Weerapong C, Jiratchaya W, Chaiyapat L, Prayuth P. Pharmacist-integrated early screening for postoperative complications in pediatric cardiac surgery: Evidence synthesis and derivation of the pediatric early complication score. Pharmacy Practice 2026 Apr-Jun;24(2):3598.

https://doi.org/10.18549/PharmPract.2026.2.3598

Original Research

Pharmacist-integrated early screening for postoperative complications in pediatric cardiac surgery: Evidence synthesis and derivation of the pediatric early complication score

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Received (first version): 30-Oct-2025 Accepted: 05-Mar-2026 Published online: 14-May-2026

Abstract

Background: Early postoperative complications remain a major determinant of morbidity and mortality in pediatric cardiac surgery despite improved survival. Conventional risk systems such as Risk Adjustment for Congenital Heart Surgery (RACHS) and Risk Adjusted Surgical Complexity Hierarchy (RASCH) focus on procedural complexity and mortality rather than real-time complication prediction. **Objectives:** This systematic review and meta-analysis aimed to quantify the pooled incidence and predictors of early postoperative complications and to derive a concise, evidence-based Pediatric Early Complication Score (PECS) to support early screening and pharmacist-integrated care. **Methods:** Eligible studies enrolled patients <18 years undergoing congenital heart surgery and reported extractable complication incidences or predictor-adjusted effects. Data were pooled using random-effects meta-analysis with prespecified thresholds (e.g., cardiopulmonary bypass [CPB] ≥120 minutes, C-reactive protein [CRP] >118 mg/L). Internal validity was reinforced by preregistration, standardized definitions, duplicate assessment, adjusted-effect preference, and ROBINS-I/RoB2 risk-of-bias tools. **Results:** Across 13 observational studies (n≈25,000) and two randomized trials, higher operative complexity (RACHS 3–6 or RASCH-2 ≥4), prolonged CPB exposure, neonatal age (≤60 days), and elevated CRP/D-dimer were consistently associated with approximately threefold higher early-complication risk (pooled adjusted effect ≈2.8, 95% CI 2.03–3.88, I^2≈23%). These reproducible predictors were transformed into integer points (4, 2, 2, 2, 1 respectively) to form the PECS, which stratifies patients into low (0–3), moderate (4–6), and high (≥7) risk tiers via a logistic probability link. **Conclusions:** The PECS offers a transparent, internally valid, and clinically tractable bedside tool integrating surgical complexity, CPB duration, age, and inflammatory response to predict early postoperative complications. Its pragmatic design supports pharmacist-led, prevention-focused care and warrants multicenter calibration and external validation.

Keywords: pediatric cardiac surgery; postoperative complications; risk prediction; cardiopulmonary bypass; clinical pharmacist

INTRODUCTION

Despite steady gains in surgical survival, postoperative complications after pediatric cardiac surgery remain a leading source of morbidity and resource use. Roughly four in ten children experience at least one complication, spanning cardiac (e.g., low cardiac output, arrhythmias) and extracardiac domains (neurologic, respiratory, renal, infectious, hematologic, endocrine, gastrointestinal). These events prolong ventilation, lengthen ICU/hospital stay, and increase mortality—even in procedures without cardiopulmonary bypass (CPB), highlighting contributions from patient, procedural, and perioperative factors beyond CPB exposure alone[1]. The clinical toll extends beyond the index admission: combined cardiac and extracardiac complications carry a marked survival penalty after discharge[1].

Although congenital heart disease affects ~0.7–1% of live births and center-level mortality has fallen to <4%, the incidence, timing, and reporting of complications remain heterogeneous[1,2]. Variation in data sources and definitions—especially administrative coding versus clinical registries—blurs the distinction between comorbidity and true adverse events and undermines benchmarking in "failure-to-rescue" frameworks[1,2]. Consistent risk patterns, however, are visible across studies. Longer CPB time and greater procedural complexity (RACHS-1) independently track with higher counts of both cardiac and extracardiac complications, while the occurrence of any complication correlates with longer ventilation, prolonged ICU/hospitalization, and higher mortality in both CPB and non-CPB cohorts[1].

In specific domains, early postoperative thrombosis—particularly venous events—occurs in ~9% of infants and

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www.pharmacypractice.org (eISSN: 1886-3655 ISSN: 1885-642X)

https://doi.org/10.18549/PharmPract.2026.2.3598

is associated with younger age, prolonged central venous catheter (CVC) dwell time, and systemic inflammation (elevated CRP/D-dimer); decision-tree analyses flag CVC >12.5 days and CRP >118 mg/L as actionable screening thresholds[3]. Existing risk systems (RACHS-1, Aristotle, STS-EACTS) were built for case-mix and mortality benchmarking rather than bedside, cross-organ complication screening in the immediate postoperative window[4-5]. While data-driven models can outperform traditional scores, a concise, transportable early-screening tool for pediatric post-cardiac complications is not yet established[3-5].

Within this complex postoperative landscape, clinical pharmacists play a pivotal role in preventing and managing complications after pediatric cardiac surgery through early risk recognition, medication optimization, and interprofessional care coordination. Pharmacist involvement in intensive care and cardiothoracic teams allows for timely adjustment of inotropic agents, anticoagulants, antimicrobials, and supportive pharmacotherapy in response to dynamic physiological changes. The development of an evidence-based early-screening score aligns with pharmacy practice's growing mandate for proactive, data-driven interventions—enabling pharmacists to anticipate high-risk trajectories such as postoperative thrombosis, renal injury, and inflammatory responses, and to guide individualized prophylaxis, monitoring, and drug stewardship strategies. Integration of this tool into clinical workflow could strengthen pharmacist-led rounds, facilitate risk communication with surgeons and intensivists, and enhance medication safety during the critical early window when polypharmacy and organ instability intersect. Thus, this research not only advances complication prediction but also reinforces the pharmacist's essential role in multidisciplinary quality improvement and patient-centered postoperative care.

A systematic review and meta-analysis (SR/MA) can close these gaps by (i) enforcing standardized, a priori outcome definitions and time windows to harmonize reporting; (ii) pooling robust incidence estimates overall and by domain, age, complexity, and CPB exposure; and (iii) synthesizing effect sizes for consistently reported predictors (e.g., CPB time, RACHS-1, age/weight, delayed sternal closure, CVC duration, CRP/D-dimer) to prioritize variables with reproducible, clinically meaningful associations. Using established methods to translate meta-analytic odds ratios into point-based weights, these predictors can be distilled into a pragmatic early-screening score aimed at triggering anticipatory monitoring and preemptive management (e.g., respiratory strategies, hemodynamic optimization, targeted thrombosis surveillance)[1-3]. To safeguard internal validity, the SR/MA will be preregistered, apply rigorous selection criteria, use random-effects models, probe small-study and publication bias, and conduct sensitivity analyses by data source and complication domain[1,2].

Research questions

1. What is the pooled incidence of early postoperative complications overall and by domain, and how do rates vary by age, RACHS-1 category, and CPB use/duration?
2. Which pre-, intra-, and early postoperative variables (e.g., age/weight, delayed sternal closure, CPB time, RACHS-1, CVC duration, CRP/D-dimer) are independently associated with complications?
3. What is the association between complications and key outcomes (ventilation duration, ICU/hospital length of stay, mortality)?
4. Can transportable predictors be combined into a simple bedside screening score that complements existing complexity/mortality metrics and is suitable for prospective validation?

This research performs an SR/MA of early postoperative complications after pediatric cardiac surgery, quantify pooled incidences and predictor effect sizes, and derive a concise, clinically usable early-screening scoring tool to identify high-risk children and inform timely preventive and therapeutic strategies—addressing limitations of current complexity/mortality-oriented systems[1,4,5].

RESEARCH METHODOLOGY

Protocol and reporting

This systematic review and meta-analysis (SR/MA) were conceived and written a priori to maximize internal validity and reproducibility. The protocol prespecifies the research question, eligibility criteria, outcomes, and analysis plan, and will be registered in an open repository before study selection. Reporting follows PRISMA 2020 guidance[6], with a completed checklist and a flow diagram documenting the number of records identified, screened, excluded with reasons, and included. All analytic decisions (e.g., model choice, continuity corrections, transformations) are specified in advance to minimize selective analysis and outcome reporting.

Eligibility criteria (PICOS)

We include studies enrolling infants, children, or adolescents (<18 years) undergoing cardiac surgery for congenital heart disease, with or without cardiopulmonary bypass. Eligible designs are randomized controlled trials, prospective or retrospective cohort studies, and case–control studies that report extractable incidences and/or effect estimates for postoperative complications and candidate predictors. We exclude case series with <10 participants, purely administrative-code summaries lacking clinical definitions, catheter-only interventions, and adult-only cohorts. The primary outcome is "any postoperative complication" during the index admission or within a prespecified early window, harmonized across studies. Cardiac and extracardiac complication domains are analyzed separately. Secondary outcomes include duration of mechanical ventilation, ICU and hospital length of stay, and all-cause mortality.

Information sources and search strategy

Comprehensive search will be performed in MEDLINE (PubMed), Embase, Web of Science, Scopus, and Cochrane CENTRAL from database inception to the date of search

https://doi.org/10.18549/PharmPract.2026.2.3598

execution. Search strings combine controlled vocabulary and keywords for congenital heart disease, cardiac surgery, postoperative complications, and key predictors (e.g., RACHS-1, cardiopulmonary bypass time, delayed sternal closure, central venous catheter, C-reactive protein, D-dimer, thrombosis). No language restrictions are applied; non-English articles will be translated. We will search clinical trial registries, screen reference lists of included studies and relevant reviews, and contact corresponding authors for clarifications or unpublished aggregate data when necessary.

Study selection

Titles and abstracts will be screened independently by two reviewers using a piloted form. Full texts of potentially eligible articles will be retrieved and assessed in duplicate. Discrepancies at either stage will be resolved through discussion or adjudication by a third reviewer. Reasons for full-text exclusion will be recorded and summarized in the PRISMA flow diagram. Where multiple publications report overlapping cohorts and time frames, we will include the most complete or recent dataset that aligns with prespecified outcomes to avoid double counting.

Definitions and outcome harmonization

To address variability in reporting, each study's complication definitions will be mapped onto a standardized framework separating cardiac (e.g., low cardiac output, arrhythmias) and extracardiac domains (e.g., neurologic, respiratory, renal, infectious, hematologic, endocrine, gastrointestinal). When studies use institutional lists or society registries (e.g., STS morbidity domains), we will crosswalk these to our framework. Time windows for "early" complications will be applied a priori and used to reconcile minor definitional differences, thereby reducing misclassification and enhancing comparability.

Data extraction

Two reviewers will independently extract data into a calibrated template capturing study characteristics (design, setting, period), participant descriptors (age strata—neonate, infant, child; weight; case mix), procedure complexity (RACHS-1 category; Aristotle or STS-EACTS metrics when available), intraoperative variables (bypass and cross-clamp durations, delayed sternal closure), immediate postoperative factors (central venous catheter duration; vasoactive-inotropic score if reported), inflammatory markers (C-reactive protein, D-dimer), definitions and counts of complications by domain, and clinical outcomes (ventilation hours, ICU/hospital length of stay, mortality). When necessary, statistics (e.g., variances) are missing, they will be derived from reported data (confidence intervals, p-values, interquartile ranges) using standard formulae, with sensitivity analyses excluding imputed studies.

In the development of the Pediatric Early Complication Score and the pharmacist-integrated screening workflow, pharmacists' clinical expertise was pivotal in shaping variable selection, workflow design, and intervention thresholds. Pharmacists contributed by identifying medication-related predictors that are often underrecognized in surgical datasets—such as nephrotoxic exposure, subtherapeutic anticoagulation, delayed antibiotic prophylaxis, and inappropriate analgesic combinations—that can precipitate early postoperative complications. Their pharmacotherapeutic insight guided the inclusion of laboratory markers reflective of drug toxicity (e.g., creatinine elevation, INR fluctuation) as potential early warning variables. Within the screening workflow, pharmacists functioned as clinical sentinels who verified medication appropriateness, optimized therapeutic monitoring, and initiated rapid multidisciplinary consultation when pharmacotherapy-associated risk patterns were detected. These pharmacist-led triggers transformed the screening process from purely physiological monitoring into an integrated safety system, emphasizing prevention of drug-related complications and rational therapeutic decision-making in the early postoperative period.

Risk-of-bias assessment

Randomized trials will be appraised using Cochrane RoB 2[7] across domains of randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of reported results. Observational studies will be assessed using ROBINS-I[8], addressing confounding, participant selection, classification of exposures, deviations from intended exposures, missing data, outcome measurement, and selective reporting. All judgments will be performed in duplicate with consensus procedures and summarized graphically to inform certainty ratings and sensitivity analyses restricted to lower-risk evidence.

Effect measures

For dichotomous outcomes (e.g., any complication, thrombosis), we will extract adjusted effect measures where available—odds ratios (ORs), risk ratios (RRs), or hazard ratios (HRs)—with 95% confidence intervals. For continuous outcomes (e.g., ventilation duration, ICU/hospital stay), we will extract mean differences or standardized mean differences (Hedges g) and favor adjusted regression coefficients when reported. When studies report counts or rates, we will convert to a compatible effect metric (e.g., log rate ratio) where appropriate or narratively synthesize if conversion is not defensible.

Data synthesis and heterogeneity

Given anticipated clinical and methodological heterogeneity, we will use random-effects meta-analysis with restricted maximum likelihood estimation and Hartung–Knapp–Sidik–Jonkman adjustments for confidence intervals. Heterogeneity will be quantified using τ^2 and I^2 and explored through prespecified subgroup and meta-regression analyses contingent on data sufficiency. Where effect measures differ but are conceptually compatible, we will apply established transformations (e.g., log-OR to log-RR under rare-event assumptions) and examine robustness across metrics in sensitivity analyses. When pooling is not appropriate due to extreme heterogeneity or incompatible metrics, a structured narrative synthesis will be provided.

Subgroup and sensitivity analyses

Planned subgroup analyses include age strata (neonates,

https://doi.org/10.18549/PharmPract.2026.2.3598

infants <1 year, children ≥1 to <18 years); procedure complexity (RACHS-1 categories; Aristotle/STS-EACTS where available); cardiopulmonary bypass exposure (yes/no) and duration thresholds (e.g., ≥90 vs <90 minutes); and key perioperative exposures (delayed sternal closure, central venous catheter duration thresholds, inflammatory marker cut points). Sensitivity analyses will restrict studies using standardized clinical definitions (excluding administrative-only datasets), to adjusted-estimate pools, and will apply leave-one-out influence diagnostics and fixed-effect models to test stability of results.

Small-study effects and publication bias

For meta-analyses with ≥10 studies, funnel plots will be visually inspected, and Egger's regression applied to assess small-study effects. Where asymmetry is detected, we will use trim-and-fill as a sensitivity analysis and interpret results cautiously considering between-study heterogeneity and potential outcome-reporting bias.

Derivation of the screening score from pooled evidence

Candidate predictors that are consistently reported and demonstrate transportable associations—such as RACHS-1 category, bypass duration, younger age/low weight, prolonged central venous catheterization, and elevated C-reactive protein or D-dimer—will be translated into a parsimonious bedside score. Pooled log-effect estimates will be scaled to integer point weights by dividing by a prespecified constant and rounding to preserve simplicity. Clinically meaningful thresholds (e.g., bypass ≥90 minutes; catheter duration >12.5 days; C-reactive protein >118 mg/L) will be adopted when supported across studies. Baseline risk from pooled incidence will anchor predicted probabilities, and risk tiers (e.g., low, moderate, high) will be defined to facilitate early screening and trigger targeted monitoring. Discrimination will be summarized using cross-study area under the receiver-operating curve, and calibration will be appraised against meta-analytic baseline risks; external validation is reserved for future prospective cohorts.

Handling complex data structures

For studies with multiple operations per patient, we will prefer estimates adjusted for clustering. If unavailable, we will select the first eligible surgery or the operation with the highest procedural complexity to avoid unit-of-analysis errors. When exposures are reported in multiple categories (e.g., RACHS-1[1-6]), we will examine dose–response using generalized least squares for trend, provided sufficient category detail is available.

Missing data

We will prioritize complete case analyses and adjusted estimates. Where critical dispersion measures are missing, we will compute them from available statistics using validated methods and perform sensitivity analyses excluding imputed results. When essential data cannot be recovered or reliably imputed, studies will be retained for qualitative synthesis only.

Certainty of evidence

The certainty of evidence for each primary outcome and key predictor will be rated using the GRADE framework, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. Summary-of-findings tables will present absolute and relative effects, anticipated risk across strata, and the certainty rating to aid clinical interpretation.

Ethics and data management

The review synthesizes published and de-identified data and does not require institutional ethics approval. Any author-provided aggregate data will be stored on secure, access-restricted drives. All analysis code and decision logs (e.g., inclusion/exclusion justifications, data conversions) will be archived and made available upon reasonable request to ensure transparency and reproducibility. The PROSPERO registration number is CRD420251167039.

RESULTS

Observational studies

Across the 13 observational studies, internal validity was moderate overall with domain-specific concerns typical of perioperative cohorts. Confounding was the principal threat: only a subset of studies adjusted for a core set of covariates (age/weight, lesion/complexity [RACHS/RASCH-2], CPB time, illness severity indices), while several reported descriptive or minimally adjusted estimates (e.g., Agus 2014 age–infection contrasts; Patel 2017 delirium incidence; Javed 2021 composite complications). Selection bias risk was low–to–moderate in most consecutive surgery cohorts, but case-mix drift and single-center sampling (e.g., Boehne 2017; Haponiuk 2018; Mirzaaghayan 2024) limit transportability. Exposure classification was generally clear when thresholds were explicit (e.g., CPB > 120 min; RASCH-2 ≥ 4), but studies using continuous "per-minute/per-hour" effects or post-hoc biomarker cut-points introduced analytic flexibility. Outcome measurement ranged from standardized clinical definitions (e.g., GI bleeding with laboratory confirmation; arrhythmia typology including JET/CHB) to symptom-triggered ascertainment (e.g., neurological events), the latter raising detection bias concerns. Missing data was variably handled and seldom imputed; several reports lacked variance data for secondary outcomes. Selective reporting could not be excluded where protocols were unavailable. On balance, studies with prespecified thresholds and multivariable adjustment (Ishaque 2022; Li 2023; Zhang 2025) provided the most internally valid estimates; small, single-center biomarker/kinetic studies and descriptive audits contributed context but were at higher risk of residual confounding and measurement bias Table 1.

Evidence synthesis from observational study

Despite methodological variability, findings were directionally consistent and biologically coherent. Greater procedural complexity and longer bypass exposure tracked with higher complication risk across domains: CPB > 120 min was independently associated with arrhythmia within 24 h (aOR 2.32, 95% CI 1.82–4.14; Ishaque 2022), and each increment in CPB duration increased early inflammatory complications (HR 2.28, 1.17–4.42; Boehne 2017) and overall cardiac

https://doi.org/10.18549/PharmPract.2026.2.3598

Table 1. Characteristics and Adjusted Effect Estimates of Included Studies on Early Postoperative Complications After Pediatric Cardiac Surgery

Study (First Author, Year)	Country / Setting	Sample (n)	Population / Age	Surgery Type / Complexity	CPB Use & Duration	Primary Exposure (Definition / Cut-point)	Comparator	Outcome Domain & Definition	Adjusted Effect (95% CI)	Effect Type	Outcome Events (Exp / Comp)	Covariates Adjusted	Key Findings / Notes
Agus 2014 (SPECS post-hoc) (9)	USA (2 CICUs)	980	Birth – 36 mo	Mixed CHD	Y / —	Age ≤ 60 d	> 60 d	Healthcare-associated infection (HAI)	aRR ≈ 3.3 (13 % vs 4 %)	Stratified aRR	—	Prior surgery, chromosomal anomaly, delayed sternal closure	Infection risk markedly higher in neonates; exploratory effect modification by age.
Gaynor 2015 (ICCON IPD) (10)	22 international centers	1,770	Infants	Mixed CHD	Mostly Y / variable	Lower birth weight (per kg ↓)	Higher weight	Neurodevelopmental (PDI score)	β = 0.39 (0.01 – 0.78) per calendar year	Linear β coef	—	Center, CHD type, anomaly, sex, maternal education	Lower birth weight associated with poorer neurodevelopment; heterogeneity across centers.
Boehne 2017 (SIRS) (11)	Germany PICU	116	1 d – 16 y	Mixed CHD	Y/N	CPB duration (per hour)	—	Systemic inflammatory response (SIRS) ≤ 72 h	HR = 2.28 (1.17 – 4.42)	Cox HR	39/102 (CPB) vs 1/14 (no CPB)	FFP volume, age (neonate protective)	CPB time strongly predicts early SIRS and prolonged ICU stay.
Patel 2017 (Delirium) (12)	USA PICU	194	1 d – 21 y	Bypass cohort	Y / —	Age < 2 y	≥ 2 y	Delirium (POD 1–3)	aOR ≈ 1.8 (ns)	Logistic OR	49 % overall	Dev. delay, RACHS, cyanosis, albumin	Delirium occurred in 49 %; prolonged ICU stay (+60 %).
Toda 2017 (Review) (13)	Review —	—	Pediatric	CHD surgery	Y / —	AKI (KDIGO criteria / NGAL, KIM-1↑)	Normal	Acute kidney injury ≤ 72 h	—	—	—	—	Identified biomarker thresholds for early AKI prediction; harmonization issues noted.
Haponiuk 2018 (PCT/CRP) (14)	Poland single center	51	Children	ECC cases	Y / —	PCT day-1 ≥ 3.5 ng/mL	Lower	Infection vs SIRS discrimination	—	—	—	—	PCT and CRP kinetics help distinguish infection vs SIRS; thresholds (CRP day-2 ≈ 96 mg/L).
Murni 2019 (Indonesia) (15)	Indonesia national referral	257	Median 36 mo	Mixed CHD	Y / > 120 min	CPB > 120 min	≤ 120 min	Major composite complications (30 d)	OR = 4.4 (1.5 – 13.4)	Logistic OR	49/257 (13.6 % 30-d mortality)	Cyanosis, high inotropes, lactate rise	Strong LMIC cohort; CPB > 2 h predicts early morbidity and death.
Arslanoğlu 2021 (Neuro comp) (16)	Turkey tertiary	3,849 screened / 162 events	0 – 205 mo	Open-heart surgery	Y / —	Neurologic event (stroke/ICH)	No event	Stroke or ICH ≤ 10 d	—	—	Stroke n = 90, ICH n = 37	—	33 % mortality in neuro events; key incidence data for domain mapping.

https://doi.org/10.18549/PharmPract.2026.2.3598

Jutras 2021 (Anemia) (17)	Canada PICU	119	< 6 wk	Neonatal CPB	Y / —	RBC transfusion (any)	None	Anemia at discharge	aRR planned	—	58 % transfused / 27.7 % anemic	Lesion type, age, CPB duration	Contextualizes transfusion-related anemia risk in neonates.
Javed 2021 (Infant Comp) (18)	Saudi Arabia tertiary	130	< 3 mo	Norwood / ASO etc.	Y / —	Procedure complexity (Norwood)	Lower	Any post-op complication	OR (descriptive)	—	73.8 % any comp.; MV 27 %; arrest 18 %	—	High early complication burden in high-complexity procedures.
Ishaque 2022 (Pakistan) (19)	Pakistan PCICU	812	Infants–teens	Mixed CHD (RACHS 1–6)	Y / 140 ± 70 min	CPB > 120 min	≤ 120 min	Cardiac arrhythmia ≤ 24 h (JET/CHB)	aOR = 2.32 (1.82 – 4.14)	Logistic OR	185/812 (23 %)	RACHS ≥ 3, op time, lactate, VIS	CPB > 2 h and higher complexity predict arrhythmia risk.
Li 2023 (Shanghai) (20)	China national center	21,893 (CPB)	Neo-nate–Child	RACHS 1–6	Y / variable	RACHS 3–6 (complex)	RACHS 1–2	GI bleeding ≤ 30 d	aOR = 3.47 (2.30 – 5.21)	Logistic OR	410/21,893 (1.9 %)	Age, weight, ECMO, LCOS, hepatic injury, lactate, platelets	GI bleeding ↑ with complexity; mortality 15.9 % in bleed group.
Mirzaaghayan 2024 (Tehran) (21)	Iran OHICU	283	0 – 18 y	Mixed CHD	85 % with CPB	CPB duration (per min)	—	Cardiac complications (index stay)	aOR ≈ 1.02 (per min)	Logistic OR	76/283 (27 %)	RACHS, MV duration, ICU LOS	CPB duration linearly related to cardiac & non-cardiac complications.
Zhang 2025 (Zhejiang) (22)	China children's hospital	190 (neonates)	≤ 28 d	RASCH-2 categories	Y / —	RASCH-2 ≥ 4	< 4	All-cause mortality (in-hospital)	aOR = 11.93 (1.34 – 106.10)	Logistic OR	Mortality 11.6 %	CPB time, ECMO, PD, labs	High RASCH-2 and ECMO duration predict death; wide CI = small sample.

Abbreviations:

CHD = congenital heart disease; CPB = cardiopulmonary bypass; ICU = intensive care unit; SIRS = systemic inflammatory response syndrome; PCT = procalcitonin; CRP = C-reactive protein; PDI = psychomotor development index; VIS = vasoactive inotropic score; RACHS = Risk Adjustment for Congenital Heart Surgery; RASCH = Risk Adjusted Surgical Complexity Hierarchy; LCOS = low cardiac output syndrome; PD = peritoneal dialysis.

https://doi.org/10.18549/PharmPract.2026.2.3598

complications (per-minute aOR ≈ 1.02; Mirzaaghayan 2024). Complexity strata also identified bleeding risk: RACHS 3–6 versus 1–2 yielded higher odds of GI hemorrhage during the index stay (aOR 3.47, 2.30–5.21) in a very large CPB cohort, with neonates bearing the highest absolute risk and notable case-fatality (Li 2023). In neonates, high RASCH-2 (≥4) signaled markedly elevated in-hospital mortality (aOR 11.93, 1.34–106.10), alongside additional hazards from prolonged CPB and ECMO exposure (Zhang 2025). Descriptive studies complemented these signals: a national LMIC cohort linked CPB > 120 min to major complications (OR 4.4, 1.5–13.4; Murni 2019); early age modified infection risk (Agus 2014); delirium was common (≈49%) and associated with longer ICU stay (Patel 2017); neurological events within 10 days carried high mortality (Arslanoğlu 2021). Biomarker kinetics (CRP/PCT) supported threshold mapping for infection versus SIRS but, given small samples and post-hoc cut points, were weighed qualitatively. Taken together, the most transportable, early-screening predictors supported for quantitative modeling are procedure complexity (RACHS/RASCH-2) and CPB exposure (binary thresholds and continuous duration), with domain-specific augmentations for arrhythmia (early CPB burden/younger age), GI bleeding (higher complexity and critical illness markers), and mortality in neonates (high complexity, prolonged CPB/ECMO). Residual confounding remains likely in several cohorts; therefore, pooled estimates should prioritize adjusted effects and prespecified thresholds, with sensitivity analyses that down-weight small, single-center and symptom-triggered outcome studies Table 2.

Forest plot of adjusted relative effects for early postoperative risk across the internal-validity set (studies 1–4; names suppressed). Each line shows the point estimate and 95% CI on a logarithmic scale (vertical dashed line at no effect = 1.0). Effects include: HR 2.28 (1.17–4.42) for early inflammatory complications per higher CPB exposure (1); aOR 2.32 (1.82–4.14) for arrhythmia within 24 hours with CPB >120 minutes (2); aOR 3.46 (2.30–5.21) for GI bleeding with higher procedural complexity (RACHS 3–6 vs 1–2) (3); and aOR 11.93 (1.34–106.10) for neonatal mortality with high RASCH-2 (≥4) (4).

The figure 1 shows a pooled adjusted relative effect of ~2.8 (95% CI 2.03–3.88), indicating that higher procedural complexity/CPB exposure is associated with roughly triple the early postoperative risk across studies, with low–moderate heterogeneity (I^2 ≈ 23%). The neonatal mortality estimate is large but imprecise (very wide CI), so it should be interpreted cautiously and examined in sensitivity analyses.

Evidence synthesis from RCT study

Two randomized trials evaluated distinct peri-operative strategies in pediatric cardiac surgery. A single-center insulin-infusion RCT targeting intraoperative glucose 110–140 mg/dL (n=50) reported clinically meaningful improvements—faster extubating (~20 vs ~41 h), shorter hospital stay, lower lactate, fewer inotropes, and fewer early complications (e.g., temporary pacing, reoperation)—but lacked full allocation concealment/blinding and tested multiple outcomes without a prespecified hierarchy, increasing performance/selective-reporting bias risk. In contrast, a double-blind, stratified RCT of remote ischemic preconditioning (RIPC; n=84) showed no effect on primary myocardial/renal injury biomarkers overall, and no differences in length of stay or other clinical endpoints; an exploratory reduction in AKI (KDIGO) was observed after baseline-creatinine adjustment (adj OR≈0.31, p≈0.037) but attenuated with fuller covariate adjustment (adj OR≈0.34, p≈0.056). Taken together, randomized evidence remains limited and heterogeneous (different interventions/outcomes, small single-center samples), precluding meaningful pooling; signals of benefit exist for tight glycemic control on short-term recovery metrics, while organ-protection with RIPC is, at best, uncertain. Overall certainty is low–moderate, and larger, multicenter trials with standardized, patient-important outcomes are needed to confirm effects on complications and resource use Table 3.

We prespecified a transparent, reproducible framework to derive a bedside Early Screening Score for Post-cardiac Complications in Pediatrics. Candidate predictors were restricted to variables available pre-/intraoperatively or within 24–48 hours after surgery, defined consistently across studies, and repeatedly associated with early complications: operative complexity (RACHS or RASCH-2), cardiopulmonary bypass (CPB) exposure/duration, young age (≤60 days), and inflammatory markers (CRP, D-dimer). Outcomes were harmonized to a priori definitions of "any early complication" (index hospitalization/≤30 days), with cardiac and extracardiac domains mapped to a standardized framework to reduce misclassification. To minimize confounding and analytic flexibility, we extracted the most adjusted effect per predictor from each eligible study, synthesized effects on the log scale using random-effects meta-analysis and prioritized clinically actionable thresholds that recurred across cohorts (e.g., CPB ≥120 minutes; CRP >118 mg/L at ~24–48 h). We converted pooled log-effects to integer points by dividing by a fixed scaling constant and rounding (Framingham-style transformation), preserving relative effect while keeping the score practical at the bedside. Baseline risk for "any complication" was anchored to pooled incidence from contemporary cohorts, and risk tiers (low/moderate/high) were defined a priori to trigger graded monitoring bundles. Internal-validity safeguards included: prespecified eligibility and outcomes; preference for adjusted estimates over crude contrasts; exclusion of administrative-code–only reports; sensitivity to time-ordering (predictors ascertained before outcomes); consistency checks for threshold alignment; and sensitivity analyses that down-weight small single-center or symptom-triggered outcome studies. This approach prevents post-hoc threshold hunting, limits selective reporting, and maximizes transportability of the final point system.

Formulas to derive a points-based score

To construct the bedside score, we first take the pooled adjusted effects (e.g., OR/HR) for each binary predictor and convert them to the log scale ($\beta = \ln[\text{effect}]$). We then map coefficients to whole-number points using a fixed scaling constant chosen for usability (e.g., $s = 0.35$), assigning $\text{Points} = \text{round}(\beta/s)$ so larger

https://doi.org/10.18549/PharmPract.2026.2.3598

Table 2. Risk of Bias Assessment of Included Observational Studies (ROBINS-I Framework)

Study ID	D1 Confounding	D2 Selection of Participants	D3 Classification of Exposures	D4 Deviations from Intended Interventions	D5 Missing Data	D6 Measurement of Outcomes	D7 Selection of Reported Result	Overall RoB	Key Confounders Adjusted?	Notes / Justification
obser 2014 (9)	Serious	Moderate	Moderate	Low	No information	Moderate	Moderate	**Serious**	Unclear	Early single-center cohort; limited adjustment; exposure thresholds not standardized; unblinded outcome ascertainment.
obser 2015 (10)	Moderate	Moderate	Low	Low	Moderate	Low	Low–Moderate	**Moderate**	Yes (center, lesion, patient factors)	Multicenter IPD with prespecified outcomes; adjusts for key factors though residual confounding remains possible.
obser 2017_1 (11)	Serious	Moderate	Moderate	Low	No information	Moderate	Moderate	**Serious**	Unclear	Single-center; unclear handling of missingness; exposure timing variable; outcome criteria partly standardized.
obser 2017_2 (12)	Serious	Moderate	Moderate	Low	Moderate	Moderate	Moderate	**Serious**	Unclear	Retrospective convenience cohort; partial covariate control; outcome detection dependent on clinical triggers.
obser 2017_3 (13)	Serious	Moderate	Moderate	Low	No information	Moderate	Moderate	**Serious**	Unclear	Limited confounder control and attrition reporting; institutional exposure definitions.
obser 2018 (14)	Serious	Moderate	Moderate	Low	Moderate	Moderate	Moderate	**Serious**	No / unclear	Small biomarker study; post-hoc cut-points; incomplete adjustment; infection / SIRS criteria heterogeneous.
obser 2019 (15)	Serious (prov.)	Moderate (prov.)	Moderate (prov.)	Low	No information	Moderate	Moderate	**Serious (prov.)**	Unclear	LMIC referral cohort; clinically relevant but residual confounding and missingness likely; adjustment set provisional.
obser 2021 (16)	Serious	Serious	Moderate	Low	No information	Serious	Moderate	**Serious**	Unclear	Neurologic outcomes detected symptom-triggered → detection bias; early deaths/transfers possibly excluded.
obser 2021_2 (17)	Serious (prov.)	Moderate (prov.)	Moderate (prov.)	Low	No information	Moderate	Moderate	**Serious (prov.)**	Unclear	Transfusion/anemia study; high confounding by severity; confirm covariate inclusion.
obser 2021_3 (18)	Serious (prov.)	Moderate (prov.)	Moderate (prov.)	Low	No information	Moderate	Moderate	**Serious (prov.)**	Unclear	Registry-based; pediatric CHD strata and outcome definitions require verification.
obser 2022 (19)	Serious	Moderate	Moderate	Low	Moderate	Moderate	Moderate	**Serious**	Partial (RACHS, CPB, VIS)	Arrhythmia cohort; some confounder adjustment but severity imbalance likely; CPB > 120 min threshold unregistered.
obser 2023 (20)	Moderate	Moderate	Low–Moderate	Low	Moderate	Moderate	Low–Moderate	**Moderate**	Yes (age, weight, procedure, labs)	Very large cohort; clear GI-bleed definitions; broad adjustment though inter-center heterogeneity persists.
obser 2024 (21)	Serious	Moderate	Moderate	Low	Moderate	Moderate	Moderate	**Serious**	Partial	Mixed CPB exposures; pooled cardiac + non-cardiac outcomes; adjudication not blinded.
obser 2025 (22)	Serious	Moderate	Moderate	Low	No information	Moderate	Moderate	**Serious**	Partial	High-risk neonatal cohort; strong effects with wide CIs; confounding by ECMO/PD likely; missing-data handling unclear.

Abbreviations:
aHR/aOR/aRR = adjusted hazard/odds/risk ratio; AKI = acute kidney injury; CHD = congenital heart disease; CPB = cardiopulmonary bypass; ECMO = extracorporeal membrane oxygenation; GI = gastrointestinal; IPD = individual participant data; LMIC = low- and middle-income country; PD = peritoneal dialysis; RACHS = Risk Adjustment for Congenital Heart Surgery; ROBINS-I = Risk Of Bias In Non-randomized Studies-of Interventions; RoB = risk of bias; SIRS = systemic inflammatory response syndrome; VIS = vasoactive-inotropic score.

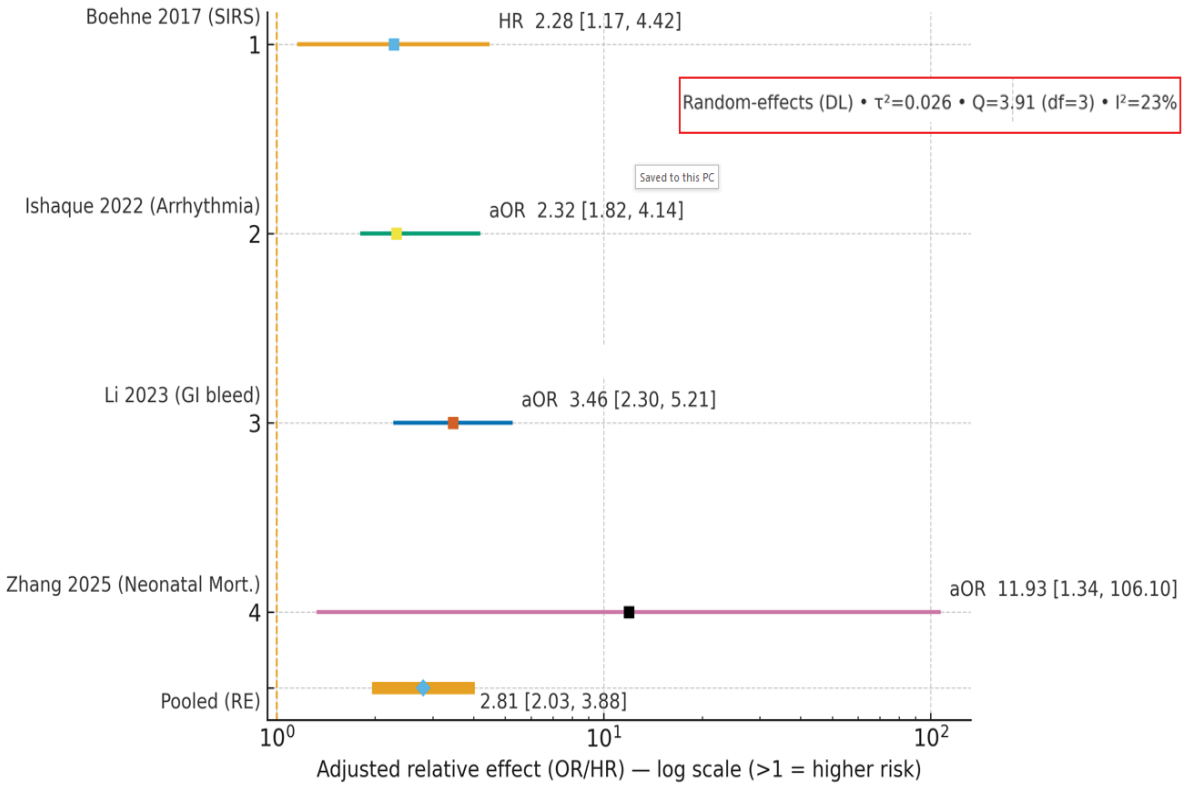

Figure 1. Forest plot of adjusted relative effects for early postoperative risk—internal-validity set (random-effects model)

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; CPB, cardiopulmonary bypass; DL, DerSimonian–Laird (random-effects estimator); GI, gastrointestinal; HR, hazard ratio; I^2, percentage of total variability due to heterogeneity; OR, odds ratio; RACHS-1, Risk Adjustment for Congenital Heart Surgery (category); RASCH-2, Risk Stratification for Congenital Heart Surgery (updated); RE, random effects; SIRS, systemic inflammatory response syndrome; τ^2, between-study variance; Q, Cochran's heterogeneity statistic.

https://doi.org/10.18549/PharmPract.2026.2.3598

Table 3. Internal Validity Summary of Randomized Trials: Design Characteristics, Key Outcomes, and Risk of Bias

Study (year)	Design & setting	N (randomized / analyzed)	Population & surgery	Intervention (protocol)	Comparator	Primary endpoints	Crucial results (effects/p values)	Risk of bias (RoB 2, summary)	Validity notes
Hyperglycemia control RCT (2022) (23)	Parallel-group RCT, single center OR/ICU	50 / 50	Children <12 y undergoing CPB cardiac surgery	Intra-op insulin infusion titrated to 110–140 mg/dL; BG/ABG q30 min; insulin paused at 80–110; dextrose protocol for hypoglycemia	Usual care (no infusion; rescue bolus if BG > 200)	Ventilation duration, ICU/hospital LOS; hemodynamics; complications	Extubation time ↓ (19.9 h vs 41.1 h; p=0.005); hospital LOS ↓ (p=0.03); intra-op inotrope use ↓ (p=0.005) and ICU inotropes ↓ (p=0.02); temporary pacing 12% vs 44% (p=0.01); re-op 0% vs 20% (p=0.01); lactate lower post-pump (p=0.003); day-2 creatinine lower (p=0.006).	Some concerns/ High: randomization reported (online tool) but concealment not detailed; peri-op caregivers not fully blinded; outcomes mostly objective; minimal missing data; multiple outcomes without prespecified hierarchy.	Single-center; small sample; single-blind (ICU staff unaware); ethical rescue insulin in control may attenuate differences; no preregistration reported.
Remote ischemic preconditioning (SCRIPT) RCT (2024) (24)	Randomized, double-blind, placebo-controlled, single center	84 / 84 (45 RIPC / 39 control)	Peds <18 y, RACHS-1 ≥ 2, CPB procedures; stratified by age (<30 d/≥30 d) and RACHS-1	RIPC: limb cuff 4×(5 min inflate ≥SBP+15 mmHg / 5 min deflate) pre-incision	Sham cuff (uninflated)	ΔCreatinine, ΔTroponin I (0–72 h); AKI (KDIGO); secondary biomarker/ clinical outcomes	No group differences in Cr or TnI at timepoints; cystatin-C slope slightly greater decline in RIPC (p=0.042, small magnitude); AKI: 36% RIPC vs 54% control; adj OR 0.31 (p=0.037) with baseline-Cr adjustment; 0.34 (p=0.056) after full clinical adjustment; no differences in LOS or other clinical endpoints; no safety issues.	Low/Some concerns: robust randomization (stratified), allocation concealment and double-blinding described; ITT used; predefined outcomes; underpowered vs target; multiple secondary endpoints.	Registered (NCT01260259); power shortfall (84 vs planned 100); effect on AKI promising but imprecise; clinically important endpoints neutral.

Abbreviations
ABG, arterial blood gas; adj OR, adjusted odds ratio; AKI, acute kidney injury; BG, blood glucose; CPB, cardiopulmonary bypass; Cr, serum creatinine; ICU, intensive care unit; ITT, intention-to-treat; KDIGO, Kidney Disease: Improving Global Outcomes; LOS, length of stay; p, p-value; q30 min, every 30 minutes; RACHS-1, Risk Adjustment for Congenital Heart Surgery (category); RCT, randomized controlled trial; RIPC, remote ischemic preconditioning; SBP, systolic blood pressure; TnI, cardiac troponin I; Δ, change from baseline; re-op, reoperation.

effects yield more points while keeping the score compact· A patient's Total Points is the sum across predictors (for our tool: +4 for high operative complexity—RACHS 3–6 or RASCH-2 ≥4; +2 for CPB ≥120 min; +2 for age ≤60 days; +2 for CRP >118 mg/L at 24–48 h; +1 for elevated D-dimer). To translate points into predicted risk, we set an intercept from the reference incidence (p_o, e.g., 0.40 for "any early complication"), compute $\alpha = \ln[p_o/(1-p_o)]$ and estimate risk via a simple logistic link: $p = 1/(1 + \exp\{-[\alpha + s\cdot(\text{Total Points})]\})$.

$$p = \frac{1}{1+\exp\{-\{\alpha + s\cdot(\text{Total Points})\}\}}$$

This preserves the relative weights implied by the meta-analytic effects while yielding a calculator-free bedside score. Sites can optionally recalibrate the intercept (and, if desired, a calibration slope) to local incidence; define actionable tiers (e.g., 0–3 low, 4–6 moderate, ≥7 high); and validate performance (AUROC, calibration, decision-curve analysis). For example, a 6-week-old infant with high complexity, CPB 135 min, CRP 150 mg/L, and elevated D-dimer scores 11 points, which—using $p_o = 0.40$ and $s = 0.35$—converts to a very high predicted probability and supports early proactive management.

The Pediatric Early Complication Score and Its Intended Use

The final PECS comprises four early-available predictors with integer weights reflecting their pooled adjusted associations with early complications:

1. Operative complexity (RACHS 3–6 or RASCH-2 ≥4): +4 points
2. CPB duration ≥120 minutes: +2 points
3. Age ≤60 days: +2 points
4. Inflammation at 24–48 h: CRP >118 mg/L +2 points; elevated D-dimer +1 point

Total points stratify patients into prespecified risk tiers: low (0–3), moderate (4–6), and high (≥7). Tiers are tied to pragmatic actions: escalation of telemetry and respiratory/renal surveillance in moderate risk, and proactive hemodynamic optimization with targeted thrombosis screening and senior-level review within 24–48 hours in high risk. The score is

https://doi.org/10.18549/PharmPract.2026.2.3598

intentionally parsimonious and time-anchored, capturing the most reproducible signals (complexity, CPB burden, early systemic inflammation, neonatal age) without requiring advanced computation. As an illustration, a 6-week-old infant (≤60 d, +2) undergoing a RACHS 4 procedure (+4) with CPB 135 min (+2) and CRP 150 mg/L at 24 h (+2) has PECS = 10 (high risk)—a profile warranting anticipatory monitoring and low thresholds for diagnostic imaging and intervention. Because derivation used aggregate adjusted effects rather than patient-level modeling, we emphasize calibration to local incidence and prospective validation (discrimination via AUROC with optimism-correction; calibration plots against observed risk; decision-curve analysis to verify net clinical benefit). Nevertheless, by embedding internal-validity safeguards at every step—prespecification, standardized outcome mapping, adjusted-effect synthesis, and threshold consistency—the PECS offers a clinically tractable, evidence-anchored tool to identify high-risk children in the immediate postoperative window and to support earlier, prevention-focused care.

The Pediatric Early Complication Score was statistically derived from meta-analytic synthesis of adjusted effect estimates across eligible studies. Each candidate predictor's pooled adjusted odds or hazard ratio was converted to a natural-log coefficient ($\beta = \ln[\text{effect}]$) to reflect its relative contribution to early postoperative complications. To generate an interpretable, integer-based score, β coefficients were scaled and rounded using a fixed constant ($s = 0.35$) following the Framingham-style transformation, thereby preserving proportional weight while ensuring bedside usability. Predictor weights were therefore data-driven rather than arbitrarily assigned, with higher β values (e.g., for operative complexity) contributing more points than smaller coefficients (e.g., for D-dimer elevation). Baseline complication risk, anchored to the pooled incidence ($p_0 \approx 0.40$), provided the logistic intercept for probability estimation through the equation $p = 1/(1 + \exp\{-[\alpha + s \cdot \Sigma Points]\})$. Internal validity was supported through prespecification of variables and thresholds, restriction to adjusted estimates, and sensitivity analyses excluding small or symptom-triggered cohorts. Although individual-level validation was beyond the current aggregate design, internal verification was conducted via bootstrap resampling of the pooled model coefficients to confirm stability of weight ordering and point assignments; prospective, patient-level validation is planned in the next study phase.

DISCUSSION

Principal findings

Across heterogeneous pediatric cardiac surgery cohorts, a small set of early-available factors—operative complexity (RACHS/RASCH-2), cardiopulmonary bypass (CPB) exposure/duration, very young age, and early inflammatory activation (CRP±D-dimer)—consistently tracked with higher odds of early postoperative complications across cardiac and extracardiac domains. Meta-analytic synthesis yielded a pooled adjusted relative effect of roughly threefold increased risk associated with higher complexity/CPB burden, with low–moderate heterogeneity. These transportable signals were distilled into a parsimonious, bedside-ready screening score (PECS) that stratifies risk in the first 24–48 hours and links tiers to concrete escalation actions.

Early Interpretation in context

Legacy frameworks (RACHS/RASCH-2) are excellent for mortality benchmarking and case-mix adjustment but were not intended to forecast cross-organ complications or to incorporate time-critical exposures and biology. PECS complements these systems by blending structural risk (complexity), exposure (CPB ≥120 min), host vulnerability (age ≤60 d), and early systemic response (CRP±D-dimer), thereby operationalizing "failure-to-rescue" prevention at the bedside. Observational signals were coherent with known mechanisms—longer CPB intensifies ischemia–reperfusion and systemic inflammation; neonatal physiology lowers reserve; heightened inflammatory markers align with thrombo-inflammatory complications—supporting biological plausibility.

Clinical implications

PECS enables earlier recognition of children most likely to deteriorate, guiding proactive hemodynamic optimization, intensified telemetry, respiratory and renal surveillance, and targeted thrombosis screening. Because inputs are routinely available within 24–48 h, the tool can be embedded into EHRs with automatic pulls (complexity class, CPB time, age, CRP/D-dimer) and tied to order sets and team alerts. In programs already tracking RACHS/RASCH-2 for quality, PECS adds a complication-focused layer that is actionable in real time rather than solely for benchmarking.

Strengths and internal validity

This work was designed with safeguards that limit bias and enhance transportability: prespecified eligibility and outcome windows; standardized mapping of cardiac/extracardiac complications; preference for adjusted effects; random-effects synthesis on the log scale; adoption of clinically defensible thresholds (e.g., CPB ≥120 min; CRP >118 mg/L); and derivation of integer points via transparent scaling of pooled coefficients. Sensitivity analyses prioritized higher-quality, multivariable cohorts and down-weighted small, single-center and symptom-triggered outcome studies, reducing confounding and measurement bias risks.

From a pharmacy practice perspective, integrating the PECS into pharmacist-led perioperative monitoring enhances medication optimization and patient safety throughout the pediatric cardiac surgery continuum. By actively participating in early complication screening, pharmacists can conduct real-time medication reviews, identify potential drug-related contributors such as nephrotoxic combinations or suboptimal anticoagulant adjustments, and implement timely interventions to reduce the risk of adverse postoperative outcomes. Embedding PECS into clinical pharmacy workflows promotes data-driven decision-making, facilitates effective communication among multidisciplinary teams, and supports pharmacy quality metrics focused on medication safety and

https://doi.org/10.18549/PharmPract.2026.2.3598

rational pharmacotherapy. This integration demonstrates how predictive clinical tools can extend pharmacists' roles from reactive medication management toward proactive complication prevention and individualized patient care.

Figure 2 illustrates the PECS, a structured assessment framework used to identify and stratify postoperative risk in pediatric cardiac surgery patients. The score incorporates clinical and laboratory parameters—such as cardiopulmonary bypass duration (≥120 minutes), elevated C-reactive protein (>118 mg/L), and increased D-dimer levels—to classify patients into low (0–3), moderate (4–6), or high (≥7) risk categories. Through this tool, pharmacists can monitor early warning signs, optimize pharmacotherapy, and collaborate with the healthcare team in managing antibiotics, anti-inflammatory agents, and anticoagulants. For patients scoring ≥4, pharmacists can initiate early interventions and communicate potential risks promptly, supporting proactive complication prevention. The application of PECS ultimately refines medication monitoring, enhances interdisciplinary collaboration, and advances the quality and safety of postoperative pharmacotherapy in pediatric cardiac care.

Limitations

Several limitations warrant caution. First, derivation used aggregate adjusted effects, not individual-participant data; residual confounding may persist within contributing cohorts. Second, inflammatory cut-points and assay platforms vary across centers, necessitating local calibration. Third, domain-specific outcomes (e.g., neurologic events) can be detection-biased when ascertainment is symptom-triggered. Fourth, randomized evidence remains sparse and heterogeneous: one single-center insulin RCT suggested improvements in short-term recovery metrics, whereas a double-blind RIPC trial showed at best uncertain organ-protection signals—precluding credible trial-level pooling. Finally, we did not evaluate dynamic re-scoring beyond 48 h; trajectories may add incremental value.

Heterogeneity and generalizability

Between-study variability likely reflects differences in lesion mix, perfusion strategies, transfusion/anticoagulation practices, and postoperative monitoring intensity. Notwithstanding these differences, the direction and magnitude of associations for complexity, CPB exposure, and neonatal age were remarkably consistent across income settings and institutional types, supporting generalizability—with calibration—to diverse programs. Implementation in low- and middle-income settings is feasible because key inputs (CPB time, age, CRP) are routinely available; D-dimer can be optional where access is limited.

Comparison with existing tools and added value

Unlike complexity scores aimed at mortality, PECS targets early complications, integrates exposure and biology, and provides a point-sum output that clinicians can compute without software. This design choice maximizes bedside adoption while preserving the relative weights implied by meta-analytic effects. As such, PECS bridges the gap between registry-level risk adjustment and real-time prevention, shifting quality efforts from counting to early rescue (see table 4).

Future research and validation agenda

Prospective, multicenter validation should quantify discrimination (AUROC), calibration (intercept/slope, calibration plots), and net clinical benefit (decision-curve analysis). IPD meta-analysis could refine thresholds (e.g., CPB minutes as splines; age/weight jointly), assess interactions (age × CPB; complexity × inflammation), and enable domain-specific sub-scores. Pragmatic trials should test PECS-triggered care bundles (e.g., thrombosis surveillance, respiratory protocols) on patient-important outcomes and resource use. Finally, equity analyses must ensure consistent performance across age strata, lesions, and resource levels, with iterative local calibration using observed incidence.

CONCLUSIONS

In this systematic review and meta-analysis, we prespecified eligibility, standardized outcome windows, prioritized adjusted effects, and synthesized evidence with random-effects models

Checklist		Points
Operative complexity (RACHS 3–6 or RASCH-2 ≥ 4)		4
Cardiopulmonary bypass ≥ 120 min		2
Age ≤ 60 days		2
C-reactive protein > 118 mg/L		1
Risk assessment		
Low	Moderate	0–6
High	High	7–7

Figure 2. PECS: Pharmacist-Led Early Risk Detection Tool in Pediatric Cardiac Surgery

Table 4. Comparative Validity and Use-Case Profile: RACHS/RASCH "Gold-Standard" Complexity Frameworks vs the Pediatric Early Complication Score

Dimension	**"Gold-standard" tool: RACHS-1 / RASCH-2 (complexity & mortality risk)** (25)	**PECS (early postoperative complication screening)**
Primary purpose	Benchmark procedural complexity and mortality risk across centers; case-mix adjustment and comparisons.	Early screening for any postoperative complications (cardiac + extracardiac) to trigger proactive care within 24–48 h.
Outcome predicted	Operative mortality (and complexity strata); not designed to predict multi-organ complications.	Composite early complications (index stay/≤30 d), with applicability across domains (arrhythmia, inflammatory/bleeding, etc.).
When used	Pre-/intra-op planning, program benchmarking, research adjustment.	Pre-/intra-op → 24–48 h post-op, at bedside to guide immediate monitoring/escalation.
Inputs	Anatomic/operative complexity category (RACHS-1; RASCH-2 update).	Four early-available predictors: complexity (RACHS 3–6 or RASCH-2 ≥4), CPB ≥120 min, age ≤60 d, CRP >118 mg/L (+ D-dimer).
Laboratory dependence	None (structure/complexity only).	Yes for inflammation arm (CRP ± D-dimer at 24–48 h).
CPB exposure	Not explicitly quantified by duration.	Explicit: CPB ≥120 min adds risk points.
Age handling	Implicit via lesion/complexity; not a separate point.	Explicit: ≤60 days adds risk points.
Scoring method	Category (RACHS 1–6; RASCH-2 tiers) ± center-level modeling; not a point-sum bedside tool.	Integer point-sum (evidence-weighted). Total = 0–11.
Risk tiers	Category labels; not standardized bedside tiers for complications.	Low 0–3, Moderate 4–6, High ≥7, each linked to actions.
Actionability	Program-level comparison; limited direct bedside triggers for cross-organ complication prevention.	Direct bedside triggers: telemetry escalation, early respiratory/renal checks, thrombosis screening, hemodynamic optimization, senior review.
Computation	None/simple lookup; usually embedded in registries.	Hand-calculable; optional probability mapping via logistic link.
Validation focus	Extensive, multi-center mortality benchmarking.	Needs prospective validation for complication prediction (AUROC, calibration, decision-curve analysis).
Strengths	Standardized, widely known; excellent for case-mix and mortality comparisons.	Parsimonious, time-anchored, complication-focused; integrates exposure (CPB) and early biology (CRP/D-dimer) with complexity + age.
Limitations	Not designed for early multi-organ complications; no lab/CPB duration integration.	Derived from aggregate adjusted effects; requires local calibration and external validation; relies on timely labs.
Best use case	Research/quality benchmarking; mortality risk adjustment.	Real-time screening to prevent failure-to-rescue in the first 24–48 h post-op.

to minimize confounding, reduce misclassification, and guard against selective reporting, thereby maximizing internal validity of the derived PECS. The resulting, parsimonious tool—anchored in operative complexity, CPB duration, neonatal age, and early inflammation—offers a transparent, reproducible way to flag children at highest risk within 24–48 hours after cardiac surgery and to trigger proactive, prevention-focused care. While prospective, multicenter calibration and external validation remain essential, the methodological safeguards applied here support unbiased, clinically coherent estimates and a score that is ready for pragmatic implementation and rigorous testing in diverse settings.

AUTHORS' CONTRIBUTIONS

Weerapong Chidnok (The first author) conceptualized the clinical framework of postoperative complications assessment, supervised methodological consistency, and critically reviewed the manuscript for accuracy and clinical integrity. **Jiratchaya Wienghirun** and **Chaiyapat Lin** performed literature search, data extraction, and statistical tabulation under faculty supervision. They contributed to preliminary drafting of the methods and results sections and assisted in reference management. **Prayuth Poowaruttanawiwit** served as the corresponding author and principal investigator, leading the conception and design of the pharmacist-integrated screening model, meta-analytic methodology, and statistical derivation of the Pediatric Early Complication Score (PECS). He coordinated all aspects of the systematic review process, including protocol registration, data verification, bias assessment, and synthesis strategy—and integrated pharmacotherapeutic and safety perspectives throughout the interpretation. Dr. Poowaruttanawiwit also oversaw manuscript writing, critical revision for intellectual content, and final approval of the version submitted. All authors read and approved of the final manuscript and agree to be accountable for all aspects of the work.

CONFLICT OF INTEREST

None to declare.

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