

Systemic Review

Probiotics in pediatric cardiac surgery: biological effects and clinical outcomes – a systematic review of randomized evidence

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Received: 25 March 2026

Accepted: 21 September 2026

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ABSTRACT

Children undergoing cardiac surgery with cardiopulmonary bypass (CPB) are vulnerable to intestinal barrier dysfunction, systemic inflammation, and postoperative infection. Probiotics may restore gut microbiota balance and modulate inflammation, but evidence in pediatric cardiac populations is limited. The objective is to systematically analyze the effects of perioperative probiotic supplementation in pediatric cardiac surgery, and incorporating indirect evidence from adult CPB trials. Following PRISMA 2020 guidelines, major databases (PubMed, Embase, Scopus, CENTRAL, and ClinicalTrials.gov) were searched through March 2025. Eligible studies were randomized controlled trial (RCTs) and pilot studies that evaluated the probiotics in pediatric or adult cardiac-surgery patients. Data extraction and risk-of-bias assessment (RoB2) were performed independently by three reviewers. Owing to clinical heterogeneity and sparse events, findings were narratively synthesized, with quantitative pooling limited to comparable continuous outcomes. Five RCTs (three pediatric, two adult) met the inclusion criteria. Pediatric trials using *Bifidobacterium breve* or *Bifidobacterium longum* demonstrated improved intestinal microbiota and trends toward reduced endotoxin and I-FABP levels, but no significant differences in infection or ICU length of stay. Adult CPB trials showed reduced acute gastrointestinal injury and nosocomial infections. No adverse events or probiotic-associated sepsis were reported. Overall certainty of evidence ranged from low to moderate, limited by sample size and outcome heterogeneity. Perioperative probiotic supplementation in pediatric cardiac surgery appears safe and biologically active but lacks conclusive evidence for clinical benefit. Larger, standardized multicenter RCTs are warranted to determine efficacy and optimize strain selection, dosing, and timing.

Keywords: Probiotics, Cardiac surgery, Cardiopulmonary bypass, Randomized controlled trials, Pilot study, Outcome

INTRODUCTION

Cardiac surgery with cardiopulmonary bypass (CPB) in children is a highly complex procedure in pediatric intensive care, requiring careful management of systemic inflammation, haemodynamics, and postoperative recovery.¹ Despite advances in surgical and anaesthetic techniques, children with congenital heart disease still face risks like infection, prolonged ventilation, and feeding

intolerance.² These complications arise from CPB stress, ischemia-reperfusion injury, antibiotics, and altered intestinal perfusion that impair gut barrier function.

Evidence from pediatric and adult studies shows that CPB causes temporary intestinal hypoperfusion and disrupts the gut microbiome.³ Dysbiosis causes pathogenic bacteria overgrowth, endotoxin translocation, and systemic inflammation through pattern recognition receptors.

Elevated plasma intestinal fatty acid-binding protein (I-FABP) and endotoxin after CPB confirm intestinal mucosal damage injury.⁴ In neonates and infants, with developing gut microbiota and immunity, such disruptions may cause necrotising enterocolitis (NEC), sepsis, and impaired enteral tolerance.

Probiotics have been studied to improve gut integrity, restore microbial balance, boost mucosal immunity, decrease endotoxin levels, reduce inflammatory cytokines like interleukin-6, and shorten intensive care unit (ICU) stays.⁵ In neonatal and pediatric populations, probiotics are well established for preventing NEC in preterm infants, but their use in the cardiac ICU has been limited to a few small-scale studies.⁶

Meta-analyses have summarized probiotics in neonatal intensive care, but none focus on perioperative or cardiopulmonary bypass in children, who differ due to hemodynamic instability and bypass-related gut ischemia, unlike prematurity-related NEC.⁷ Despite potential benefits, clinicians are cautious for safety concerns, strain selection issues, and uncertain efficacy. Limited pediatric RCTs prevent detailed analysis, but synthesizing evidence is vital for assessing feasibility, safety, biological plausibility, and guiding future trials.

Objectives

This review systematically identifies, evaluates, and synthesises RCTs and pilot studies on perioperative probiotic supplementation in pediatric cardiac surgery, including adult CPB RCTs as indirect evidence.

METHODS

This systematic review was conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA 2020) statement.⁸ The design adhered to the methodological standards of the Cochrane handbook for systematic reviews of interventions.⁹

Given the scarcity of pediatric RCTs and the heterogeneity of outcomes, the review was prespecified as a systematic

review with narrative synthesis, with meta-analytic pooling limited to continuous outcomes for which ≥ 2 trials provided compatible numerical data. Adult CPB trials were incorporated as indirect evidence, analyzed separately, and not statistically combined with pediatric data, consistent with GRADE guidance on indirectness.¹⁰ Eligibility criteria were determined using the population, intervention, comparator, outcome (PICO) framework, with inclusion and exclusion criteria outlined in Table 1.

A comprehensive literature search was conducted in PubMed/MEDLINE, Embase (Elsevier), Scopus, and clinicalTrials.gov (to identify ongoing or unpublished RCTs). Searches were updated through March 2025. Reference lists of all included studies and relevant reviews were manually screened for additional trials.

The PubMed search string was structured around the PICO terms using MeSH and free-text keywords: ("probiotics"[Mesh] OR probiotic* OR synbiotic* OR "bifidobacterium" OR "lactobacillus") AND ("congenital heart disease" OR "cardiac surgery" OR "cardiopulmonary bypass" OR "cardiac ICU") AND ("randomized controlled trial" OR randomised OR RCT OR pilot study). Equivalent strategies were adapted for Embase and Scopus using Emtree terms and Boolean syntax. Figure 1 shows the PRISMA flow diagram and the research strategy. All retrieved citations were imported into EndNote for deduplication and screening (Table 1).

Three reviewers independently screened titles and abstracts. Full-text articles were retrieved when eligibility was uncertain. Disagreements were resolved by consensus or consultation with a third reviewer. Data was extracted independently by two reviewers using a pre-piloted excel form that covered the study characteristics: author, year, country, design, sample size, population details: age range, surgery type, CPB use, and baseline characteristics. Intervention: probiotic strain(s), dosage, timing, duration, comparator: placebo, usual care, or blank control and outcomes: primary: postoperative infection rate, NEC incidence, gut biomarkers (I-FABP, IL-6) and secondary: microbiota diversity indices, ICU length of stay (LOS), ventilation time, mortality, and adverse events.

Table 1: Study method with inclusion and exclusion criteria using the PICO framework.

Criterion	Inclusion	Exclusion
Population	Neonates, infants, or children (0–18 years) undergoing cardiac surgery with CPB or postoperative cardiac ICU admission; adult cardiac-surgery patients included as indirect evidence	Non-surgical critical care patients or non-cardiac surgeries
Intervention	Any probiotic or synbiotic (single or multistrain) administered pre-, intra-, or postoperatively via enteral route, regardless of dose or duration	Prebiotics alone, fermented foods, or topical applications
Comparator	Placebo, standard care, or no probiotic	Absence of a comparator group (observational or uncontrolled studies)
Outcomes	Microbiota changes, gut injury biomarkers (I-FABP, IL-6, endotoxin), postoperative infection rates, NEC, feeding intolerance, ICU stay, and mortality	Animal studies, reviews, non-randomized or non-controlled designs

Continued.

Criterion	Inclusion	Exclusion
Study design	Randomized controlled trials (parallel, double-blind, or single-blind) or a pilot study	Observational studies, case series, or case reports
Language and period	English-language studies, no date restriction (inception–2025)	Non-English without translation or incomplete data

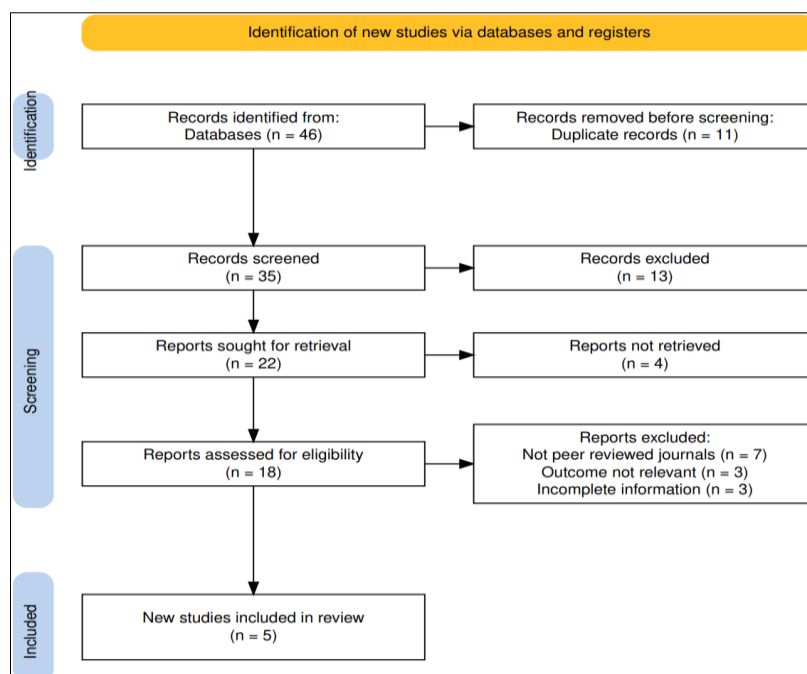


Figure 1: PRISMA flow diagram for prebiotic studies in cardiac surgery.

Statistical data was assessed with means, SDs, medians, or event counts as available. When data were reported as medians and IQRs, conversion to mean±SD was performed using established methods.¹¹ Each included RCT was assessed using the Cochrane risk of bias 2.0 (RoB2) tool.¹² The following domains were evaluated: randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, selection of reported results. Judgments were categorized as low risk, some concerns, or high risk. Given substantial clinical and methodological heterogeneity (different probiotic strains, dosing, and outcomes), a narrative synthesis was chosen as the principal analytic approach.¹³ Studies were grouped by population (pediatric versus adult) and outcome domain (microbiota, biomarkers, clinical outcomes).

When ≥ 2 studies reported comparable continuous outcomes (e.g., ICU LOS), quantitative pooling was attempted using RevMan 5.4 (Cochrane collaboration). Random-effects models were applied to compute pooled mean differences (MD) with 95% confidence intervals (CI). For binary outcomes, risk ratios (RR) were calculated only when ≥ 2 studies reported events; otherwise, results were described qualitatively.¹⁴

During protocol development, a quantitative meta-analysis of infection rates was planned; however, this was modified to a narrative synthesis after determining that two pediatric

RCTs had no events in either arm. Such studies cannot contribute to pooled RR calculations without misleading precision.¹⁵ This review analyzed previously published data and therefore did not require institutional ethics approval. Ethical approval was confirmed for all included RCTs. No patient-level data were accessed.

RESULTS

A total of 46 records were identified through database searches and manual reference screening. After removal of 11 duplicates, 35 titles and abstracts were screened, and 13 were excluded that were not relevant. 22 studies were tried to be retrieved. 4 reports not retrieved. 18 full-text articles were reviewed in detail. Of these, five randomized controlled trials (RCTs) met the inclusion criteria (Figure 1).

Three trials were conducted in pediatric cardiac surgery populations: Ellis et al, Umenai et al, and Toritsuka et al.¹⁶⁻¹⁸ Two additional trials were identified in adult cardiac surgery with CPB, Liu et al and Yang et al.^{5,19} No ongoing or unpublished trials meeting the criteria were found on ClinicalTrials.gov or the WHO ICTRP at the time of the final search (March 2025).

Three pediatric RCTs together included 119 participants (Table 2). All were single-center, parallel-group designs with sample sizes ranging from 16 to 82.

Ellis et al randomized 16 neonates with congenital heart disease (CHD) to receive *Bifidobacterium longum ssp. infantis* (4.2×10^9 CFU twice daily) or placebo for eight weeks postoperatively.

Primary outcomes were gut microbiota composition and plasma cytokine profiles.¹⁶

Umenai et al enrolled 21 neonates (7-21 days old) undergoing cardiac surgery, who received *Bifidobacterium breve* (3×10^9 CFU/day) preoperatively and for 1 week postoperatively. Outcomes included stool microbiota composition and gut barrier biomarkers.¹⁷

Toritsuka et al studied 82 children (0-15 years) undergoing CPB, randomized to *Bifidobacterium breve* BBG-01 (0.5×10^9 CFU per dose, thrice daily) versus control. Outcomes included microbiota diversity, I-FABP, and postoperative infection rates.¹⁸

All three pediatric trials used enteral administration via milk or water, starting preoperatively or within 48 hours

post-surgery, and continued until hospital discharge. No study reported probiotic-associated bacteremia or serious adverse events.

While, two adult RCTs contributed 82 participants (Liu et al and Yang et al), Liu et al randomized 30 adults undergoing valve surgery with CPB to receive a combination of probiotics (*Lactobacillus*, *Bifidobacterium*, and *Enterococcus faecium*) as part of selective digestive decontamination (SDD) versus standard care.¹⁹

Yang et al enrolled 52 adults scheduled for valve replacement under CPB and received a multistrain probiotic (6×10^9 CFU/day) for 7 days preoperatively. The primary outcome was acute gastrointestinal injury (AGI) incidence; secondary outcomes included nosocomial infections and ICU length of stay.⁵

All adult trials were double-blind and placebo-controlled, unlike the open-label design of some pediatric studies.

Table 2: Characteristics of included randomized controlled trials.

Study and year	Country	Population (age range)	Surgery type	Probiotic strain(s) and dose	Compare	Duration/timing	Primary outcomes	Key findings
Ellis et al, 2013	USA	Neonates with CHD (≥ 34 weeks GA)	Post-cardiac surgery	<i>Bifidobacterium longum ssp. infantis</i> 4.2×10^9 CFU BID	Placebo	8 weeks post-op	Gut microbiota, cytokines	$\uparrow$ <i>Bifidobacterium</i> , safe, no infection or NEC
Umenai et al, 2014	Japan	Neonates (7-21 days)	CHD repair with CPB	<i>Bifidobacterium breve</i> 3×10^9 CFU/day	No probiotic	1 week pre- and post-op	Microbiota, fecal endotoxin, I-FABP	Improved microbiota, $\downarrow$ endotoxin, no infection
Toritsuka et al, 2024	Japan	Children (0-15 years)	CPB for CHD	<i>Bifidobacterium breve</i> BBG-01, 0.5×10^9 CFU TID	No probiotic	Preop + POD1-discharge	Dysbiosis, I-FABP, infection	Corrected dysbiosis, infection 25.6% versus 28.2%, safe
Liu et al, 2018	China	Adults (18-70 years)	Valve surgery with CPB	Multistrain (<i>Lactobacillus</i> , <i>Bifidobacterium</i> , <i>Enterococcus</i>)	Standard care	Pre-postoperative	IL-6, endotoxin	$\downarrow$ IL-6, safe, no infection
Yang et al, 2025	China	Adults (18-70 years)	Valve replacement (CPB)	<i>Lactobacillus rhamnosus</i> + <i>E. faecium</i> , 6×10^9 CFU/day $\times 7$ days preop	Placebo	Preop only	AGI, infection, ICU LOS	$\downarrow$ AGI, $\downarrow$ infection, $\downarrow$ ICU LOS

CHD=Congenital heart disease; CPB=cardiopulmonary bypass; I-FABP=intestinal fatty acid-binding protein; AGI=acute gastrointestinal injury; LOS=length of stay

Table 3: Cochrane risk of bias 2.0 assessment.

Domain	Ellis (2013)	Umenai (2014)	Toritsuka (2024)	Liu (2018)	Yang (2025)
Randomization process	Low	Some concerns	Low	Low	Low
Allocation concealment	Low	High	Low	Some concerns	Low

Continued.

Domain	Ellis (2013)	Umenai (2014)	Toritsuka (2024)	Liu (2018)	Yang (2025)
Blinding of participants/personnel	Low	High	High	Some concerns	Low
Blinding of outcome assessment	Low	Some concerns	Some concerns	Some concerns	Low
Incomplete outcome data	Low	Low	Low	Low	Low
Selective reporting	Low	Low	Low	Low	Low
Other bias	Small pilot	Small, open-label	None	Mixed intervention	None
Overall judgment	Low-moderate	Moderate-high	Moderate	Moderate	Low

Table 4: GRADE summary of evidence.

Outcome	No. of studies	Participants (N)	Effect direction	Certainty (GRADE)	Main reasons for downgrade
Microbiota composition	3 pediatric, 2 adult	201	Consistent improvement	Moderate	Imprecision (small n)
Biomarkers (I-FABP, IL-6)	2 pediatric, 2 adult	150	Biochemical improvement	Low-moderate	Heterogeneity, indirectness
Infection rate	1 pediatric, 1 adult	134	↓ only in adults	Low	Sparse events, imprecision
ICU length of stay	2 pediatric, 2 adult	160	Mildly shorter LOS	Low	Small effect, heterogeneity
Mortality/adverse events	5 RCTs	201	No events	High	None

Table 5: Summary of outcome effects by domain.

Outcome domain	Pediatric evidence (Ellis, Umenai, Toritsuka)	Adult evidence (Liu, Yang)	Overall direction of effect	Certainty (GRADE)
Gut microbiota restoration	↑ <i>Bifidobacterium</i> , ↓ <i>Enterobacteriaceae</i>	Improved diversity, ↓ endotoxin species	Consistent improvement	Moderate
Biomarkers (I-FABP, IL-6, endotoxin)	↓ endotoxin trend, no I-FABP change	↓ IL-6 and endotoxin (significant)	Consistent biochemical benefit	Low–Moderate
Postoperative infections	0-28%, no significant reduction	↓ infection (11.5% versus 34.6%, $p<0.05$)	Benefit in adults only	Low
ICU length of stay	Trend ↓ (mean 7.8 versus 8.1 days)	↓ LOS (5 versus 6 days, $p<0.05$)	Mild benefit, not consistent	Low
Mortality/safety	No deaths or probiotic sepsis	None reported	Safe in all trials	High (safety)

Outcomes

All three pediatric RCTs assessed fecal microbiota composition by culture or 16S rRNA sequencing. *Bifidobacterium* abundance increased significantly in intervention groups across all studies.¹⁶⁻¹⁸ Ellis and Umenai observed reduced *Enterobacteriaceae* counts compared with baseline.¹⁶⁻¹⁸ Toritsuka demonstrated partial restoration of microbiota diversity post-CPB, but the effect dissipated after 14 days.¹⁸ Similarly, adult RCTs confirmed normalisation of the microbiota and reduced levels of endotoxin-producing bacteria postoperatively in probiotic groups.^{5,19}

Biochemical markers were inconsistently reported. Ellis measured plasma cytokines (IL-6, IL-10) and intestinal fatty acid-binding protein (I-FABP) and found no significant differences between groups. Umenai found lower fecal endotoxin and improved fecal bifidobacteria-to-enterobacteria ratio in the probiotic arm, though I-FABP differences were not important. Toritsuka observed postoperative increases in I-FABP in both groups, suggesting persistent mucosal injury despite correction of the microbiota. demonstrated significantly lower AGI incidence and endotoxin levels in adults ($p<0.05$), supporting a protective effect on the gut barrier.

Two pediatric studies (Ellis, Umenai) reported no infections in either group, while Toritsuka found no significant difference between the probiotic and control arms (25.6% versus 28.2%, $p=0.78$). In adults, Yang (2025) reported significantly fewer nosocomial infections (11.5% versus 34.6%, $p=0.04$), whereas found none in either group ($n=30$). Hence, quantitative pooling of infection rates was not possible for pediatric or adult datasets due to sparse events and heterogeneous definitions of infection. While ICU length of stay (LOS) and recovery were median LOS 8 versus 9 days (intervention versus control) in Umenai. It was mean LOS 7.8 ± 2.3 versus 8.1 ± 2.5 days in Toritsuka. Although directionally shorter, differences were not statistically significant ($p>0.05$). Among adults, Yang reported a significant reduction in ICU LOS (mean 5 versus 6 days, $p=0.03$), while Liu observed similar trends without statistical testing (Tables 3-5).

Across five RCTs ($n=201$ total participants), probiotic supplementation was safe and biologically active in modulating intestinal microbiota and inflammatory markers. The clinical benefits of infection and ICU stay remain inconclusive, primarily due to limited sample sizes and event rates in pediatric studies. Adult CPB data suggest potential benefits on AGI and nosocomial infections, providing indirect support for probiotic prophylaxis in high-risk pediatric populations.

Formal assessment of publication bias (funnel plot or Egger's test) was not performed due to <10 eligible trials. Sensitivity analyses were limited to descriptive reanalysis, excluding high-risk studies, yielding consistent qualitative findings.

DISCUSSION

This systematic review synthesized all available randomized evidence evaluating the use of probiotics in pediatric cardiac surgery and relevant adult CPB contexts. Across five RCTs comprising 201 participants, probiotic supplementation consistently demonstrated safety and microbiota modulation, but the clinical benefits on infection rates or length of stay remained inconclusive. Pediatric studies, though limited in sample size, collectively showed correction of gut dysbiosis and trends toward improved intestinal barrier markers.

In adults, larger trials suggested reductions in AGI and postoperative infections, supporting the biological plausibility that probiotics may mitigate CPB-associated intestinal dysfunction.

These findings highlight that perioperative probiotic therapy is feasible and safe in both pediatric and adult cardiac-surgery patients, but definitive efficacy on hard clinical endpoints remains unproven. The evidence base is constrained by small pediatric cohorts and heterogeneity in probiotic strains, dosing, and outcome definitions.

The consistent finding across studies was improved intestinal microbiota composition following probiotic administration. *Bifidobacterium breve* and *Bifidobacterium longum* strains restored microbial diversity disrupted by perioperative antibiotics and CPB exposure.¹⁶⁻¹⁸ This aligns with studies in other surgical populations showing that probiotics replenish beneficial genera and enhance short-chain fatty acid production.²⁰

In adults, Liu et al and Yang et al reported reductions in endotoxin and IL-6 concentrations, biomarkers linked to systemic inflammation and organ dysfunction after CPB.^{5,19} These observations mirror earlier meta-analyses in general ICU populations, which show that probiotics can lower levels of inflammatory cytokines and bacterial translocation. The parallel trends across pediatric and adult trials strengthen the hypothesis that probiotic-mediated gut stabilization may modulate systemic inflammation during cardiac surgery.²¹

Despite biological plausibility, infection outcomes in pediatric studies were rare events. Both Ellis and Umenai reported no infections, whereas Toritsuka found no significant differences between groups. In contrast, Yang demonstrated a 23% absolute reduction in nosocomial infections among adults. This discrepancy may reflect differences in sample size, surgical complexity, and the maturity of gut microbiota.

A meta-analysis of probiotics in adult non-cardiac surgical reduced the risk of developing postoperative infectious complications by 37% (relative risk (RR)=0.63, 95% confidence interval (CI) 0.54-0.74, $p<0.001$), whereas pediatric cardiac-surgery data remain too limited to confirm this effect.²² Furthermore, outcome definitions varied: some trials defined infection clinically, others microbiologically, and the timing of follow-up ranged from seven days to discharge. Standardization of outcome definitions is therefore essential in future studies.

Safety is a central concern when introducing live microorganisms to critically ill children. Importantly, none of the included studies reported probiotic-related sepsis or bacteremia, corroborating systematic reviews in neonatal and ICU populations where such complications are exceedingly rare.²³ The probiotic strains used (*Bifidobacterium breve*, *Lactobacillus rhamnosus*, and *Enterococcus faecium*) have long safety records in pediatrics and are widely used in NEC prevention. The absence of mortality across all trials supports their safe perioperative use when high-quality products are employed under controlled hospital conditions.

Cardiopulmonary bypass induces systemic inflammatory response syndrome (SIRS) through ischemia-reperfusion injury, endotoxemia, and cytokine release.²⁴ Gut barrier dysfunction and translocation of lipopolysaccharides contribute to postoperative complications such as sepsis, prolonged ventilation, and multiorgan dysfunction. Probiotics may mitigate these effects via multiple

mechanisms: restoring microbial diversity and lowering intestinal pH; inhibiting pathogen overgrowth; enhancing mucosal tight junction integrity; modulating innate immunity through toll-like receptor (TLR) signaling; and producing metabolites (short-chain fatty acids) that support mucosal healing.^{25,26} In both pediatric and adult CPB contexts, these mechanisms are biologically relevant. However, the small pediatric trials were underpowered to capture clinical benefits resulting from subtle biochemical changes.

Timing of probiotic administration emerged as a crucial variable. Yang initiated supplementation 7 days preoperatively, achieving significant improvements in biomarkers, whereas pediatric trials began either immediately before or after surgery.⁵ Early initiation may be necessary to precondition the gut microbiota before CPB-induced insult. Moreover, strain selection matters: multistrain formulations with *Bifidobacterium* and *Lactobacillus* species appear synergistic, whereas single-strain trials show limited efficacy. Dose optimization and duration beyond hospital discharge warrant investigation.

Strengths

This is the first systematic synthesis focusing exclusively on perioperative probiotic therapy in pediatric cardiac-surgery patients, integrating mechanistic and clinical data from both pediatric and adult CPB RCTs. Strengths include: comprehensive multi-database search and adherence to PRISMA 2020; inclusion of both biological and clinical outcomes; dual independent screening, extraction, and risk-of-bias assessment; unlike prior probiotic reviews in general neonatal populations, this study contextualizes results within the unique inflammatory environment of CPB and uses adult evidence to strengthen mechanistic understanding.

Clinical implications

Although current evidence does not support routine use of probiotics for infection prevention after pediatric cardiac surgery, the demonstrated safety and microbiota benefits justify considering pilot implementations under research supervision. Clinicians may consider probiotics for selected stable patients once enteral feeding is initiated, provided product quality and strain documentation are ensured.

Routine prophylactic use cannot be recommended until larger multicenter RCTs establish efficacy. However, the consistent safety findings, along with the sound mechanistic rationale, clearly indicate the importance of pursuing further investigation rather than discontinuing this strategy.

Research implications

Future pediatric probiotic trials should be multicenter with at least 200 participants, stratified by age and surgery type.

Standardized multistrain formulations, such as *Bifidobacterium breve* and *Lactobacillus rhamnosus*, are recommended. Supplementation needs to start 5-7 days before surgery and continue for a minimum of two weeks postoperatively. Clinical outcomes infection, ICU length of stay, and feeding tolerance should be uniformly reported using validated definitions. Rigorous design and outcome consistency will enhance the reliability of future findings.

Limitations

Despite rigorous methods, the review is limited by the inclusion of only five RCTs, restricting quantitative synthesis and generalizability. Potential unpublished or non-indexed studies may have been missed. Variation in probiotic formulations hinders direct comparisons, and pooled meta-analysis for infection outcomes was not feasible due to zero-event trials. These challenges reflect the emergent evidence base; larger collaborative studies are needed to address sample-size limitations.

CONCLUSION

Perioperative probiotic supplementation in children undergoing cardiac surgery appears safe, biologically active, and feasible, but current evidence is insufficient to confirm clinical efficacy. Microbiota modulation and improved gut barrier markers suggest a protective mechanism analogous to that observed in adults, yet pediatric RCTs remain underpowered to demonstrate outcome benefits. Larger, standardized trials ideally harmonized with adult protocols are warranted to determine whether probiotics can translate biological plausibility into tangible clinical improvement. Until then, probiotics in pediatric cardiac ICUs should remain an experimental adjunct used within research frameworks.

ACKNOWLEDGEMENTS

Authors would like to acknowledge the supervision received from consultants in Pediatric CSICU, Dr. Reem Beherei, Dr. Yasser Alheraish, and Dr. Khaled Alarwan.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Shahzad M, Aldughaythir MS, Alanazi F, Alanazi A, Alghamdi M, Alharbi H, et al. Probiotics in pediatric cardiac surgery: biological effects and clinical outcomes – a systematic review of randomized evidence. *Int J Contemp Pediatr* 2026;13:2322-9.