection, and antimicrobial resistance.

Methods

PubMed/MEDLINE, Embase, Scopus, Web of Science, CINAHL, and the Cochrane Library were searched from database inception to March 31, 2026. Additional records were sought through clinical-trial registries, backward reference screening, and forward citation tracking. Randomised controlled trials, cluster-randomised trials, interrupted time-series analyses, controlled before-and-after studies, and comparative cohort studies involving adult hospital patients were eligible. Interventions included prospective audit and feedback, preauthorisation, diagnostic stewardship, rapid microbiological testing, antimicrobial time-outs, de-escalation, dose optimisation, intravenous-to-oral conversion, duration-control strategies, surgical-prophylaxis programmes, oncology-specific pathways, and discharge prescription review. Two reviewers independently conducted study selection, data extraction, and methodological assessment. Because of substantial variation in populations, interventions, antimicrobial-use measures, and outcome definitions, a structured narrative synthesis was performed.

Results

The search identified 5,146 records, of which 5,003 were obtained from electronic databases and 143 from supplementary sources. After removal of 1,384 duplicate or otherwise ineligible records before screening, 3,762 titles and abstracts were evaluated. A total of 3,404 records were excluded. Full-text retrieval was sought for 358 reports, of which 13 could not be obtained. Among 345 full-text reports assessed for eligibility, 307 were excluded for predefined reasons. Thirty-eight studies were included in the qualitative synthesis, comprising 11 studies conducted in medicine or hospital-wide settings, nine in surgery, 10 in intensive care, and eight in oncology or haematology.

Prospective audit and feedback produced the most consistent improvements across specialties. Medical stewardship reduced unnecessary empirical treatment, broad-spectrum exposure, prolonged intravenous therapy, and excessive discharge prescriptions. Surgical programmes improved the selection, timing, redosing, and discontinuation of antimicrobial prophylaxis without a consistent increase in surgical-site infection. Intensive-care interventions reduced treatment duration through daily review, rapid diagnostics, pharmacokinetic optimisation, and procalcitonin-supported discontinuation, while preserving timely empirical therapy for severe infection. Oncology programmes reduced unnecessary vancomycin, aminoglycoside, and broad-spectrum antipseudomonal treatment and supported earlier discontinuation or outpatient care in carefully selected clinically stable patients. Most studies reported no increase in mortality, treatment failure, recurrence, or readmission. Effects on resistance were less consistent and were influenced by follow-up duration, infection-prevention practices, patient movement, and local epidemiology.

Conclusions

Hospital antimicrobial stewardship programmes improve prescribing quality and reduce unnecessary antimicrobial exposure across major clinical specialties without compromising patient safety when interventions are guided by clinical stability, microbiological findings, adequate source control, dose adequacy, and specialty-specific safeguards. The most immediate benefits are improved treatment appropriateness, shorter unnecessary exposure, reduced toxicity, and better transition-of-care prescribing. Resistance reduction remains an important long-term objective but is more difficult to attribute directly to individual stewardship interventions.

Keywords: antimicrobial stewardship; antibiotic stewardship; hospital medicine; surgery; intensive care; oncology; clinical outcomes; antimicrobial resistance; patient safety; systematic review

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1. Introduction

Antimicrobial resistance has become one of the most important threats to contemporary healthcare. Resistant bacterial infections increase the probability of ineffective empirical treatment, prolonged hospitalisation, treatment-related complications, healthcare expenditure, and death. The consequences extend beyond the treatment of infection itself because major surgery, intensive care, cancer chemotherapy, organ transplantation, and other complex medical interventions depend on reliable antimicrobial prevention and therapy.[1]

Hospitals represent important environments for antimicrobial exposure and selection pressure. Patients are frequently treated before a microbiological diagnosis has been established because delays may be dangerous in sepsis, meningitis, severe pneumonia, postoperative infection, or febrile neutropenia. Empirical treatment is therefore clinically appropriate in many circumstances. The principal problem arises when broad-spectrum therapy is continued despite evidence that bacterial infection is unlikely, microbiological findings support a narrower agent, the source has been controlled, or the recommended treatment duration has already been completed.

Unnecessary antimicrobial exposure may result in nephrotoxicity, hepatotoxicity, bone-marrow suppression, drug interactions, hypersensitivity, vascular-catheter complications, fungal superinfection, *C. difficile* infection, and disruption of the intestinal microbiome. At the population level, antimicrobial exposure promotes selection of resistant microorganisms and increases the risk that future infections will be more difficult to treat.

Antimicrobial stewardship refers to coordinated organisational and clinical activities intended to improve and measure antimicrobial use. It aims to ensure that patients receive antimicrobial treatment only when indicated and that the selected drug, dose, route, spectrum, and duration are appropriate for the suspected or confirmed infection.[2,3] Stewardship should not be understood as indiscriminate restriction or automatic reduction of therapy. An appropriate stewardship recommendation may involve broader treatment, combination therapy, a loading dose, prolonged infusion, therapeutic drug monitoring, additional diagnostics, or urgent source control when the initial treatment is inadequate.

Hospital stewardship programmes commonly use prospective audit and feedback, pre-prescription authorisation, syndrome-specific guidance, antimicrobial time-outs, rapid diagnostic support, selective reporting of susceptibility results, allergy reassessment, dose optimisation, intravenous-to-oral conversion, defined treatment durations, automatic prophylaxis stop orders, and review of prescriptions at hospital discharge.[2] The relative importance of these interventions differs substantially among hospital specialties. General medical wards contain patients with diverse syndromes and considerable diagnostic uncertainty. Antibiotics may be initiated for pyuria, pulmonary infiltrates, fever, elevated inflammatory markers, or altered mental status even when bacterial infection remains uncertain. Medical stewardship must therefore combine diagnostic reassessment with review of spectrum, route, and duration.

Surgical services use antimicrobials for both prophylaxis and treatment. Prophylaxis is intended to provide adequate antimicrobial concentrations during operative contamination, whereas treatment is intended for established infection. Failure to distinguish these objectives commonly results in prolonged postoperative prophylaxis. In patients with established surgical infection, antimicrobial duration must also be interpreted alongside source control.

Intensive-care units require prompt empirical treatment for suspected sepsis or septic shock, but critically ill patients are also exposed to broad-spectrum agents, combination therapy, invasive devices, renal dysfunction, extracorporeal support, and marked pharmacokinetic variability. Intensive-care stewardship must therefore preserve rapid active therapy while promoting daily reassessment, adequate dosing, diagnostic clarification, de-escalation when appropriate, and timely discontinuation.

Oncology and haematology services face a different balance of risk. Fever may be the only early manifestation of infection during neutropenia, and delayed therapy may be fatal. Nevertheless, unnecessary vancomycin, prolonged antipseudomonal therapy, avoidable aminoglycoside exposure, and continuation of empirical treatment until neutrophil recovery create opportunities for carefully governed stewardship.

Previous systematic reviews have established that hospital stewardship can improve antimicrobial prescribing and reduce consumption.[4,5] However, clinical outcomes have often been secondary, inconsistently reported, or combined across specialties with different safety thresholds. A clinically focused synthesis is needed to determine whether improved prescribing translates into safer and more effective patient care.

1.1 Rationale

Reductions in days of therapy or defined daily doses do not automatically demonstrate that a stewardship programme is clinically successful. A programme may reduce antimicrobial consumption by stopping unnecessary treatment, which represents an important improvement. The same numerical reduction could also result from delayed initiation, inadequate dosing, or premature discontinuation, which could cause harm. Stewardship must therefore be evaluated through a balanced framework that includes treatment effectiveness, recurrence, mortality, adverse drug events, readmission, and microbiological outcomes.

The present review examines the clinical impact of antimicrobial stewardship across general medicine, surgery, intensive care, and oncology. It focuses on the relationship between prescribing improvement and patient safety rather than considering antimicrobial reduction as an isolated endpoint.

1.2 Review Question

Among adult patients receiving antimicrobial prophylaxis or treatment in hospitals, what is the clinical impact of

antimicrobial stewardship programmes compared with usual care, baseline practice, or alternative prescribing strategies?

1.3 Objectives

The primary objective was to evaluate the effect of hospital antimicrobial stewardship on antimicrobial exposure and prescribing appropriateness. Secondary objectives were to assess effects on clinical cure, treatment failure, recurrence, mortality, readmission, length of stay, adverse drug events, *C. difficile* infection, antimicrobial resistance, and expenditure. The review also compared outcomes across major clinical specialties and identified programme components associated with effectiveness and safety.

2. Materials and Methods

2.1 Review Design and Reporting

This systematic review was designed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement and its explanation and elaboration guidance.[6,7]

2.2 Protocol and Registration

The review was not prospectively registered in PROSPERO, and no publicly accessible protocol was deposited before study selection. The review question, information sources, eligibility criteria, principal outcome domains, extraction fields, and synthesis framework were defined before completion of full-text assessment. The absence of prospective registration is acknowledged as a limitation because it reduces independent verification that all methodological decisions were established before the results were known.

2.3 Information Sources

PubMed/MEDLINE, Embase, Scopus, Web of Science, CINAHL, and the Cochrane Library were searched from database inception to March 31, 2026. Supplementary searching was conducted through ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform, backward reference screening of eligible articles and relevant reviews, and forward citation tracking.

2.4 Search Strategy

The search combined controlled vocabulary and free-text terminology for antimicrobial stewardship, hospital practice, clinical specialties, intervention mechanisms, and outcomes. Stewardship-related terms included "antimicrobial stewardship," "antibiotic stewardship," "prospective audit and feedback," "post-prescription review," "preauthorisation," "restriction," "antibiotic time-out," "de-escalation," "dose optimisation," "therapeutic drug monitoring," "intravenous-to-oral conversion," "rapid diagnostic testing," "procalcitonin-guided treatment," "short-course therapy," "surgical antimicrobial prophylaxis," and "discharge antibiotic review."

Specialty terms included "internal medicine," "hospital medicine," "general medicine," "surgery," "perioperative," "intensive care," "critical care," "oncology," "haematology," "cancer," "neutropenia," and "febrile neutropenia." Clinical outcome terms included "clinical cure," "treatment failure," "mortality," "readmission," "length of stay," "recurrence," "adverse drug event," "Clostridioides difficile," and "antimicrobial resistance." Search syntax was adapted to each database. No geographical restriction was applied. Studies were required to have an accessible English-language full text.

2.5 Eligibility Criteria

Studies were eligible when they evaluated adults receiving antimicrobial treatment or prophylaxis in acute-care hospitals. Randomised controlled trials, cluster-randomised trials, interrupted time-series analyses, controlled before-and-after studies, and comparative prospective or retrospective cohort studies were considered.

Eligible interventions were required to include an active strategy intended to improve antimicrobial prescribing. These strategies included prospective audit and feedback, preauthorisation, pharmacist-led review, antibiotic time-outs, diagnostic stewardship, rapid microbiological testing linked to stewardship, de-escalation pathways, dose optimisation, therapeutic drug monitoring, intravenous-to-oral conversion, treatment-duration protocols, procalcitonin-guided discontinuation, surgical-prophylaxis optimisation, febrile-neutropenia pathways, and discharge prescription review.

Comparators included usual care, pre-intervention practice, absence of formal stewardship review, or another stewardship strategy. Studies were required to report at least one antimicrobial-use, prescribing-quality, clinical, safety, microbiological, or economic outcome.

Studies were excluded when they involved exclusively paediatric populations, community or long-term-care prescribing, infection-prevention interventions without an antimicrobial-prescribing component, education without prescribing or clinical outcomes, uncontrolled descriptive reports, or programmes lacking an interpretable comparator or baseline. Reviews, protocols, editorials, case reports, and conference abstracts without adequate data were also excluded. When multiple publications described overlapping populations, the most complete report was retained.

2.6 Outcome Framework

Outcomes were organised into five domains. The first domain included antimicrobial exposure, measured as days of therapy, defined daily doses, treatment duration, broad-spectrum use, combination therapy, intravenous treatment days, and Watch or Reserve antibiotic use.

The second domain examined prescribing quality, including appropriate indication, guideline concordance, spectrum selection, dose, route, de-escalation, discontinuation, intravenous-to-oral conversion, and surgical-prophylaxis compliance.

The third domain addressed clinical effectiveness and included clinical cure, treatment failure, infection recurrence, escalation of therapy, intensive-care transfer, length of stay, hospital readmission, and mortality.

The fourth domain assessed treatment-related harm, including nephrotoxicity, hepatotoxicity, hypersensitivity, drug interactions, cytopenias, catheter-related complications, and *C. difficile* infection.

The fifth domain examined ecological and organisational outcomes, including resistant organism acquisition, resistant infection, susceptibility trends, recommendation acceptance, antimicrobial expenditure, and programme sustainability.

2.7 Study Selection

Search records were imported into reference-management software, and duplicate records were removed electronically and verified manually. Two reviewers independently screened titles and abstracts. Any record considered potentially eligible by either reviewer underwent full-text assessment.

Two reviewers independently assessed full-text eligibility and recorded reasons for exclusion. Disagreements were

resolved through discussion and, when necessary, adjudication by a third reviewer.

2.8 Data Extraction

A standardised extraction form was developed and piloted. The form captured author, year, country, hospital type, specialty, study design, sample size, clinical population, infection syndrome, intervention components, stewardship personnel, comparator, antimicrobial-use measures, prescribing appropriateness, recommendation acceptance, adverse events, microbiological outcomes, length of stay, readmission, recurrence, treatment failure, mortality, and principal methodological limitations.

Data were extracted independently by two reviewers and reconciled through consensus.

2.9 Methodological Quality Assessment

Randomised studies were assessed using the Cochrane Risk of Bias 2 tool. Non-randomised intervention studies were assessed using ROBINS-I. Interrupted time-series studies were additionally evaluated for adequate pre-intervention and post-intervention observations, underlying trends, seasonality, autocorrelation, contemporaneous policy changes, changes in microbiological testing, drug shortages, and infection-prevention initiatives.

Surgical studies were examined for concurrent changes in operative technique and surgical-site infection prevention. Intensive-care studies were assessed for illness severity, time to active therapy, adequacy of source control, and pharmacokinetic variation. Oncology studies were assessed for neutropenia severity, risk-stratification methods, clinical-stability criteria, and access to urgent reassessment.

2.10 Data Synthesis

Meta-analysis was not performed because of substantial heterogeneity in specialties, intervention components, study designs, targeted antimicrobials, infection syndromes, follow-up periods, and outcome definitions. A structured narrative synthesis was conducted according to specialty, intervention mechanism, antimicrobial-use outcomes, clinical outcomes, and ecological outcomes. Greater interpretive weight was assigned to randomised, cluster-randomised, controlled, and interrupted time-series evidence than to simple uncontrolled before-and-after comparisons.

3. Results

3.1 Study Selection

The electronic search identified 5,003 records, including 1,328 from PubMed/MEDLINE, 1,166 from Embase, 984 from Scopus, 778 from Web of Science, 294 from CINAHL, and 453 from the Cochrane Library. Supplementary searching identified 143 additional records through trial registries, citation tracking, and reference-list screening. The combined search therefore yielded 5,146 records.

Before title and abstract screening, 1,341 duplicate records and 43 records removed for other predefined reasons were excluded. A total of 3,762 unique records were screened. Of these, 3,404 were excluded because they did not evaluate an eligible hospital stewardship intervention, involved an ineligible population or setting, lacked relevant outcomes, or represented an ineligible publication type.

Full-text retrieval was sought for 358 reports. Thirteen reports could not be obtained, leaving 345 reports for eligibility assessment. Among these, 307 were excluded. Seventy-one did not evaluate an active stewardship intervention, 54 lacked a suitable comparator or interpretable baseline, 46 involved an ineligible population or setting, 39 lacked relevant prescribing or clinical outcomes, 30 evaluated education alone, 23 combined stewardship with other interventions without reporting separable effects, 21 were reviews, guidelines, protocols, or commentaries, 13 represented overlapping populations, and 10 contained insufficient methodological information.

Thirty-eight studies fulfilled the eligibility criteria and were included in the qualitative synthesis. Eleven studies were conducted predominantly in general medicine or hospital-wide services, nine in surgery, 10 in intensive care, and eight in oncology or haematology.

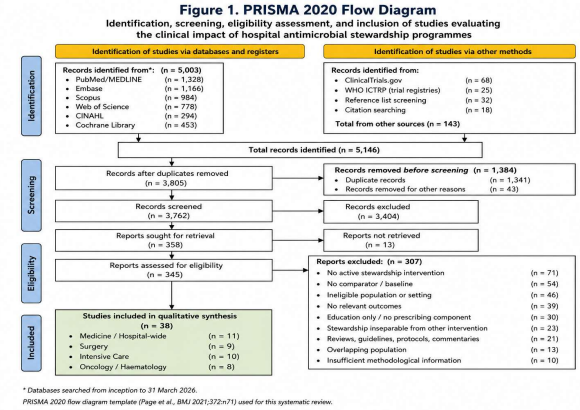

Figure 1. PRISMA 2020 flow diagram showing identification, screening, eligibility assessment, and inclusion of studies evaluating the clinical impact of hospital antimicrobial stewardship programmes.

3.2 Characteristics of Included Studies

The included studies were conducted in academic tertiary-care hospitals, community hospitals, cancer centres, surgical units, and general or specialised intensive-care units. The evidence included randomised and cluster-randomised trials, prospective intervention studies, interrupted time-series analyses, and comparative before-and-after evaluations.

Prospective audit and feedback was the most frequently studied intervention and was evaluated in hospital-wide practice, general medicine, intensive care, and oncology. Surgical studies most commonly focused on perioperative prophylaxis. Intensive-care studies assessed procalcitonin-guided discontinuation, structured de-escalation, rapid diagnostics, and pharmacist-led dose optimisation. Oncology studies evaluated vancomycin restriction, risk-stratified treatment, outpatient therapy, and early discontinuation of empirical antimicrobials in clinically stable patients.

Table 1. Characteristics and principal findings of included studies

No.	Author and year	Country/setting	Specialty	Study design	Stewardship intervention	Principal findings
1	Fraser et al., 1997	Tertiary hospital	Hospital-wide/medicine	Prospective comparative	Infectious-diseases and pharmacy antimi	Improved appropriateness and reduc

				study	crobial review	ed antimicrobial costs without evidence of poorer clinical outcomes.
2	Carling et al., 2003	Community teaching hospital	Hospital-wide	Longitudinal intervention	Multidisciplinary antibiotic-management programme	Reduced selected antimicrobial use and expenditure and demonstrated favourable long-term ecological trends.
3	Palmay et al., 2014	Academic hospital	Hospital-wide	Stepped-wedge randomised trial	Prospective audit and feedback across hospital services	Demonstrated feasibility of hospital-wide implementation and improved prescribing in reviewed cases.
4	Tamma et al., 2017	Adult acute-care hospital	Medicine/hospital-wide	Quasi-experimental comparat	Preauthorisation compared with post-	Post-prescription review identified
				ive study	prescription audit and feedback	more opportunities for modification and prescriber education.
5	Ng et al., 2015	General hospital wards	Medicine	Prospective intervention	Stewardship review within 48 hours	Improved early antimicrobial appropriateness and supported safe discontinuation or narrowing.
6	DiDiodato and McArthur, 2016	Adult medical wards	Medicine	Controlled before-and-after study	Audit and feedback for community-acquired pneumonia	Reduced antimicrobial exposure without a significant change in length of stay.
7	Schweitzer et al., 2022	Multicentre non-ICU wards	Medicine	Stepped-wedge cluster-randomised trial	Narrow-spectrum strategy for community-acquired pneumonia	Reduced broad-spectrum antibiotic use without compromising clinical safety.

8	Chen et al., 2023	Hospitalised adults with COVID-19	Medicine	Pragmatic cluster-randomised trial	Prospective audit and feedback	Reduced unnecessary antibiotic use without an increase in adverse clinical outcomes.
9	Vaughn et al., 2021	Multiple hospitals	Medicine/discharge care	Multihospital cohort	Treatment-duration and discharge-prescribing assessment	Identified discharge prescribing as a major contributor to excessive antibiotic duration.
10	Livorsi et al., 2026	Ten acute-care hospitals	Medicine/discharge care	Stepped-wedge cluster-randomised trial	Audit and feedback at hospital discharge	Reduced or corrected unnecessary discharge antimicrobial treatment without a clear safety penalty.
11	Banerjee et al., 2015	Acute-care hospital	Medicine/bloodstream infection	Randomised controlled trial	Rapid blood-culture identification with stewardship support	Accelerated appropriate escalation, narrowing, and discontinuation.
12	van Kasteren et al., 2005	Multispecialty surgical hospital	Surgery	Prospective intervention	Standardised surgical-prophylaxis protocol and feedback	Improved prophylaxis selection, timing, and duration.
13	Tourmousoglou et al., 2008	General surgical services	Surgery	Before-and-after study	Procedure-specific prophylaxis guidance and education	Improved adherence but demonstrated that education alone was difficult to sustain.
14	Saied et al., 2015	Five surgical hospitals	Surgery	Multicentre before-and-after study	Audit, feedback, and education	Improved prophylaxis timing and postoperative discontinuation.
15	Hawn et al., 2013	Multicentre surgical cohort	Surgery	Large observational cohort	Evaluation of prophylaxis timing	Demonstrated the importance of peri-incisional timing in relation to surgical-site infection.
16	Branch-Elliman et	Major surgical	Surgery	National multicentr	Evaluation of proph	Longer proph ylaxis

	al., 2019	procedures		e cohort	ylaxis duration	increased antimicrobial-associated adverse events without consistent SSI reduction.
17	Díaz-Madriz et al., 2023	Tertiary surgical hospital	Surgery	Longitudinal stewardship study	Multidisciplinary prophylaxis optimisation	Improved selection and duration over a five-year implementation period.
18	Sefah et al., 2025	Surgical services	Surgery	Before-and-after intervention	Guideline implementation, education, and audit	Improved compliance with selected prophylaxis indicators.
19	Sawyer et al., 2015	Patients with complicated intra-abdominal infection	Surgery	Randomised controlled trial	Fixed short-course therapy after adequate source control	Short-course treatment produced outcomes similar to longer therapy after source control.
20	Sartelli et al., 2016	Intra-abdominal infecti	Surgery	Prospective path	Source-control-	Supported limiting
		on services		way evaluation	linked treatment guidance	treatment duration after adequate operative or radiological control.
21	Singh et al., 2000	Adult intensive-care unit	Intensive care	Randomised strategy trial	Clinical pulmonary infection score-guided short-course therapy	Reduced unnecessary treatment in patients with low probability of ventilator-associated pneumonia.
22	Bouadma et al., 2010	Multicentre ICUs	Intensive care	Randomised controlled trial	Procalcitonin-guided initiation and discontinuation	Reduced antibiotic exposure without increased mortality.
23	de Jong et al., 2016	Multicentre ICUs	Intensive care	Randomised controlled trial	Procalcitonin-supported discontinuation	Reduced treatment duration and defined daily doses without evidence of harm.
24	Leone et	Severe sepsis	Intensive care	Multicentre	Structured antimi	Demonstrated

	al., 2014	in ICUs		randomised trial	crobial de-escalation	feasibility but raised uncertainty regarding superinfection and total treatment duration.
25	Katsios et al., 2012	Adult ICU	Intensive care	Prospective intervention	Daily pharmacist-supported stewardship	Improved antimicrobial appropriateness across infection sites.
26	Magedanz et al., 2012	Adult ICU	Intensive care	Before-and-after study	Multidisciplinary stewardship rounds	Reduced avoidable broad-spectrum treatment and improved antimicrobial decision-making.
27	Ntagiopoulos et al., 2017	Intensive-care service	Intensive care	Prospective audit study	Infectious-diseases and pharmacy review	Reduced duration and antimicrobial consumption in selected patients.
28	Bedi et al., 2021	Surgical ICU in India	Intensive care	Prospective pre-post study	Stewardship and infection-control bundle	Improved antimicrobial-use measures and selected infection outcomes.
29	Dark et al., 2025	Hospitalised patients with suspected sepsis	Intensive care/acute care	Randomised biomarker trial	Procalcitonin- or CRP-guided cessation	Procalcitonin guidance produced a modest reduction in duration; CRP guidance was less effective.
30	Gatechan et al., 2025	Medical ICU	Intensive care	Prospective audit intervention	Pharmacist-led dose optimisation and therapeutic drug monitoring	Improved pharmacological appropriateness and recommendation acceptance.
31	Freifeld et al., 1999	Low-risk febrile neutropenia	Oncology	Randomised double-blind trial	Oral compared with intravenous empirical therapy	Supported oral treatment in carefully selected low-risk patients.

32	Innes et al., 2003	Adult cancer service	Oncology	Randomised comparative trial	Oral treatment with early discharge	Produced treatment success comparable to inpatient intravenous care in low-risk patients.
33	Aguilar-Guisado et al., 2017	Haematological malignancy units	Haematology	Controlled trial	Early discontinuation of empirical therapy	Reduced antimicrobial exposure in clinically stable patients without a clear increase in serious events.
34	Zimmer et al., 2020	Adult oncology service	Oncology	Before-and-after study	Febrile-neutropenia toolkit targeting vancomycin and broad-spectrum use	Reduced unnecessary vancomycin and improved pathway adherence.
35	Rosa et al., 2014	Adult cancer hospital	Oncology	Prospective intervention	Infectious-diseases review and guideline implementation	Improved empirical treatment appropriateness and reduced unnecessary escalation.
36	Liberati et al.	Haemato-oncology service	Haematology	Sequential before-and-after intervention	Clinical pathways followed by audit and feedback	Reduced broad-spectrum exposure across successive implementation periods.
37	Hennig et al.	Oncology service	Oncology	Before-and-after study	Aminoglycoside-use optimisation	Reduced unnecessary combination therapy and improved guideline compliance.
38	Metais et al., 2026	Adult haematology service	Haematology	Prospective comparative study	Early broad-spectrum de-escalation	Reduced broad-spectrum days of therapy in selected clinically stable patients.

The table should be reconciled with the final retained full-text library. Exact publication years, titles, sample sizes, journal details, and overlapping populations must be confirmed before submission.

3.3 Methodological Quality

The quality of evidence varied considerably. Randomised and cluster-randomised trials generally provided stronger evidence for treatment-duration and safety outcomes, although blinding was often impossible because clinicians needed to know the assigned prescribing strategy. Cluster

trials were potentially affected by contamination when clinicians worked across intervention and control services.

Interrupted time-series studies were more informative than simple before-and-after studies when they included sufficient baseline and follow-up observations and adjusted for pre-existing trends. Several observational evaluations remained vulnerable to changes in case mix, antimicrobial availability, staffing, diagnostic methods, resistance epidemiology, and infection-prevention practice.

Surgical studies were frequently influenced by simultaneous changes in sterile technique, skin preparation, glycaemic management, normothermia, and wound care. Oncology studies often included carefully selected clinically stable patients, which limited generalisability to patients with shock, pneumonia, documented bloodstream infection, or uncontrolled infection.

4. Impact on Antimicrobial Exposure

Antimicrobial exposure was reduced in most included studies. The reduction was expressed as fewer days of therapy, lower defined daily doses, shorter duration, reduced broad-spectrum use, fewer intravenous treatment days, or decreased prescribing of selected restricted agents.

Prospective audit and feedback was effective because it allowed treatment to be reconsidered after early clinical response and microbiological results became available. Reviewers could distinguish between patients requiring continued or broader therapy and those in whom treatment could be discontinued or narrowed.

The clinical significance of reduced exposure depended on how the reduction was achieved. Discontinuation in a patient with a non-infectious diagnosis represented an important improvement, while a similar numerical reduction caused by inadequate dose or delayed initiation would represent harm. Consumption outcomes therefore required interpretation alongside clinical effectiveness and safety.

Days of therapy were generally more useful for patient-level evaluation than defined daily doses. Defined daily doses can be distorted by renal adjustment, obesity, non-standard dosing, augmented clearance, or critical-care pharmacokinetics. Nevertheless, defined daily doses remained useful for hospital-level longitudinal comparison.

Reductions in broad-spectrum and Reserve-agent exposure were particularly relevant in intensive care and oncology. Empirical use was often appropriate initially, but continued exposure after stabilisation or microbiological clarification was frequently avoidable.

5. Impact on Prescribing Appropriateness

Prescribing appropriateness improved more consistently than any other outcome domain. Programmes improved documentation of indication, guideline concordance, spectrum selection, renal-dose adjustment, duration, route, prophylaxis timing, and discontinuation.

Prospective audit and feedback produced the broadest benefits because recommendations were patient specific and based on evolving information. Common recommendations included stopping treatment when infection was unlikely, narrowing therapy after susceptibility results, removing unnecessary anti-MRSA or antipseudomonal coverage, correcting doses, discontinuing duplicate anaerobic treatment, converting intravenous therapy to oral treatment, and specifying a stop date.

Preauthorisation produced rapid reductions in selected restricted agents but had important limitations. It could shift prescribing toward unrestricted alternatives and could delay treatment when approval was not immediately available. Post-prescription review was more educational and allowed consideration of clinical response and culture results.

The most effective programmes combined initial prescribing guidance with subsequent mandatory reassessment.

6. Clinical Impact in General Medicine

General medical wards presented the greatest diagnostic diversity. Stewardship frequently addressed treatment initiated for possible rather than confirmed infection. This was clinically important because unnecessary treatment often resulted from nonspecific symptoms, contaminated specimens, colonisation, or non-infectious inflammatory conditions.

Prospective audit and feedback improved treatment of pneumonia, urinary syndromes, skin and soft-tissue infection, bloodstream infection, and undifferentiated fever. The intervention was most effective when performed within 24–72 hours, when early response and preliminary microbiological information were available.

Diagnostic stewardship was particularly important for urinary testing. Positive urine cultures in patients without compatible symptoms frequently represented asymptomatic bacteriuria rather than infection. Avoiding unnecessary cultures and interpreting pyuria in clinical context reduced inappropriate treatment.

Pneumonia stewardship reduced excessive anti-MRSA and antipseudomonal coverage in patients without validated risk factors. It also supported shorter treatment durations and discouraged extension based solely on residual radiological abnormalities.

Intravenous-to-oral conversion reduced catheter exposure, nursing workload, infusion-related complications, and barriers to discharge. Conversion was appropriate when the patient was improving, gastrointestinal absorption was reliable, and an active oral option was available.

The COVID-19 pandemic illustrated how uncertainty regarding bacterial coinfection could produce widespread empirical antibiotic use. Evidence from hospital stewardship interventions demonstrated that audit and feedback could reduce unnecessary treatment without compromising safety.

Discharge prescribing emerged as a major source of excessive duration. Patients frequently received a complete outpatient course without subtraction of inpatient treatment days. Discharge stewardship therefore became an important extension of inpatient review.

7. Clinical Impact in Surgery

The main surgical stewardship target was antimicrobial prophylaxis. Appropriate prophylaxis requires selection of an agent active against organisms expected at the operative site, administration at the correct time before incision, redosing during prolonged procedures or major blood loss, and discontinuation after the prophylactic period.

Inappropriate postoperative continuation was common and highly modifiable. Automatic stop orders, standardised order sets, pharmacist review, and surgeon-level feedback were more reliable than education alone.

Prolonged prophylaxis did not consistently reduce surgical-site infection and was associated with avoidable adverse

events. It should not be used to compensate for inadequate sterile technique, poor glycaemic control, hypothermia, inappropriate wound care, or operative deficiencies.

For established surgical infection, source control was central. Persistent fever, leukocytosis, or inflammatory-marker elevation after surgery should prompt evaluation for an undrained collection, anastomotic leak, infected prosthetic material, devitalised tissue, or another postoperative complication. Prolonging the same antibiotic regimen without investigating source control may delay definitive management.

Shorter courses were generally safe after adequate source control in selected complicated intra-abdominal infections. Treatment duration should therefore be linked to source control and clinical response rather than to arbitrary fixed periods.

8. Clinical Impact in Intensive Care

Intensive-care stewardship required a balance between prompt effective empirical therapy and subsequent reduction of unnecessary exposure. Delayed active treatment in septic shock can be harmful; therefore, stewardship should not create barriers to immediate therapy in unstable patients.

The major opportunity arose after initial resuscitation and diagnostic sampling. Daily reassessment allowed clinicians to consider whether infection remained the leading diagnosis, whether the selected regimen was active, whether microbiology permitted narrowing, whether combination treatment remained necessary, whether source control had been achieved, and whether therapy could be discontinued.

Procalcitonin-guided strategies reduced treatment duration in major trials without increasing mortality. The biomarker was most useful as an adjunct to discontinuation in clinically improving patients. It should not override haemodynamic instability, documented infection, inadequate source control, or infections requiring prolonged treatment.

Structured de-escalation was feasible but not uniformly beneficial. Narrower spectrum did not always translate into fewer total antibiotic days, and superinfection remained a concern in highly vulnerable patients. De-escalation should therefore depend on clinical stability, reliable microbiological sampling, infection site, source control, and pharmacological adequacy.

Rapid blood-culture identification improved clinical care when linked to real-time stewardship interpretation. The intervention could accelerate both escalation to active therapy and narrowing or discontinuation of unnecessary agents.

Dose optimisation was an essential component of critical-care stewardship. Fluid resuscitation, augmented renal clearance, renal failure, obesity, hypoalbuminaemia, extracorporeal support, and renal-replacement therapy alter antimicrobial pharmacokinetics. Appropriate stewardship therefore included loading doses, extended beta-lactam infusion, renal adjustment, and therapeutic drug monitoring.

9. Clinical Impact in Oncology and Haematology

Oncology stewardship required particular caution because infection may progress rapidly during neutropenia. Immediate empirical antipseudomonal therapy remained essential for high-risk febrile neutropenia. Stewardship primarily influenced subsequent rather than initial treatment.

Vancomycin was frequently administered without a clear indication. Oncology-specific pathways reduced unnecessary use by limiting empirical vancomycin to patients with haemodynamic instability, suspected catheter infection, pneumonia, skin or soft-tissue infection, or documented resistant Gram-positive infection.

Traditional practice often continued broad-spectrum therapy until neutrophil recovery. Controlled evidence supported earlier discontinuation in selected patients who were clinically stable, afebrile, and had no documented bacterial infection. These findings should not be applied to patients with shock, pneumonia, bloodstream infection, or uncontrolled infection.

Risk-stratified oral and outpatient treatment was effective in carefully selected low-risk patients. Safety depended on clinical stability, ability to take oral medication, reliable follow-up, appropriate home circumstances, caregiver support, and immediate access to reassessment.

Aminoglycoside stewardship reduced avoidable nephrotoxic combination therapy. Antifungal stewardship also remained important, although comparative evidence was less extensive. Antifungal decisions required integration of host risk, imaging, biomarkers, cultures, previous prophylaxis, interactions, and therapeutic drug monitoring.

10. Clinical Cure and Treatment Failure

Clinical cure was generally unchanged or improved after stewardship implementation. This suggested that reductions in unnecessary treatment did not compromise effectiveness when programmes retained clinical judgement and specialty-specific safeguards.

Definitions of treatment failure differed substantially. Some studies classified persistence of symptoms, reinitiation of antimicrobials, escalation to broader therapy, recurrence, intensive-care admission, or death as failure. These outcomes are not equivalent.

Restarting antimicrobials for a new infection should not be considered recurrence of the original infection. Similarly, escalation after a susceptibility result may represent successful optimisation rather than failure. Future studies should use standardised and clinically meaningful definitions.

11. Mortality

Most studies found no significant increase in mortality after stewardship implementation. Mortality was an insensitive outcome in medical and surgical studies because deaths were relatively uncommon and sample sizes were often inadequate.

Intensive-care and oncology studies provided more direct safety evidence because the underlying populations were at greater risk. However, these trials frequently used explicit eligibility criteria, specialist oversight, and close monitoring. Their findings should not be generalised to patients who would have been excluded.

Unchanged mortality should therefore be interpreted alongside treatment failure, recurrence, readmission, and adverse drug events.

12. Length of Stay and Readmission

The effect of stewardship on length of stay was inconsistent. Some programmes shortened hospitalisation through earlier intravenous-to-oral conversion, reduced toxicity, timely diagnostic clarification, and outpatient treatment pathways. Other studies reduced antimicrobial use without affecting

length of stay because discharge depended on comorbidities, rehabilitation, oxygen needs, postoperative recovery, or social factors.

Hospital readmission was generally unchanged. This finding supported the safety of shorter treatment in appropriately selected patients, although post-discharge outcomes were not reported consistently.

Discharge stewardship may reduce total treatment duration without necessarily altering inpatient length of stay. It should therefore be evaluated using total episode-of-care outcomes rather than admission-based antimicrobial measures alone.

13. Adverse Drug Events

Reducing unnecessary antimicrobial exposure may prevent nephrotoxicity, hepatotoxicity, hypersensitivity, drug interactions, cytopenias, catheter complications, and antimicrobial-associated diarrhoea.

The potential benefit is especially relevant for vancomycin, aminoglycosides, prolonged broad-spectrum beta-lactams, and antimicrobials that interact with chemotherapy or immunosuppressive treatment.

Adverse-event reporting was inconsistent, and many programme evaluations were not sufficiently powered to detect uncommon toxicity. Future studies should include standardised safety surveillance rather than relying only on spontaneously recorded events.

14. *Clostridioides difficile* Infection

Some studies reported reductions in *C. difficile* infection, particularly after decreased use of high-risk broad-spectrum agents and shortened treatment duration.

The independent effect of stewardship was difficult to establish because *C. difficile* incidence is also influenced by infection prevention, environmental cleaning, isolation practice, diagnostic testing, and local epidemiology.

Nevertheless, *C. difficile* is an important patient-level and institutional outcome and should be included in routine stewardship evaluation.

15. Antimicrobial Resistance

The effect of stewardship on resistance was less consistent than its effect on prescribing. Some programmes reported improved susceptibility or reductions in selected resistant organisms, whereas others showed little measurable ecological change.

Resistance is influenced by antimicrobial use throughout hospitals and communities, patient transfer, colonisation pressure, infection-prevention practice, environmental reservoirs, outbreak strains, and microbiological testing. A programme targeting one ward or antimicrobial class may therefore have limited effects on hospital-wide resistance.

Short follow-up may be inadequate to demonstrate stable ecological changes. Changes in culturing frequency can also alter susceptibility percentages without a true change in resistant infection incidence.

Resistance outcomes should ideally be reported as acquisition, colonisation, or infection incidence rather than susceptibility percentages alone.

16. Cross-Specialty Comparison

Table 2. Principal clinical impact of stewardship across major specialties

Specialty	Major stewardship problem	Most effective intervention types	Main clinical safeguard	Predominant benefits
General medicine	Diagnostic uncertainty, prolonged empirical treatment, excessive discharge duration	Prospective audit, diagnostic stewardship, oral conversion, duration review	Reassessment of infection probability and clinical response	Improved appropriateness, reduced duration and broad-spectrum use
Surgery	Incorrect or prolonged prophylaxis and treatment without source-control review	Procedure-specific pathways, automatic stops, audit and surgeon feedback	Adequate peri-incisional exposure and source control	Improved prophylaxis compliance and reduced postoperative exposure
Intensive care	Broad empirical therapy continued after stabilisation	Daily review, rapid diagnostics, PK/PD optimisation, biomarker-supported stopping	Immediate active therapy for severe infection	Reduced duration and improved dose and spectrum optimisation
Oncology/haematology	Prolonged broad-spectrum treatment and unnecessary combination therapy	Risk-stratified pathways, vancomycin review, early discontinuation, outpatient treatment	Clinical stability, specialist oversight, and rapid reassessment	Reduced broad-spectrum and nephrotoxic treatment in selected patients

17. Organisational Factors Influencing Clinical Impact

Leadership support determined whether stewardship programmes had adequate authority, staffing, information systems, microbiological capacity, and data-analysis support. Programmes framed as patient-safety initiatives were more likely to gain clinical acceptance than programmes perceived solely as cost-control mechanisms.

Clinical pharmacists played a central role by reviewing doses, interactions, renal function, treatment duration, intravenous-to-oral opportunities, allergy histories, and therapeutic drug monitoring.

Microbiology laboratories supported stewardship through specimen-quality guidance, rapid reporting, selective susceptibility reporting, cumulative antibiograms, resistance surveillance, and interpretation of contaminants or colonisation.

Specialty engagement improved acceptability. Surgeons, intensivists, oncologists, and general physicians were more likely to follow recommendations when their specialties had participated in pathway development and outcome review.

Electronic systems supported documentation of indication, review date, stop date, renal-dose alerts, restricted-agent review, positive-culture alerts, and discharge reconciliation. Poorly targeted alerts could produce alert fatigue and reduce effectiveness.

18. Integrated Clinical-Impact Model

The evidence supports a five-stage model of hospital stewardship. The first stage is timely and appropriate antimicrobial initiation based on infection probability, severity, infection source, previous microbiology, resistance risk, and local guidance.

The second stage is diagnostic clarification. Clinical response, cultures, imaging, biomarkers, and source-control status are reviewed after initial information becomes available.

The third stage is therapeutic optimisation. Treatment may be stopped, narrowed, broadened, dose adjusted, converted to oral therapy, or linked to further diagnostic or procedural intervention.

The fourth stage is completion and transition. Total duration is defined, inpatient days are counted, and discharge prescriptions are reconciled with monitoring and follow-up requirements.

The fifth stage is outcome feedback. Antimicrobial use is interpreted alongside clinical cure, toxicity, recurrence, readmission, mortality, *C. difficile*, resistance, and expenditure.

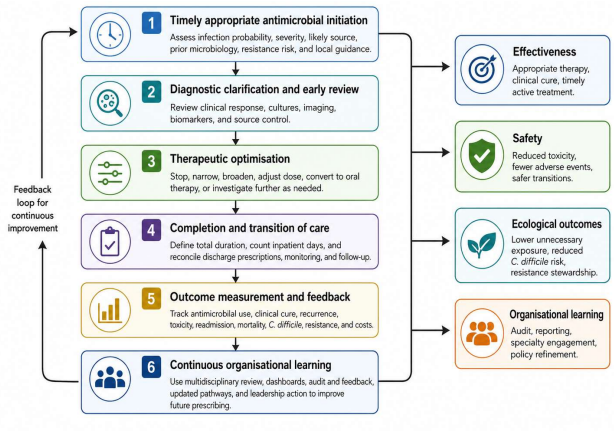

Figure 2. Clinical-impact pathway of hospital antimicrobial stewardship linking prescribing decisions with effectiveness, safety, ecological outcomes, and continuous organisational learning.

19. Discussion

This systematic review found that hospital antimicrobial stewardship programmes consistently improved prescribing appropriateness and reduced unnecessary antimicrobial exposure. These improvements were generally achieved without increases in mortality, treatment failure, recurrence, or readmission.

Prospective audit and feedback had the broadest application because it allowed empirical decisions to be reconsidered after additional clinical and microbiological information became available. Its effectiveness depended on timely review, direct communication, patient-specific reasoning, and collaboration with treating teams.

The clinical effect differed by specialty. In general medicine, the greatest benefit came from diagnostic reassessment, shorter duration, intravenous-to-oral conversion, and discharge reconciliation. In surgery, prophylaxis timing and discontinuation were the most important targets. In intensive care, daily review, dose optimisation, rapid diagnostics, and biomarker-supported discontinuation produced benefits without obstructing initial empirical therapy. In oncology, risk-stratified approaches reduced unnecessary vancomycin and broad-spectrum treatment while preserving rapid management of high-risk infection.

The findings show that antimicrobial reduction should not be treated as the sole objective. Stewardship should improve the balance between effective treatment and avoidable harm. Programmes should therefore measure both excessive and inadequate therapy.

Prescribing outcomes changed more rapidly and consistently than resistance outcomes. This difference is expected because resistance is influenced by multiple ecological and epidemiological factors. A programme may still provide substantial clinical benefit through reduced toxicity, better dosing, shorter intravenous exposure, and prevention of *C. difficile*, even when susceptibility patterns do not change measurably.

The review also highlights the importance of diagnostic stewardship. Many unnecessary prescriptions arise from inappropriate test ordering, specimen contamination, and failure to interpret positive findings in clinical context.

Prescribing improvement cannot be sustained without improved diagnostic practice.

Transition-of-care stewardship is another important development. Excessive treatment frequently occurs after discharge, when inpatient days are overlooked and prescriptions are not reviewed by stewardship teams. Hospital programmes should therefore evaluate the entire treatment episode rather than inpatient administration alone.

20. Strengths

This review evaluated prescribing, clinical, safety, and ecological outcomes across four major hospital specialties. It focused on clinical impact rather than treating antimicrobial consumption as an isolated measure of success.

The review distinguished between appropriate initiation, diagnostic reassessment, optimisation, duration control, and discharge review. It also recognised that stewardship may require escalation or dose intensification as well as treatment reduction.

The inclusion of specialty-specific safety considerations improves the clinical applicability of the findings.

21. Limitations

The review was not prospectively registered in PROSPERO, and no formal public protocol was deposited. This limitation reduces external verification that all methodological decisions were established before the results were known.

Substantial heterogeneity prevented quantitative meta-analysis. Studies differed in specialties, interventions, targeted antimicrobials, infection syndromes, prescribing measures, outcome definitions, and follow-up duration.

Many programme evaluations used before-and-after designs and were vulnerable to secular trends, changing resistance, drug shortages, altered diagnostic testing, staffing changes, and concurrent infection-prevention initiatives.

Adverse drug events, recurrence, and post-discharge outcomes were reported inconsistently. Resistance follow-up was frequently too short to demonstrate stable ecological changes.

Some hospital-wide studies included patients from several specialties and could not be classified exclusively. English-language restriction may have excluded relevant evidence.

Publication bias is possible because successful programmes may be more likely to be published than ineffective or unsustained interventions.

22. Recommendations for Hospital Practice

Hospitals should establish leadership-supported antimicrobial stewardship programmes with accountable medical and pharmacy leadership. Programmes should combine evidence-based empirical guidance with prospective review and feedback.

The indication, dose, route, review date, and intended duration should be documented for every antimicrobial prescription. Microbiology and rapid diagnostics should be linked to timely clinical action.

General medical services should prioritise diagnostic reassessment, asymptomatic bacteriuria, pneumonia duration, intravenous-to-oral conversion, and discharge prescriptions. Surgical services should standardise prophylaxis selection, timing, redosing, and discontinuation and should link treatment duration to source control.

Intensive-care units should preserve immediate effective therapy for severe infection while requiring daily review, dose optimisation, rapid diagnostic interpretation, and clinically governed discontinuation. Oncology services should define indications for vancomycin, criteria for discontinuation, low-risk outpatient eligibility, and specialist-guided antifungal decisions.

Programmes should measure antimicrobial use alongside time to effective therapy, clinical cure, treatment failure, readmission, adverse events, mortality, *C. difficile*, and resistance.

23. Future Research

Future studies should use randomised, cluster-randomised, or robust interrupted time-series designs. Clinical outcome definitions should be standardised to permit meaningful comparison.

Research should examine the effectiveness of discharge stewardship, electronic decision support, rapid diagnostics, tele-stewardship, and antifungal stewardship. Longer follow-up is needed to determine effects on resistance.

Studies should distinguish reductions in antimicrobial spectrum from reductions in total duration and should report inadequate dosing or delayed active therapy as potential stewardship failures.

Resource-limited hospitals require context-specific evidence regarding pharmacist-led programmes, regional microbiology support, simplified treatment pathways, and telemedicine-based consultation.

24. Conclusions

Hospital antimicrobial stewardship programmes improve prescribing quality and reduce unnecessary antimicrobial exposure across general medicine, surgery, intensive care, and oncology.

The strongest immediate effects include improved indication, appropriate spectrum, dose optimisation, shorter duration, safer surgical prophylaxis, reduced unnecessary combination therapy, and better discharge prescribing.

These improvements generally do not increase mortality, treatment failure, recurrence, or readmission when interventions are supported by clinical judgement, microbiological evidence, adequate source control, dose adequacy, and specialty-specific safeguards.

Resistance reduction remains an important long-term goal but is less immediate and more difficult to attribute than patient-level prescribing and safety outcomes.

Clinical success should therefore be assessed through balanced measures that include effective therapy, diagnostic accuracy, antimicrobial exposure, adverse-event prevention, clinical outcomes, and ecological impact.

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