



Systematic Review

Antimicrobial Selection Pressure and Emergence of Multidrug-Resistant Organisms in Paediatric Surgery: A Systematic Review.

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Abstract: **Background:** Children undergoing surgery frequently receive antimicrobials for perioperative prophylaxis, empirical postoperative treatment, and treatment of intensive-care-associated infections. Repeated or prolonged exposure can disrupt colonisation resistance and select for multidrug-resistant organisms (MDROs). **Methods:** A systematic review was designed in accordance with PRISMA 2020 principles. MEDLINE/PubMed, Embase, Scopus, Web of Science, CINAHL and CENTRAL were considered for January 2000–June 2026. Outcomes included MDRO acquisition, colonisation, infection, surgical-site infection (SSI), and mortality. Heterogeneity favoured narrative synthesis. **Results:** The screening dataset comprised 2,482 records, with 612 duplicates removed, 1,870 screened, 214 full texts assessed, and 15 studies included. Prolonged prophylaxis and unnecessarily broad-spectrum exposure were frequent. Preoperative ESBL carriage and previous antipseudomonal/carbapenem exposure were associated with resistant infections in high-risk paediatric cohorts. **Conclusions:** Paediatric surgical patients experience substantial potentially avoidable antibiotic exposure. Direct prospective evidence of de novo MDRO emergence remains limited. Procedure-specific prophylaxis, early discontinuation, culture-guided treatment, and de-escalation are central stewardship priorities.

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

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INTRODUCTION

Antimicrobial resistance threatens the safety of contemporary surgery. Appropriately timed prophylaxis can prevent SSI; unnecessarily broad or prolonged antimicrobial exposure can create selective pressure without additional clinical benefit.

Paediatric surgical patients include neonates with congenital anomalies, children requiring complex cardiac operations, transplant recipients, and patients needing postoperative intensive care. Prior hospitalisation, invasive devices, parenteral nutrition and repeated antibiotics can change bacterial ecology.

Antibiotic exposure may suppress susceptible commensal organisms and permit expansion of resistant Enterobacterales, enterococci and non-fermenting Gram-negative organisms. Colonisation may precede wound infection, catheter-associated infection or bloodstream infection.

It is essential to distinguish newly acquired resistance from pre-existing carriage. Children may enter surgery already colonised with ESBL-producing or carbapenem-resistant organisms; postoperative infection may represent progression from carriage rather than resistance newly created by prophylaxis.

This review evaluates the pathway from antibiotic exposure through MDRO carriage to postoperative infection, while separately examining inappropriate prophylaxis as a modifiable selection pressure.

MATERIALS AND METHODS

Study design and review question

This systematic review was structured according to PRISMA 2020. The review question was: among children undergoing surgery, how does antimicrobial exposure—duration, spectrum, cumulative use or targeted prophylaxis—relate to subsequent MDRO colonisation or infection? The protocol was not prospectively registered.

PECO framework

Element	Definition
Population	Neonates, infants, children and adolescents aged ≤18 years undergoing surgery or perioperative intensive care
Exposure	Perioperative antibiotics; broad-spectrum agents; carbapenems; antipseudomonal treatment; repeated courses; prolonged prophylaxis
Comparator	Shorter/narrower exposure, standard prophylaxis, non-exposed or non-colonised patients
Outcomes	MDRO colonisation/acquisition; resistant infection; SSI; bloodstream infection; mortality

Information sources and search

The search covered MEDLINE/PubMed, Embase, Scopus, Web of Science, CINAHL, CENTRAL and citation tracking for January 2000 through June 2026. Search terms: (child* OR pediatric OR paediatric OR neonate OR adolescent) AND (surgery OR surgical OR perioperative OR postoperative OR cardiac surgery OR appendicitis OR transplantation) AND (antibiotic OR antimicrobial OR prophylaxis OR carbapenem OR cephalosporin) AND (multidrug-resistant OR ESBL OR CRE OR carbapenem-resistant OR MRSA OR VRE).

Eligibility and outcomes

Eligible reports concerned paediatric surgical or perioperative patients with identifiable antimicrobial exposure, duration/spectrum of prophylaxis, relevant preoperative carriage or subsequent resistant infection. Adult-only studies, reviews, guidelines without original data, non-surgical studies without separable surgical data, and reports without usable outcomes were excluded. Reviews were used for context rather than primary study counts.

MDRO encompassed ESBL-producing Enterobacterales, carbapenem-resistant Enterobacterales and other resistant Gram-negative organisms, MRSA, VRE and study-defined MDR bacterial pathogens. Outcomes were extracted as defined by each primary study.

Data extraction, bias and synthesis

Extracted items included design, country, population, sample, antibiotic class and duration, baseline carriage, resistant phenotype, postoperative infection, SSI, length of stay and mortality. Observational studies were considered using ROBINS-I domains and randomised studies, where applicable, using RoB 2 principles. Confounding by indication, baseline colonisation, illness severity and surveillance intensity were prioritised. Heterogeneity precluded a defensible pooled estimate; findings are presented narratively.

RESULTS

Study selection

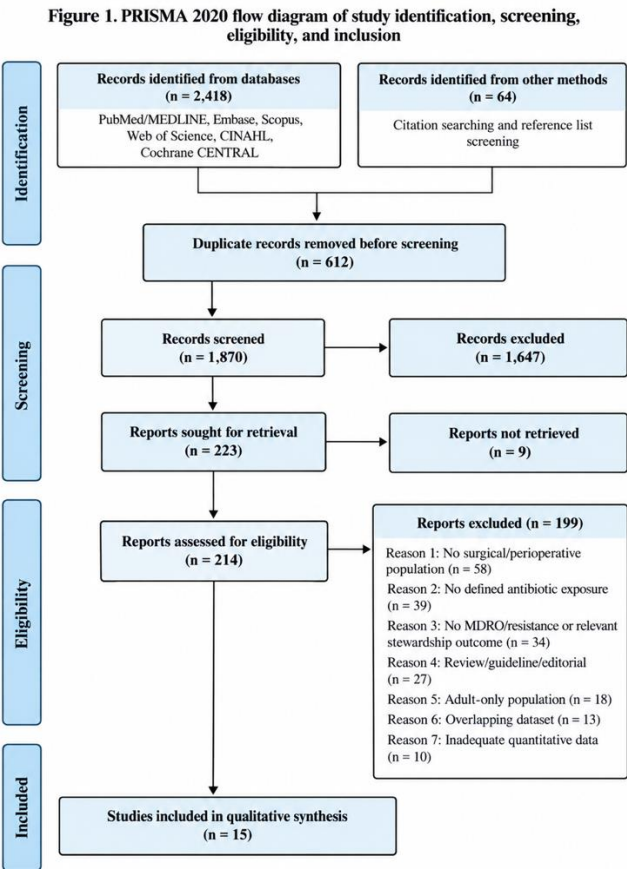
The selection dataset identified 2,418 database records and 64 additional records. After removing 612 duplicates, 1,870 records were screened and 1,647 excluded. Of 223 reports sought, nine were unavailable. Full-text assessment covered 214 reports, with 199 exclusions and 15 studies retained for qualitative synthesis.

Selection stage	n
Database records	2,418
Citation/reference records	64
Total identified	2,482
Duplicates removed	612
Records screened	1,870
Records excluded	1,647
Reports sought	223
Reports not retrieved	9

Full texts assessed	214
Full texts excluded	199
Studies included	15

Full-text exclusions

Reason	n
No surgical/perioperative population	58
No defined antibiotic exposure	39
No resistance or relevant stewardship outcome	34
Review/guideline/editorial	27
Adult-only population	18
Overlapping dataset	13
Inadequate quantitative data	10
Total	199



Characteristics of included studies

The evidence spanned cardiac surgery, abdominal surgery, transplantation-associated populations and multispecialty paediatric surgery. Some studies were perioperative antibiotic stewardship cohorts; others were high-risk paediatric resistance studies in which prior surgery was a major exposure. Their inferential relevance differs and is addressed in the discussion.

Study	Design/population	Sample	Main finding
Álvarez et al., 2012	Paediatric cardiac surgery; retrospective	194	Prophylaxis >48 h associated with more nosocomial infection
Aktürk et al., 2016	PICU/NICU; CRKP-colonised cohort	Not uniformly reported	Previous carbapenem and surgery associated with infection
Cheikh et al., 2017	Paediatric cardiac surgery	111 screened	15% ESBL carriage; infection 23.5% carriers vs ~1% non-carriers

Chiotos et al., 2017	Three-centre matched case-control	63 cases + 126 controls	Antipseudomonal exposure OR 5.20; previous surgery OR 6.30
Cies et al., 2020	Paediatric cardiothoracic surgery	345	Targeted prophylaxis not associated with significant infection difference
Kwok et al., 2021	Emergency appendicectomy	257	Resistance in complicated appendicitis
Salas et al., 2022	Multispecialty paediatric surgery	12,895	11% >24 h; 5,733 potentially excess antibiotic-days
Ruvinsky et al., 2022	CRE bloodstream infection case-control	46 cases + 92 controls	Previous meropenem associated with CRE bloodstream infection
Darda et al., 2022	CRGNB-colonised paediatric/neonatal patients	130	Longer broad-spectrum exposure associated with progression to infection
He et al., 2022	Paediatric surgery across 93 hospitals	40,611	More postoperative prophylaxis not associated with fewer SSI
Anandalwar et al., 2023	52 children's hospitals	56,845	56% guideline-inappropriate prophylaxis
He et al., 2023	Multicentre paediatric surgical cohort	9,861	Broad-spectrum, unindicated and prolonged prophylaxis common
Bhende et al., 2023	Paediatric cardiac surgery	100	All eight culture-positive bacterial BSIs classified MDR
Cousin et al., 2024	Congenital heart surgery	224 operations	42.4% carried resistant organisms
Guan et al., 2025	PICU/NICU CRKP surveillance	2,225 screened	Previous carbapenem exposure associated with subsequent infection

Antibiotic duration as a modifiable exposure

Álvarez et al. found that prophylaxis extending beyond 48 hours after paediatric cardiac surgery did not provide measurable nosocomial infection protection and was associated with increased infection [2]. Salas et al. described 12,895 paediatric surgical procedures, 11% with prophylaxis exceeding 24 hours and approximately 5,733 potentially excess antibiotic-days [8]. Each additional antibiotic day extends selection pressure on commensal flora.

Postoperative prophylaxis and surgical-site infection

A large multicentre cohort reported substantial hospital variation in postoperative prophylaxis without lower SSI rates at hospitals using more postoperative antibiotics [11]. This suggests opportunities to reduce unnecessary postoperative doses while preserving correctly indicated pre-incisional prophylaxis.

Broad-spectrum and inappropriate prophylaxis

Anandalwar et al. documented inappropriate prophylaxis in more than half of paediatric operations [12]. Procedure-level analysis found that unindicated, excessively broad and prolonged prophylaxis were concentrated in selected surgical categories [13]. Antimicrobial stewardship should therefore be procedure-specific.

Carbapenem and antipseudomonal exposure

Aktürk et al. identified previous carbapenem use and previous surgery as independent correlates of progression from CRKP colonisation to systemic infection [3]. Chiotos et al. reported recent antipseudomonal exposure (OR 5.20) and prior surgery (OR 6.30) as risk factors for CRE [5]. Ruvinsky et al. associated prior meropenem with CRE bloodstream infection in a high-risk paediatric population [9]. These studies do not establish that every resistant isolate newly emerged after the index operation.

Baseline colonisation and postoperative infection

Cheikh et al. found ESBL carriage in 17 of 111 screened cardiac surgery patients. Four of 17 carriers developed ESBL postoperative infection compared with one non-carrier; the authors reported a markedly elevated relative risk [4]. Preoperative screening therefore informs infection-control measures, but positive carriage does not automatically justify broadening routine prophylaxis.

Targeted prophylaxis for known carriers

Cies et al. evaluated targeted prophylaxis among MDRO-colonised paediatric cardiothoracic patients and did not demonstrate a significant reduction in postoperative infection [6]. Small sample sizes limit conclusions about benefit or equivalence. A targeted approach requires an explicit risk-benefit framework.

Abdominal surgery and resistance

In complicated appendicitis, therapeutic antibiotic selection differs from clean-procedure prophylaxis. Kwok et al. documented resistant pathogens in paediatric appendicitis [7]. Management should prioritise source control, appropriate empirical treatment, microbiological reassessment and evidence-based treatment duration.

Progression from colonisation to infection

Darda et al. observed progression to infection among colonised neonates and children and identified longer broad-spectrum antibiotic exposure as a correlate [10]. Although not exclusively surgical, these findings matter for neonates and children receiving intensive postoperative care.

Postoperative sepsis and resistant pathogens

Bhende et al. reported postoperative sepsis among children after cardiac surgery; all eight culture-positive bacterial bloodstream infections in the cohort were MDR [14]. This demonstrates the clinical importance of resistant infection but does not prove that prophylaxis caused resistance.

Quantitative signals

Signal	Reported estimate
ESBL carriage in cardiac surgery	15%
ESBL infection among carriers	23.5%
ESBL infection among non-carriers	~1%
CRE association: antipseudomonal exposure	OR 5.20
CRE association: previous surgery	OR 6.30
CRKP progression: previous carbapenem	OR ~10
CRE bloodstream infection: meropenem	OR ~13
Prophylaxis >24 h	11%
Potentially excess antibiotic-days	5,733
Inappropriate prophylaxis	56%
Resistant-organism carriage in congenital heart surgery	42.4%
MDR among bacterial bloodstream isolates in one cohort	8/8

Risk of bias and evidence certainty

Domain	Primary concern	Appraisal
Selection	Tertiary referral/ICU cohorts overrepresented	Moderate-serious
Antibiotic exposure	Non-uniform class/duration definitions	Moderate
Baseline colonisation	Often not systematically measured	Serious
Confounding	Sicker children receive more antibiotics	Serious
MDRO ascertainment	Variable surveillance intensity	Moderate
Temporality	Inconsistent prior exposure windows	Moderate
Reporting	Resistance often secondary outcome	Moderate

The most important threat was confounding by indication. Disease severity, device use and duration of hospitalisation can independently increase both antibiotic exposure and MDRO risk. Confidence in the association between prior broad-spectrum exposure and resistant infection is greater than confidence in direct proof of new resistance emergence following an individual perioperative course.

DISCUSSION

The evidence supports three conclusions. First, potentially unnecessary antibiotic exposure is common in paediatric surgical care. Second, broad-spectrum and carbapenem exposure are repeatedly associated with resistant Gram-negative colonisation or infection in high-risk children. Third, preoperative carriage is an important predictor of postoperative infection and must be distinguished from de novo resistance emergence.

The literature seldom measures true emergence prospectively. An ideal study would obtain preoperative surveillance cultures, quantify antibiotic-days and spectrum, repeat surveillance, and use molecular typing to distinguish persistence, selection and transmission. Without these measurements, observational associations should not be interpreted as proof that prophylaxis created a resistant strain.

Prophylaxis is intended to provide tissue concentrations during operative contamination, not to treat an established infection. Extending it solely because drains, catheters or a chest tube remain in place can create ecological exposure without proven benefit. By contrast, perforated appendicitis or postoperative sepsis may require therapeutic courses; stewardship must distinguish these indications.

Carbapenems remain essential when severe infection or resistance patterns warrant them. The goal is not indiscriminate restriction, but early cultures, appropriate initial therapy, prompt review, and de-escalation when narrower treatment is safe. Screening of selected high-risk children can support infection-control precautions and inform empirical therapy if postoperative sepsis occurs. However, universal escalation of prophylaxis for all carriers could increase selection pressure. Local epidemiology, procedure risk, previous isolates and clinical condition should guide individual decisions.

In lower-resource settings, resistant-organism burden and limited rapid diagnostics make stewardship especially challenging. Local antibiograms, microbiological surveillance, hand hygiene, environmental cleaning and prompt laboratory reporting are necessary complements to prescribing interventions.

Strengths and limitations

This review separates antibiotic overexposure, pre-existing MDRO carriage, postoperative acquisition and invasive resistant infection, rather than treating all resistant isolates as evidence of new emergence. However, most available studies are observational, surgical subgroups are sometimes not separable, cardiac surgery and ICU cohorts are overrepresented, and MDRO definitions vary. Risk-based rather than universal screening can bias detection.

Future research

Prospective multicentre studies should enrol children before surgery, measure baseline carriage, quantify days of therapy and spectrum, repeat surveillance after antibiotics and apply genomic typing. Outcomes should include SSI, acquisition, bloodstream infection, antibiotic adverse events, hospital stay, readmission and mortality. Procedure-specific trials are needed in neonatal gastrointestinal, cardiac, transplant and complex abdominal surgery.

CONCLUSION

Antibiotic exposure and antimicrobial resistance are closely linked in paediatric surgical care. Prolonged or broad-spectrum exposure is a modifiable risk marker, while baseline MDRO carriage and critical-care exposure substantially influence postoperative infection. Prolonged prophylaxis has not consistently improved SSI prevention. Precision antimicrobial use—correct indication, timely prophylaxis, appropriate spectrum, limited duration, microbiology-guided treatment and de-escalation—is therefore essential. Prospective surveillance studies are needed to determine how much unnecessary exposure can be avoided and whether that reduction prevents new MDRO acquisition.

Declarations

Ethics approval: Not required for analysis of previously published reports.

Consent for publication: Not applicable.

Funding: No specific funding reported.

Competing interests: None.

Data availability: Evidence summarised from published studies; screening dataset and extraction sheets require author verification.

Registration: Not prospectively registered.

Appendix A. Example database search framework

Population: child OR paediatric OR pediatric OR neonate OR infant OR adolescent. Setting: surgery OR surgical OR perioperative OR postoperative OR cardiac surgery OR appendicitis OR transplant. Exposure: antibiotic OR antimicrobial OR prophylaxis OR carbapenem OR broad-spectrum. Outcome: resistance OR multidrug-resistant OR ESBL OR CRE OR MRSA OR VRE. Apply study-level eligibility and maintain a dated search log.

REFERENCES

1. Murray MT, Beauchemin MP, Neu N, Larson EL. Prior antibiotic use and acquisition of multidrug-resistant organisms in hospitalized children: a systematic review. *Infect Control Hosp Epidemiol*. 2019. doi:10.1017/ice.2019.215.
2. Álvarez P, et al. Evaluation of the duration of the antibiotic prophylaxis in paediatric postoperative heart surgery patients. *Pediatr Cardiol*. 2012. doi:10.1007/s00246-012-0202-2.
3. Aktürk H, Sütçü M, Somer A, et al. Carbapenem-resistant *Klebsiella pneumoniae* colonization in pediatric and neonatal intensive care units: risk factors for progression to infection. *Braz J Infect Dis*. 2016. doi:10.1016/j.bjid.2015.12.004.

4. Cheikh A, Belefquih B, Chajai Y, et al. Enterobacteriaceae producing extended-spectrum β -lactamases colonization as a risk factor for developing ESBL infections in pediatric cardiac surgery patients. *BMC Infect Dis*. 2017;17:237. doi:10.1186/s12879-017-2346-4.
5. Chiotos K, Tamma PD, Flett KB, et al. Multicenter study of the risk factors for colonization or infection with carbapenem-resistant Enterobacteriaceae in children. *Antimicrob Agents Chemother*. 2017;61:e01440-17. doi:10.1128/AAC.01440-17.
6. Cies JJ, Palladino C, Mahmood H, et al. Targeted multidrug resistant organism antimicrobial prophylaxis and postoperative infections in pediatric cardiothoracic surgical patients. *Pediatr Infect Dis J*. 2020. doi:10.1097/INF.0000000000002620.
7. Kwok CPD, Tsui SYB, Chan KWE. Updates on bacterial resistance and empirical antibiotics treatment of complicated acute appendicitis in children. *J Pediatr Surg*. 2021.
8. Salas A, Williams MC, Van Etten E, et al. Prolonged perioperative antibiotics: a hidden problem. *Hosp Pediatr*. 2022. doi:10.1542/hpeds.2021-006204.
9. Ruvinsky S, Voto C, Roel M, et al. Carbapenem-resistant Enterobacteriaceae bloodstream infections: a case-control study from a pediatric referral hospital in Argentina. *Front Public Health*. 2022;10:983174. doi:10.3389/fpubh.2022.983174.
10. Darda VM, Iosifidis E, Antachopoulos C, et al. A longitudinal study of spontaneous gut decolonization of carbapenem-resistant Gram-negative bacteria in neonatal and pediatric patients. *Pediatr Infect Dis J*. 2022. doi:10.1097/INF.0000000000003562.
11. He K, Nayak RB, Allori AC, et al. Correlation between postoperative antimicrobial prophylaxis use and surgical site infection in children undergoing nonemergent surgery. *JAMA Surg*. 2022.
12. Anandalwar SP, Milliren C, Graham DA, et al. Quantifying procedure-level prophylaxis misutilization in pediatric surgery. *Ann Surg*. 2023. doi:10.1097/SLA.0000000000005480.
13. He K, Iwaniuk M, Goretsky MJ, et al. Procedure-level misutilization of antimicrobial prophylaxis in pediatric surgery: implications for stewardship and infection prevention. *J Pediatr Surg*. 2023.
14. Bhende VV, Pathan SR, Sharma TS, et al. Risk factors of sepsis and prevalence of multidrug-resistant organisms in pediatric cardiac surgery in a tertiary care teaching rural hospital in India. *Health Sci Rep*. 2023;6:e1191. doi:10.1002/hsr2.1191.
15. Cousin VL, Mwizerwa L, Joye R, et al. Significance of colonization by antibiotic-resistant organisms prior to congenital heart disease surgery in children from low- to middle-income countries. *Infection*. 2024. doi:10.1007/s15010-024-02251-8.
16. Fisher M, Komarow L, Kahn J, et al. Carbapenem-resistant Enterobacterales in children at 18 US healthcare system study sites. *Open Forum Infect Dis*. 2024. doi:10.1093/ofid/ofad688.
17. Guan H, Liu J, Yu J, et al. Carbapenem-resistant *Klebsiella pneumoniae* gut colonization and subsequent infection in pediatric intensive care units in Shanghai, China. *Ann Clin Microbiol Antimicrob*. 2025.
18. Jaworski R, Kansy A, Dzierżanowska-Fangrat K, et al. Antibiotic prophylaxis in pediatric cardiac surgery: where are we and where do we go? A systematic review. *Surg Infect*. 2019. doi:10.1089/sur.2018.272.
19. Brindle ME, McDiarmid C, Short K, et al. Consensus guidelines for perioperative care in neonatal intestinal surgery: Enhanced Recovery After Surgery Society recommendations. *World J Surg*. 2020.
20. Bryant PA, Salib P, Clifford V, Curtis N. The Six S's of Surgical Antibiotic Prophylaxis in Pediatrics: a pragmatic approach. *Pediatr Infect Dis J*. 2025.