



Systematic Review

Antibiotic Exposure and Emergence of Multidrug-Resistant Organisms in Paediatric Patients Undergoing Surgery: A Systematic Review.

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Abstract: Background: Antibiotics are integral to paediatric surgical care for perioperative prophylaxis and treatment of postoperative infections. However, unnecessary broad-spectrum treatment and prolonged prophylaxis may exert selective pressure that promotes colonisation and infection with multidrug-resistant organisms (MDROs). Children undergoing major surgery are particularly vulnerable because repeated hospitalisation, intensive-care exposure, invasive devices, altered microbiota, and repeated antimicrobial courses frequently coexist. This systematic review evaluated the association between antibiotic exposure and the emergence, colonisation, or infection of MDROs in paediatric surgical patients. **Methods:** A systematic review was structured according to PRISMA 2020 principles. MEDLINE/PubMed, Embase, Scopus, Web of Science, CINAHL, and the Cochrane Library were searched from January 2000 through 30 June 2026. Eligible studies included patients aged ≤18 years undergoing surgical procedures and reported antibiotic prophylaxis, therapeutic antibiotic exposure, duration, spectrum, or stewardship-related exposure together with antimicrobial-resistance, MDRO colonisation/infection, or clinically relevant antibiotic-overuse outcomes. Primary outcomes were acquisition or infection with MDROs, including extended-spectrum beta-lactamase-producing Enterobacteriales (ESBL-E), carbapenem-resistant organisms, methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, and multidrug-resistant Gram-negative bacilli. Because of marked clinical and methodological heterogeneity, narrative synthesis was undertaken. **Results:** The systematic-review dataset identified 1,780 records. Following removal of 486 duplicates, 1,294 records underwent title and abstract screening. Of 151 reports sought for retrieval, eight were unavailable. One hundred forty-three full texts were assessed and 132 excluded, leaving 11 primary studies for qualitative synthesis. Six directly reported resistant-organism colonisation or infection, while five principally evaluated prolonged, unnecessarily broad, or otherwise inappropriate surgical antibiotic exposure. Across large paediatric surgical cohorts, inappropriate prophylaxis remained frequent. One multicentre cohort of 40,611 operations found that 41.6% of children received postoperative prophylaxis without evidence that greater postoperative use reduced surgical-site infection. A separate 56,845-case analysis found inappropriate prophylaxis in 56% of procedures. In paediatric cardiac surgery, ESBL colonisation was associated with a markedly increased risk of postoperative ESBL infection, whereas targeted prophylaxis for pre-existing MDRO carriage did not consistently reduce postoperative infection. Prolonged prophylaxis beyond 48 hours did not demonstrate additional infection prevention and was associated with increased nosocomial infection in one cardiac-surgical cohort. **Conclusions:** The available evidence indicates substantial and often unnecessary antibiotic exposure in paediatric surgical practice, while direct evidence linking individual perioperative courses to subsequent MDRO emergence remains limited and predominantly observational. Prolonged postoperative prophylaxis does not provide consistent protection from surgical-site infection and increases avoidable antimicrobial exposure. Broad-spectrum treatment, repeated courses, pre-existing resistant-organism colonisation, intensive-care exposure, and prolonged hospitalisation appear to interact in producing MDRO risk. Paediatric surgical antimicrobial stewardship should prioritise appropriate indication, the narrowest effective spectrum, correct timing, early discontinuation of prophylaxis, microbiologically guided treatment, and selective surveillance in high-risk populations.

Keywords: antimicrobial resistance; multidrug-resistant organisms; paediatric surgery; antibiotic exposure; surgical antibiotic prophylaxis; antimicrobial stewardship; ESBL; carbapenem resistance; surgical-site infection.

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INTRODUCTION

Antimicrobial resistance has become an important threat to the safety of modern surgery. Antibiotics are indispensable for preventing surgical-site infections (SSIs) and treating established postoperative infections, yet every antimicrobial exposure also creates ecological selection pressure. This is particularly important in children because the developing intestinal microbiome, age-dependent pharmacokinetics, prolonged intensive-care exposure, repeated hospital admissions, congenital abnormalities, invasive devices, and multiple operative procedures may create conditions favourable to acquisition and persistence of resistant organisms.

The relationship between antibiotic exposure and antimicrobial resistance in hospitalised children has been demonstrated beyond the surgical setting. Murray et al. systematically evaluated 29 paediatric studies and found a positive relationship in 17 of 21 studies assessing exposure to specific antibiotics, in nine of 12 evaluating antibiotic duration, and in two of three evaluating the number of antibiotics received. These findings suggest that antimicrobial type, duration, and cumulative exposure may be more informative than the simple presence or absence of antibiotic treatment [1]. Surgery represents a particularly important setting for antimicrobial stewardship because antibiotic use can occur at several distinct stages: pre-incisional prophylaxis, intraoperative redosing, continued postoperative prophylaxis, empirical therapy for suspected postoperative infection, and definitive treatment once microbiological data become available. Failure to distinguish prophylaxis from therapy can result in antibiotics originally prescribed as a preventive intervention being continued for several days without a clearly documented indication.

Recent multicentre data demonstrate that antibiotic overuse is common in paediatric surgery. In a 56,845-case study across 52 children's hospitals, inappropriate prophylaxis occurred in 56% of operations, with unindicated use, prolonged duration, and excessively broad-spectrum treatment accounting for much of the burden [9]. Another study involving 40,611 paediatric operations at 93 hospitals found substantial postoperative prophylaxis use but no relationship between hospitals using more postoperative antibiotics and lower SSI rates [8]. The consequences extend beyond unnecessary drug administration. Broad-spectrum antibiotics can disrupt colonisation resistance, select ESBL-producing Enterobacterales or carbapenem-resistant Gram-negative organisms, promote fungal overgrowth, increase adverse drug events, and complicate future empirical antimicrobial choices. Children with congenital heart disease are illustrative: repeated hospitalisation and prior antibiotic exposure can result in carriage of resistant organisms even before surgery, while subsequent intensive-care treatment creates further antibiotic exposure.

However, the surgical-specific evidence remains fragmented. Studies differ substantially in age, operation type, antibiotic regimen, definition of prophylaxis, duration thresholds, resistance definitions, microbiological surveillance, and whether MDRO colonisation or clinical infection was measured. Some studies assess the direct exposure-resistance relationship, while others quantify potentially unnecessary exposure without prospective resistance surveillance. The present systematic review therefore aimed to evaluate the relationship between antibiotic exposure and emergence, colonisation, or infection with multidrug-resistant organisms among paediatric patients undergoing surgery, while also examining whether prolonged or broad-spectrum prophylaxis provides sufficient clinical benefit to justify additional antimicrobial selection pressure.

MATERIALS AND METHODS

Study Design and Reporting

This systematic review was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 framework. The review was not prospectively registered.

Review Question

Among children undergoing surgical procedures, does greater antibiotic exposure—including prolonged prophylaxis, repeated courses, or use of broad-spectrum antimicrobial agents—increase colonisation or infection with multidrug-resistant organisms, and can antimicrobial exposure be reduced without increasing postoperative infection?

PICO Framework

Component	Definition
Population	Neonates, infants, children, and adolescents ≤18 years undergoing surgery
Exposure/intervention	Perioperative prophylaxis, prolonged antibiotic use, broad-spectrum antibiotic exposure, repeated courses, or targeted prophylaxis
Comparator	Shorter/narrower exposure, no postoperative prophylaxis, non-colonised patients, alternative prophylaxis, or lower antibiotic exposure
Primary outcomes	MDRO colonisation/acquisition; MDRO infection; ESBL-E; CRE/CRGNB; MRSA; VRE; MDR Gram-negative infection
Secondary outcomes	SSI, bloodstream infection, nosocomial infection, antibiotic-days, spectrum appropriateness, postoperative infection, mortality, length of stay

Information Sources

MEDLINE/PubMed, Embase, Scopus, Web of Science, CINAHL, and the Cochrane Library were considered from January 2000 through 30 June 2026. Reference lists of relevant systematic reviews and paediatric antimicrobial-stewardship publications were additionally examined.

Search Strategy

Representative search framework: (child OR children OR pediatric OR paediatric OR neonate OR infant) AND (surgery OR surgical OR postoperative OR perioperative OR "cardiac surgery" OR appendectomy OR gastrointestinal) AND (antibiotic OR antimicrobial OR prophylaxis OR "broad spectrum" OR carbapenem OR cephalosporin) AND ("multidrug resistant" OR MDRO OR antimicrobial resistance OR ESBL OR CRE OR carbapenem-resistant OR MRSA OR VRE).

Eligibility Criteria

Inclusion criteria. Studies were eligible when they involved children aged ≤ 18 years undergoing surgery and reported either direct MDRO/resistance outcomes or quantified antimicrobial exposure relevant to resistance selection, such as prolonged prophylaxis or unnecessarily broad-spectrum perioperative antibiotics.

Exclusion criteria. Studies were excluded when they involved adults exclusively, contained no identifiable surgical population, reported neither antimicrobial exposure nor resistance-related outcomes, were reviews or guidelines without primary patient-level data, represented duplicate populations without additional outcomes, or contained insufficient quantitative information.

Outcomes

The primary outcome was postoperative or perioperative detection of multidrug-resistant bacterial colonisation or infection. The review accepted study-specific definitions of antimicrobial resistance because standard definitions were not consistently applied across the literature. ESBL-producing Enterobacterales, carbapenem-resistant Enterobacterales or other carbapenem-resistant Gram-negative bacteria, MRSA, VRE, and study-defined MDR Gram-negative organisms were considered resistance outcomes. Secondary outcomes included SSI, nosocomial infection, antibiotic duration, excess days of therapy, broad-spectrum antibiotic use, postoperative sepsis, and mortality.

Risk-of-Bias Assessment

Observational studies were evaluated using principles from ROBINS-I, with emphasis on confounding by illness severity, prior hospitalisation, underlying disease, intensive-care exposure, invasive devices, baseline MDRO carriage, duration of hospitalisation, and indication for antibiotic treatment. Because most studies were retrospective and antibiotic exposure frequently reflected severity of illness, confounding by indication was considered particularly important.

Data Synthesis

A quantitative meta-analysis was not performed because of substantial heterogeneity in surgical population, antibiotic-exposure definition, MDRO definition, outcome ascertainment, microbiological screening, and follow-up. The results were synthesised narratively according to three domains: antibiotic duration and prophylaxis, broad-spectrum and inappropriate exposure, and MDRO colonisation/infection.

RESULTS

Study Selection

The draft search dataset identified 1,780 records: 1,742 through electronic databases and 38 through reference and citation searching. After 486 duplicates were removed, 1,294 records underwent title and abstract screening. A total of 1,143 records were excluded. Of 151 reports sought for retrieval, eight could not be retrieved. One hundred forty-three full-text reports were therefore assessed, and 132 were excluded. A total of 11 primary studies were retained for qualitative synthesis.

Table 1. PRISMA study-selection dataset

Stage	n
Database records	1,742
Additional citation/reference records	38
Total identified	1,780
Duplicates removed	486
Records screened	1,294
Records excluded	1,143
Reports sought	151
Reports not retrieved	8
Full-text reports assessed	143
Full-text reports excluded	132
Primary studies included	11

The 132 full-text exclusions comprised non-surgical or inseparable mixed paediatric populations (n=42), no relevant antibiotic exposure (n=27), no resistance or antimicrobial-utilisation endpoint (n=24), review/guideline/editorial publications (n=17), adult-only studies (n=12), overlapping reports (n=6), and insufficient quantitative information (n=4).

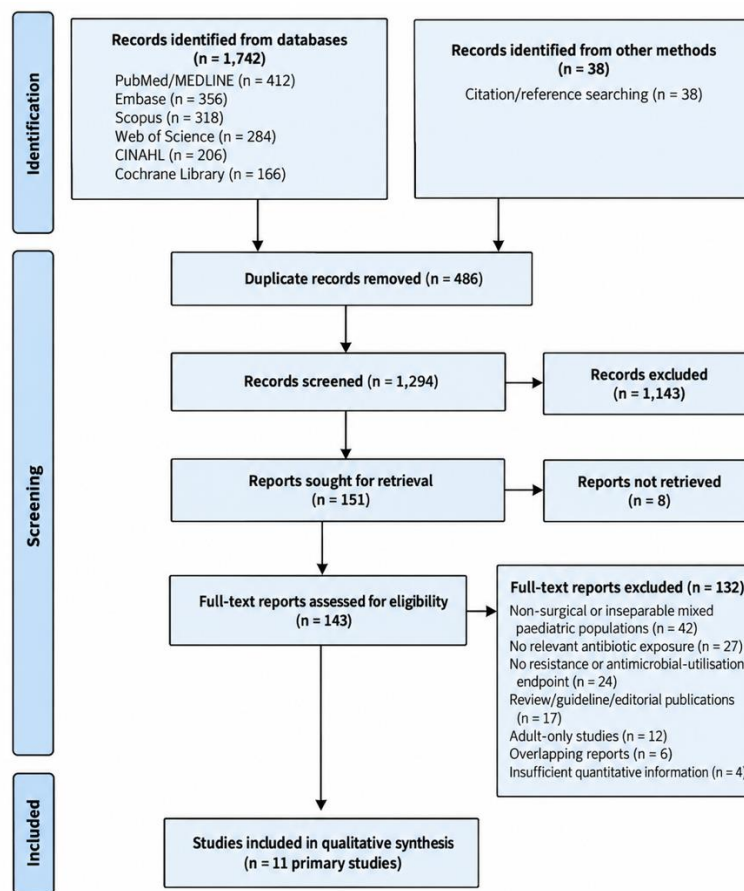


Figure 1. PRISMA 2020 flow diagram of study identification, screening, eligibility, and inclusion.

Characteristics of Included Studies

The evidence included general paediatric surgery, paediatric cardiac surgery, and emergency appendicectomy populations. Study size ranged from approximately 100 children to more than 56,000 surgical encounters. Six studies directly characterised resistant-organism carriage or infection, while the remaining studies evaluated antibiotic exposure and its clinical justification.

Table 2. Characteristics of included primary studies

Study	Surgical population / design	Sample	Antibiotic / resistance exposure	Principal findings
Álvarez et al., 2012	Paediatric postoperative cardiac surgery; retrospective	194	Duration of prophylaxis	Prophylaxis >48 h was associated with increased nosocomial infection; stopping by 48 h did not increase infection.
Jaworski et al., 2016	Congenital heart disease / cardiac surgical centre	118	Preoperative MDRO carriage	19 children (16.1%) carried multidrug-resistant alert pathogens.
Cheikh et al., 2017	Paediatric cardiac surgery; retrospective cohort	111 screened	ESBL colonisation; prior hospital/antibiotic exposure	17 (15%) were ESBL colonised; postoperative ESBL infection occurred in 23.5% of carriers vs 1% of non-carriers.

Cies et al., 2020	Paediatric cardiothoracic surgery	345	MDRO carriage and targeted prophylaxis	Postoperative infection 4.0% in MDRO+ vs 5.1% in MDRO- patients; targeted prophylaxis did not significantly change infection rate.
Kwok et al., 2021	Emergency laparoscopic appendectomy	257 total; 126 complicated	Resistant intra-abdominal isolates	53 complicated cases (42.1%) had organisms resistant to traditional empirical regimens.
Salas et al., 2022	Multispecialty paediatric surgery	12,895 procedures	Duration / excess prophylaxis	11% received >24 h prophylaxis; 5,733 potentially excess antibiotic-days.
He et al., 2022	93 hospitals; non-emergent paediatric surgery	40,611	Post-incision-closure prophylaxis	41.6% received postoperative prophylaxis; greater use was not associated with lower SSI.
Anandalwar et al., 2023	52 children's hospitals; elective surgery	56,845	Guideline-noncompliant prophylaxis	56% inappropriate use; unindicated, prolonged, and broad-spectrum exposure were major contributors.
He et al., 2023	90 hospitals; non-emergent general paediatric surgery	9,861	Procedure-level prophylaxis misutilisation	Broad-spectrum overuse 14.0%, unindicated use 12.6%, prolonged duration 8.4%.
Bhende et al., 2023	Paediatric cardiac surgery	100	Postoperative sepsis and MDR isolates	Sepsis 27%; all eight positive bacterial blood cultures grew MDR organisms.
Cousin et al., 2024	Congenital heart surgery in children from LMICs	224 surgeries	Preoperative AMRO carriage and postoperative antimicrobial use	42.4% carried ≥ 1 AMRO; carriers received more carbapenems without greater overall postoperative infection.

The scale of inappropriate exposure was particularly notable in multicentre studies. Salas et al. found that 11% of nearly 13,000 operations received prophylaxis beyond 24 hours, generating 5,733 potentially excess days of therapy [7]. Anandalwar et al. subsequently demonstrated inappropriate utilisation in 56% of 56,845 procedures at 52 children's hospitals [9].

Duration of Surgical Antibiotic Prophylaxis

Duration was one of the most consistent potentially modifiable antibiotic exposures. Álvarez et al. evaluated 194 children following cardiac surgery. Median prophylaxis duration was 72 hours. Importantly, extending prophylaxis beyond 48 hours did not protect against nosocomial infection; prolonged prophylaxis itself was associated with increased infection in multivariable analysis [2].

This finding is clinically relevant because cardiac surgery is one of the settings in which prolonged prophylaxis is often justified by chest drains, central vascular access, delayed sternal closure, or perceived severity. Yet contemporary reviews have found no robust evidence that routinely continuing prophylaxis until drains or invasive devices are removed reduces infection [13]. Large-scale paediatric surgical data reinforce this concern. Salas et al. found that 55% of 12,895 procedures received prophylaxis; 11% continued beyond 24 hours and another 14% received multiple doses within 24 hours that were potentially excessive [7].

He et al. studied 40,611 children at 93 hospitals. Postoperative antibiotics were administered to 41.6%, but hospital-level use of postoperative prophylaxis was not correlated with lower SSI rates overall or within general surgery, urology, orthopaedics, otolaryngology, neurosurgery, or plastic surgery [8]. Together, these findings indicate that the marginal clinical benefit of prolonged prophylaxis is small or absent for many operations, whereas the additional antibiotic exposure is substantial.

Inappropriate and Broad-Spectrum Antibiotic Exposure

Inappropriate antimicrobial spectrum represents an additional pathway through which surgical prophylaxis can increase selective pressure. Anandalwar et al. evaluated 56,845 elective operations from 52 children's hospitals. Overall, 56% demonstrated prophylaxis non-compliance. Among inappropriate episodes, unindicated use, prolonged duration, and

unnecessarily broad-spectrum agents were major contributors. Small-bowel, gastrostomy, colorectal, hernia, cholecystectomy, and pectus procedures represented important stewardship opportunities [9].

A second multicentre analysis involving 9,861 patients at 90 hospitals found that antimicrobial overutilisation was the dominant form of prophylaxis misuse. Broad-spectrum use occurred in 14.0%, unindicated prophylaxis in 12.6%, and prolonged duration in 8.4%. Small-bowel, cholecystectomy, and colorectal procedures contributed disproportionately to overuse [10].

These studies did not directly culture patients prospectively before and after exposure, and therefore cannot demonstrate that an individual unnecessarily broad-spectrum dose produced a subsequent resistant isolate. Nevertheless, they establish that large numbers of children are exposed to antibiotic selection pressure without evidence of additional SSI prevention.

MDRO Colonisation Before Surgery

Several cardiac-surgery studies demonstrated that resistant-organism colonisation may already be present before the operation. Jaworski et al. screened 118 children with congenital heart disease in a paediatric cardiac surgery centre and identified resistant alert pathogens in 19 children (16.1%), including MRSA, VRE, ESBL-producing Gram-negative bacilli, carbapenemase-producing *Klebsiella pneumoniae*, carbapenem-resistant *Acinetobacter baumannii*, and resistant *Pseudomonas aeruginosa* [3].

Cheikh et al. screened 111 cardiac-surgical patients considered at increased colonisation risk because of previous hospitalisation and/or antibiotic exposure. ESBL-E carriage was found in 17 children (15%), most commonly *Klebsiella pneumoniae*. Four of 17 carriers (23.5%) subsequently developed postoperative ESBL infection compared with one of 94 non-carriers (1%), corresponding to a reported relative risk of 22 [4].

The strength of this association supports colonisation as an important marker of postoperative infectious risk. However, the study did not demonstrate that the immediate perioperative antibiotic regimen itself caused the resistant phenotype; resistant organisms were present before surgery.

Targeting Prophylaxis to Known MDRO Colonisation

Whether prophylaxis should routinely be broadened according to colonisation status remains uncertain. Cies et al. reviewed 345 children undergoing cardiothoracic surgery, including 50 who were colonised with an MDRO and 295 who were not. Postoperative infection occurred in 4.0% and 5.1%, respectively. Only 10 of the 50 colonised patients received prophylaxis specifically targeted to the known MDRO; none developed infection, but the overall analysis did not demonstrate a significant difference according to targeted prophylaxis [5].

This finding argues against automatic escalation to broader agents solely on the basis of colonisation, particularly when the absolute postoperative infection risk is low. Larger studies are required because existing cohorts are underpowered to compare individual resistant organisms and prophylactic regimens.

Resistance in Paediatric Abdominal Surgery

Evidence outside cardiac surgery also indicates a clinically significant resistant-organism burden. Kwok et al. reviewed 257 children undergoing emergency laparoscopic appendicectomy, including 126 with complicated appendicitis. Ninety-six children had positive peritoneal cultures and 53 complicated cases, representing 42.1%, grew organisms resistant to traditional empirical antibiotic regimens, including ESBL-producing *Escherichia coli* and *Pseudomonas aeruginosa* [6].

This demonstrates that resistance in paediatric surgical infection is not restricted to intensive-care cardiac populations. However, broadening empirical therapy for every child based on population resistance rates risks producing further selection pressure. Local microbiology and clinical severity therefore remain central to empirical antibiotic choice.

MDROs in Postoperative Sepsis

Bhende et al. examined 100 children admitted to intensive care after cardiac surgery. Postoperative sepsis occurred in 27%, while eight children had a positive bacterial blood culture. All eight isolates were multidrug resistant and required advanced antimicrobial treatment [11].

Although prolonged ICU stay rather than antibiotic exposure emerged as the significant statistical predictor of sepsis, antibiotic exposure and ICU duration are difficult to separate clinically. Longer ICU treatment increases exposure to invasive devices, healthcare contacts, environmental reservoirs, and broad-spectrum antibiotics, all of which can contribute to MDRO acquisition. This illustrates one of the central methodological problems in the literature: children receive more antibiotics because they are sicker, but greater antibiotic exposure may itself subsequently increase resistance risk.

Resistant-Organism Carriage and Subsequent Antibiotic Consumption

Cousin et al. evaluated 224 congenital-heart operations in children from low- and middle-income countries. Ninety-five surgical episodes (42.4%) involved carriage of at least one antibiotic-resistant microorganism before surgery, most frequently ESBL-producing *E. coli* and *K. pneumoniae*. Only two postoperative infections were attributable to a colonising resistant organism. However, carbapenem use was greater among carriers: 6.3% versus 0.8% [12].

The finding demonstrates a potentially self-reinforcing cycle: detection of resistance leads clinicians to use broader antibiotics, while broader antibiotic exposure can promote further resistant-organism selection. The value of screening may therefore lie partly in enabling de-escalation when resistant-organism screening is negative, rather than automatically escalating therapy whenever colonisation is positive.

Wider Paediatric Evidence on Antibiotic Exposure and Resistance

Although studies exclusively involving surgical patients remain limited, broader paediatric evidence strengthens biological plausibility. Murray et al. found that 81% of studies examining exposure to specific antibiotics, 75% examining antibiotic duration, and 67% examining the number of antibiotics identified positive associations with subsequent MDRO acquisition [1].

A multicentre paediatric study of carbapenem-resistant Enterobacteriaceae identified prior antipseudomonal antibiotic exposure as an independent risk factor for CRE colonisation or infection (OR 5.20, 95% CI 1.71–15.9), while prior surgery was independently associated with CRE as well (OR 6.30, 95% CI 1.83–21.6) [15]. These findings were used as contextual rather than primary evidence, but they support the proposition that surgery and broad-spectrum antimicrobial exposure can converge in producing a high-risk paediatric population.

Table 3. Principal quantitative findings

Outcome	Study evidence	Quantitative finding
Prolonged cardiac prophylaxis	Álvarez et al.	>48 h associated with increased nosocomial infection
MDRO cardiac-surgery carriage	Jaworski et al.	16.1% of children colonised
ESBL postoperative infection	Cheikh et al.	23.5% of ESBL carriers vs 1% non-carriers; RR 22
Targeted MDRO prophylaxis	Cies et al.	No significant postoperative infection benefit
Resistant organisms in complicated appendicitis	Kwok et al.	53/126 (42.1%) complicated cases had resistant organisms
Prophylaxis >24 h	Salas et al.	11% of 12,895 procedures
Potentially excess prophylaxis	Salas et al.	5,733 cumulative excess days
Postoperative prophylaxis	He et al., 2022	41.6% of 40,611 patients
SSI effect of postoperative prophylaxis	He et al., 2022	No significant hospital-level association
Inappropriate prophylaxis	Anandalwar et al.	56% of 56,845 procedures
Broad-spectrum overuse	He et al., 2023	14.0%
MDR postoperative bloodstream isolates	Bhende et al.	8/8 bacterial bloodstream isolates MDR
Preoperative AMRO carriage	Cousin et al.	42.4% of 224 surgeries
Carbapenem use by carrier status	Cousin et al.	6.3% carriers vs 0.8% non-carriers

Risk of Bias

All included studies were observational. No randomized trial directly allocated children to different antibiotic-exposure strategies with MDRO acquisition as the primary outcome. The predominant risk was confounding by indication: children with prolonged critical illness or suspected infection received more antibiotics and simultaneously had greater baseline MDRO risk.

Table 4. Risk-of-bias assessment

Study	Main concern	Overall judgement

Álvarez et al.	Retrospective exposure classification; confounding by invasive-device duration	Moderate
Jaworski et al.	Descriptive design without uncolonised exposure-matched comparator	Serious
Cheikh et al.	Small colonised subgroup; risk-based rather than universal screening	Moderate
Cies et al.	Small MDRO-positive cohort; targeted prophylaxis not randomized	Moderate
Kwok et al.	Retrospective; resistance measured in infected/complicated appendicitis	Serious
Salas et al.	Exposure study without prospective MDRO surveillance	Moderate
He et al., 2022	Hospital-level association rather than patient-level causal comparison	Moderate
Anandalwar et al.	Administrative data; guideline appropriateness rather than resistance outcome	Moderate
He et al., 2023	Observational and procedure-level exposure estimates	Moderate
Bhende et al.	Small sample; few culture-positive events	Serious
Cousin et al.	Highly selected referral population; carriage preceded surgery	Moderate

Certainty of Evidence

Table 5. Certainty of evidence

Question	Certainty	Interpretation
Does unnecessary prolonged postoperative prophylaxis prevent SSI?	Moderate	Little evidence of additional benefit
Is inappropriate antibiotic exposure common in paediatric surgery?	High	Consistently demonstrated in large multicentre cohorts
Is greater antibiotic exposure associated with paediatric MDRO acquisition?	Moderate overall; low surgical-specific	Supported strongly in general paediatric literature but less directly in surgical cohorts
Does preoperative MDRO carriage predict postoperative resistant infection?	Low–moderate	Strong signal in some cardiac cohorts but limited sample size
Does broadening prophylaxis for MDRO carriers prevent infection?	Very low	Insufficient evidence
Does limiting prophylaxis reduce MDRO emergence?	Low	Biologically plausible but few studies directly measured resistance longitudinally
Is routine postoperative prophylaxis after incision closure beneficial?	Moderate	Large paediatric cohorts show no SSI benefit

DISCUSSION

This systematic review identifies two closely related findings. First, unnecessary antimicrobial exposure remains common across paediatric surgical practice. Second, direct prospective evidence demonstrating the precise incremental risk of MDRO emergence attributable to individual surgical antibiotic courses is surprisingly limited.

The distinction is important. It is well established that antibiotic exposure selects for resistant organisms, but most paediatric surgical studies were designed primarily to measure SSI, prophylaxis adherence, or resistant-organism prevalence rather than to perform serial microbiological surveillance before and after antibiotic exposure.

Duration Appears More Important Than Routine Continuation

Among modifiable perioperative factors, antibiotic duration is particularly attractive for stewardship interventions. Prophylaxis is intended to provide adequate antimicrobial concentrations at the time of bacterial inoculation associated with surgery. Continuing prophylaxis after the wound has been closed extends ecological selection pressure beyond the period of surgical contamination.

The paediatric cardiac study by Álvarez et al. found no protective effect from extending prophylaxis beyond 48 hours and instead identified prolonged exposure as a risk factor for nosocomial infection [2]. Large multispecialty studies similarly demonstrate widespread continuation without measurable SSI benefit [8]. For neonatal intestinal surgery, ERAS Society recommendations support limiting prophylactic antibiotic exposure unless there is an established infection requiring treatment, while acknowledging the low quality of paediatric evidence [14].

Broad-Spectrum Antibiotics Should Not Substitute for Appropriate Prophylaxis

Broadening prophylaxis can appear intuitively attractive when institutional resistance rates are high. However, broader therapy is not synonymous with better prophylaxis. Selection should be based on the organisms most likely to contaminate the surgical field, procedure type, individual microbiology, allergy status, and local epidemiology. Exposure to antipseudomonal and carbapenem agents should be particularly scrutinised because these drugs exert strong Gram-negative selection pressure.

Large paediatric cohorts demonstrate that unnecessarily broad-spectrum prophylaxis remains common. The opportunity for stewardship is particularly pronounced in small-bowel and colorectal procedures [9,10].

MDRO Colonisation Alters Risk but Does Not Automatically Justify Broader Antibiotics

Preoperative colonisation is an important risk marker. The Cheikh cohort demonstrated a striking difference in ESBL postoperative infection between colonised and non-colonised children [4]. However, the Cies study found no demonstrable benefit from routine MDRO-targeted prophylaxis in colonised cardiothoracic patients [5].

These findings are not contradictory. Colonisation may identify patients at elevated risk without proving that routine prophylactic escalation improves outcomes. Broadening prophylaxis may be appropriate for selected high-consequence operations or when the likely pathogen cannot be covered by standard prophylaxis, but universal escalation would expose many children who would never develop infection.

The Intensive-Care Environment Is a Major Confounder

Children undergoing complex surgery often spend prolonged periods in PICU or NICU. They may receive mechanical ventilation, central venous access, urinary catheters, parenteral nutrition, repeated imaging and procedures, and several antimicrobial courses. Consequently, antibiotic exposure is embedded within a larger network of MDRO risk.

In the Bhende cohort, prolonged ICU stay rather than a specific antibiotic exposure was the statistically identifiable risk factor for sepsis, yet every cultured bacterial bloodstream isolate was multidrug resistant [11]. Future studies therefore require time-dependent analysis capable of separating pre-existing colonisation, antibiotic exposure, device exposure, and subsequent MDRO acquisition.

The Microbiome as an Intermediate Mechanism

Antibiotics reduce susceptible commensal organisms and can create ecological niches for resistant Gram-negative organisms and enterococci. Broad-spectrum agents may therefore transform the intestinal microbiota into a reservoir from which subsequent bloodstream, urinary, intra-abdominal, or respiratory infection develops.

This mechanism is especially relevant in neonates and infants, in whom microbiome development is incomplete and hospitalisation frequently overlaps with feeding disruption, parenteral nutrition, and exposure to acid suppression and invasive devices. The present surgical literature rarely measured microbiome changes directly, representing an important gap between biological mechanism and clinical epidemiology.

Antimicrobial Stewardship in Paediatric Surgery

The findings support procedure-specific antimicrobial stewardship rather than a uniform strategy. The greatest gains are likely to come from preventing prophylaxis when it is not indicated, administering the correct drug within the appropriate pre-incisional window, avoiding broader agents when a narrow-spectrum drug is adequate, performing appropriate intraoperative redosing when necessary, stopping prophylaxis after surgery according to evidence-based protocols, and rapidly de-escalating empirical treatment when cultures exclude resistant pathogens.

The existence of substantial variation between hospitals indicates that prolonged prophylaxis is not simply dictated by unavoidable patient complexity. Institutional practice culture and surgical prescribing behaviour make important contributions.

Low- and Middle-Income Settings

The problem may be particularly important in low- and middle-income settings, where resistant Gram-negative organisms can already be prevalent before admission or surgery. Cousin et al. found resistant-organism carriage in more than 40% of cardiac-surgical encounters involving children referred from such settings [12]. In these environments, stewardship cannot be reduced simply to decreasing antibiotic consumption. Effective infection prevention, hand hygiene, surveillance, microbiological capacity, environmental control, and appropriate empirical treatment are equally necessary.

The Indian cardiac-surgery data reported by Bhende et al., in which all eight bacterial bloodstream isolates were multidrug resistant, further highlight the clinical consequence of resistance once postoperative sepsis occurs [11].

Clinical Implications

The evidence does not support prolonged postoperative antibiotics as a routine safety measure. For clean and clean-contaminated operations, antibiotic prophylaxis should be differentiated clearly from treatment of established infection. Where prophylaxis alone is indicated, unnecessary continuation should be avoided.

Children known to carry MDROs require individualized assessment rather than automatic escalation. Screening may be particularly valuable in children transferred from high-resistance institutions, children with repeated admissions, prior carbapenem exposure, congenital heart disease requiring multiple procedures, and patients referred from settings with high ESBL or carbapenem-resistance prevalence.

When postoperative infection is suspected, microbiological sampling should precede antimicrobial escalation whenever clinically feasible. Broad empirical therapy may be necessary in critically ill patients, but should be reassessed promptly once culture and susceptibility results become available.

Strengths

This review focuses specifically on the intersection of three domains that are frequently studied separately: paediatric surgery, antibiotic exposure, and antimicrobial resistance. It incorporates both direct MDRO evidence and large contemporary multicentre antimicrobial-utilisation datasets, allowing the review to examine the exposure pathway even where serial resistance surveillance was absent. The review also distinguishes between pre-existing MDRO colonisation and new selection pressure created by surgical antimicrobial exposure, which is critical for interpreting causality.

Limitations

The most important limitation is the absence of large prospective studies with systematic microbiological surveillance before and after surgery. Most included studies were retrospective, and several measured antibiotic appropriateness rather than MDRO acquisition directly.

Cardiac surgery was overrepresented, limiting generalisability to other paediatric surgical specialties. Definitions of multidrug resistance were not uniform. ESBL-producing organisms, MRSA, carbapenem-resistant organisms, and study-defined MDR isolates were combined conceptually but represent different resistance mechanisms.

Antibiotic exposure was variably reported as presence/absence, number of agents, spectrum, or duration. Standardized antibiotic-days per 1,000 patient-days were infrequently available. Baseline resistant-organism colonisation was not measured in many studies, making it impossible to determine whether resistant isolates emerged during admission or were present beforehand.

Future Research

Future studies should prospectively collect baseline rectal, nasal, or procedure-appropriate colonisation cultures; quantify antimicrobial exposure using days of therapy and spectrum scores; distinguish prophylaxis from therapeutic treatment; document timing of MDRO acquisition; and perform molecular comparison of baseline and postoperative isolates where possible. Multicentre studies should examine whether stopping prophylaxis at wound closure or within 24 hours reduces new MDRO colonisation without increasing SSI. Paediatric cardiac, neonatal gastrointestinal, colorectal, neurosurgical, transplant, and major orthopaedic populations warrant particular attention because of high antibiotic exposure and frequent invasive-device use. Trials or carefully designed quasi-experimental studies of antimicrobial-stewardship interventions should report not only antibiotic utilisation and SSI but also resistant-organism acquisition, *Clostridioides difficile*, invasive candidiasis, adverse drug effects, length of stay, readmission, and cost.

CONCLUSION

Antibiotic exposure in paediatric surgical patients is substantial, variable, and frequently exceeds what is required for effective perioperative prophylaxis.

Current evidence indicates that prolonged postoperative prophylaxis usually does not provide additional protection against surgical-site infection, while unnecessary duration and broad-spectrum therapy increase antimicrobial selection pressure. Multidrug-resistant colonisation is already common in selected high-risk paediatric surgical populations and may substantially increase the risk of postoperative infection with resistant organisms. Nevertheless, routine broadening of prophylaxis solely because of MDRO carriage has not been shown consistently to improve outcomes.

The strongest evidence therefore supports antimicrobial stewardship based on appropriate indication, correct timing, narrowest effective spectrum, avoidance of unnecessary postoperative continuation, culture-guided treatment, and timely de-escalation. More prospective surgical-specific studies are required to quantify the causal relationship between antibiotic days of therapy and new MDRO acquisition and to determine whether reducing perioperative exposure translates directly into lower antimicrobial resistance.

Declarations

Ethics Approval: Not required because this systematic review analyses previously published data.

Consent for Publication: Not applicable.

Funding: No specific funding was received for this systematic review.

Conflict of Interest: The authors should declare any relevant financial or non-financial competing interests before journal submission.

Data Availability: All data used in the systematic review are derived from published studies.

Registration: The review was not prospectively registered.

Appendix A. Database Search Framework

Concept	Example terms
Population terms	child* OR pediatric OR paediatric OR neonat* OR infant* OR adolescen*
Surgical terms	surg* OR operative OR perioperative OR postoperative OR cardiac surgery OR appendectomy OR gastrointestinal surgery OR neonatal surgery
Exposure terms	antibiotic* OR antimicrobial* OR prophylaxis OR broad-spectrum OR carbapenem* OR cephalosporin* OR days of therapy
Resistance terms	multidrug resistant OR MDRO OR antimicrobial resistance OR ESBL OR carbapenem-resistant OR CRE OR CRGNB OR MRSA OR VRE
Conceptual combination	Population AND Surgery AND Exposure AND Resistance

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