Appendix B

Pediatric Life Support – 2025 Evidence Updates
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PLS 4160.02 – Extracorporeal Cardiopulmonary Resuscitation for Cardiac Arrest in Pediatrics

Worksheet Author(s): Anne-Marie Guerguerian
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:
Population: Infants and children (excluding newborn infants) with in-hospital or out-of-hospital cardiac arrest

Intervention: ECPR, including extracorporeal membrane oxygenation or cardiopulmonary bypass during resuscitation of cardiac arrest

Comparators: Conventional or manual CPR without ECPR

Outcomes: Any clinical outcome

Time frame: June 2022 to October 1, 2024

Year of last full review: (*insert year where this PICOST was most recently reviewed)*
2020 EvUP 2024
Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:
2021 ILCOR COSTR
We suggest ECPR may be considered as an intervention for selected children with in-hospital cardiac arrest refractory to conventional CPR in settings where resuscitation systems allow ECPR to be implemented (weak recommendation, very low certainty of evidence).
There is insufficient evidence in pediatric out-of-hospital cardiac arrests to formulate a recommendation for the use of ECPR.

Search Strategy:
Database searched: Medline
Time Frame: (existing PICOST) – updated from end of last search conducted for systematic review published[(1)] starting June 2022 up to October 2024
Date Search Completed: September 7, 2024, and re-run October 1, 2024.
Search Results (Number of articles identified and number identified as relevant): 61 articles found and of which 40 were included as relevant. Exclusions were adult population only, pediatric studies with the wrong population or editorials.

Summary of Evidence Update:

Relevant Guidelines or Systematic Reviews: 6 manuscripts (5 reviews and 1 ILCOR guideline).

Organization (if relevant); Author; Year Published	Guideline or systematic review	Topic addressed or PICO(S)T	Number of articles identified	Key findings	Treatment recommendations
Andre 2023[(2)]	Systematic Review of Case Reports and Case Series	Drowning and cardiac arrest with rewarming with ECMO or ECLS or ECPR	24 reports with 56 children; 44 with extracorporeal rewarming	Mortality/unfavorable outcomes are unacceptably high in ECMO-treated drowned children (≤ 6 yr, temperature ≤ 28°C). Conventional mortality rate 8%; ECMO rewarming 59% mortality.	They suggest conventional therapy (& aggressive rewarming) should be initiated for all drowned children (≤ 6 yr, temperature ≤ 28°C) with OHCA. If this therapy does not result in ROSC, a discussion of a withdrawal of intensive care might be prudent when core temperature has reached 34°C.

Sperotto 2023[3]	Narrative review	Cardiac arrest and cardiopulmonary resuscitation in pediatric cardiac disease	2 articles on ECPR & CPR	Rapid adoption occurring across cardiac centers	NA
Berg 2023[4]	Consensus Guideline	Resuscitation guidelines generated by ILCOR	4 articles in pediatrics identified in the Systematic Review[1] used to generate recommendations in pediatrics.	Observational studies in pediatric patients with IHCA. These 4 pediatric studies favored no ECPR, but the CIs, when available, were broad, and risk of bias was assessed as critical for all studies.	ECPR may be considered as an intervention for selected infants and children (eg, pediatric cardiac populations) with IHCA refractory to conventional CPR in settings where resuscitation systems allow ECPR to be well performed and implemented (weak recommendation, very low–certainty evidence). There is insufficient evidence in pediatric OHCA to formulate a treatment recommendation for the use of ECPR.
Sperotto 2023[5]	Systematic review	Trends in pediatric IHCA and mortality among children with cardiac disease in ICU	25 studies for qualitative meta-analysis and 19 for meta-analysis.	In ECMO centers, 22%(95%CI, 14%-33%) underwent ECPR, 22%(95%CI, 12%-38%) were unable to be resuscitated.	ECPR vs CPR was not the main research question and analyses are limited for this question.
Maier 2024[6]	Systematic review	Intoxication and overdoses in adults and pediatrics treated with ECMO	145 studies with 539 ECMO with 257 ECPR; 13 studies were pediatric case reports.	ECMO can be used in intoxication as a “bridge to elimination” or “bridge to antidote.” When ECMO is applied due to intoxication, the interaction of the extracorporeal circuit and toxin-removal measures must be considered.	NA
Sperotto 2024[7]	Secondary analysis of a Systematic review: meta-analysis and meta-regression	ECPR in children with cardiac disease in the ICU	9 (17,669 patients). 8 cohort studies, 1 was a case-control, 8 were retrospective, 1 was prospective, 6 were single-	Pooled 21% (95% CI, 15-29%) of pediatric cardiac disease experiencing IHCA were supported with ECPR. Meta-regression adjusted for category of patients (surgical vs.	20% of pediatric cardiac patients experiencing IHCA were supported with ECPR. ECPR use significantly increased over time. This may explain in part the increased trends in survival demonstrated for

			center, and 3 were multicenter. 7 included in meta-analysis	general cardiac), use ECPR in critically ill children with cardiac disease significantly increased over time (p = 0.026).	the cardiac ICU population.

RCT: No RCT comparing ECPR vs conventional CPR

Nonrandomized Trials, Observational Studies (in alphabetical order of last name of first author): There are 21 studies.

Study Acronym; Author; Year Published	**Study Type/Design; Study Size (N) Study Type:**	**Patient Population Inclusion Criteria:**	**Primary Endpoint and Results (include P value; OR or RR; & 95% CI) 1° endpoint:**	**Summary/Conclusion Comment(s)**
Bakos 2023[8] *PDF not retrievable*	Retrospective single center observational study from Zagreb, Croatia 2009-2020	17 ECPR/52 ECMO	Insufficient information from abstract	NA
Beni 2023[9]	ELSO Registry 2017-2019	ECPR without congenital heart disease; 567 patients	In-hospital mortality 59%. Obesity (aOR, 2.28; 95% CI, 1.21-4.31), traumatic injury (aOR, 6.94; 95% CI, 1.55-30.88) associated with greater odds of in-hospital mortality. White race (aOR, 0.64; 95% CI, 0.45-0.91), ventricular tachycardia as an initial arrest rhythm (aOR, 0.36; 95% CI, 0.16-0.78), ROSC before cannulation (aOR, 0.56; 95% CI, 0.35-0.9), and acquired cardiac disease (aOR, 0.43; 95% CI, 0.29-0.64). Respiratory disease greater odds of severe neurologic complications (aOR, 1.64; 95% CI, 1.06-2.54).	NA
Bilodeau 2024[10]	ELSO Registry 2010-2019	Pediatric OHCA (N 66) or cardiac arrest in the emergency department (EDCA) (N74) (> 28 d-< 18y)	Survival to hospital discharge 31% (20% OHCA survival vs. 41% EDCA survival, p = 0.008). In adjusted analyses, OHCA was associated with 3.9 times greater odds of mortality (95% confidence interval [CI] 1.61, 9.81) when compared to compared to EDCA. Location of cannulation was not associated with mortality (odds ratio 1.8, 95% CI 0.75, 4.3).	ECPR for pediatric patients with refractory OHCA is associated with poor survival compared to patients with EDCA.
Brunetti 2024[11]	PC4 Registry 2014-2019, 37 hospitals	ECMO use across hospitals focused on surgical hospitalizations.	ECPR rates were similar across all tertiles of ECMO use.	Incorporating adjusted ECMO use rates in quality metrics is consistent with developing non-mortality metrics of

				perioperative quality of care.
Choi 2024[12]	Multicenter retrospective study across 14 hospitals in Korea 2012-2021	255 ECPR/1032 ECMO	Overall survival rate ECPR 32.2%.	NA
Gottschalk 2023[13]	Retrospective single center case series 2005-2016 Germany	Drowning	4 of 11 survivors to hospital discharge.	NA
Gutierrez-Soriano 2023[14]	ELSO Registry 2007-2018	Myocarditis < 18 y; Pre ECMO CA or ECPR (N 273)	Focus on evaluating the impact of the interval of time between intubation and ECMO cannulation and cardiac arrest (either pre ECMO or ECPR).	Myocarditis supported with ECMO without ECPR or pre-ECMO CA have higher survival. Earlier cannulation onto ECMO after intubation is associated with improved survival-to-discharge rates.
Han 2024[15]	Retrospective review of 2013-2021 of defibrillator & bedside monitor recordings to evaluate chest compression interruptions	41 ECPR Events	Survival to hospital discharge and PCPC on discharge. Adjusting for interaction between CCI variability and duration, age, sex, location of cannulation (PICU vs. CVICU) survival to discharge was associated with lower variability in CCI duration (OR = 1.12; 95% CI, 1–1.24; p = 0.04), maximum CCI duration (OR = 0.91; 95% CI, 0.86–0.95; p < 0.001), maximum CCI duration in the final 5 minutes (OR = 0.95; 95% CI, 0.92–0.98; p = 0.001), and daytime ECPR events (OR = 3.96; 95% CI, 1.75–8.97; p = 0.001). Similar results were observed for survival with favorable neurologic outcomes.	Chest compression interruptions deserve to be studied and optimized.
Joye 2024[16]	ELSO registry 2017-2021 with ECPR > 29 d < 18y	2209 ECPR with death by neurologic criteria (DNC) in 138.	Factors associated with DNC	Older age, pre-ECPR lactate, and CO2 before and during ECMO warrant further study.
Kaku 2024[17] PDF ordered	Retrospective cohort across 4 Japanese centers 2010-2019	Pediatric ECMO cases (N 155)	Survival and neurologic outcomes across regions	NA
Kamsheh 2024[18]	KID inpatient database 2003-2016	Myocarditis treated with mechanical support with 32 ECPR cases	Overall mortality is not significantly different between those that receive VAD or combination MCS as compared to non-ECPR ECMO.	NA

Loec 2024[19]	GWTG-Resuscitation multicenter registry 2000-2021, propensity matched analysis regression & Bayesian analysis	Pediatric IHCA noncardiac illness > 30 min CPR, 875 patients, 159 ECPR and 716 CCPR.	No differences in survival to discharge ECPR group (21.4%) and C-CPR group (16.2%) in univariable analysis (p = 0.13) or propensity-weighted multivariable logistic regression (aOR ratio 1.42 [95% CI, 0.84-2.40; p = 0.19])	No significant association between ECPR and survival to hospital discharge; post hoc Bayesian analysis suggested a survival benefit (85% posterior probability).
Mowrer 2024[20]	Multi-institutional, retrospective	Pediatric oncological cases or HCT supported with ECMO (N149) with 51 with CPR before ECMO and 14 ECPR	CPR increased odds of mortality (either CPR only or ECPR). Survival to hospital discharge was 2/14 ECPR.	CPR increases odds of mortality.
Olson 2024[21]	ELSO registry 2020-2023	Pediatric OHCA, 80 cases	23/80 (30%) survived to hospital discharge. Variables associated with survival (shockable rhythm, signs of life, lactate on ECMO)	Survival rate is lower than for pediatric IHCA ECPR however higher than previously reported.
Ortmann 2023[22]	Retrospective multicenter observational study of 5 US sites 2012-2019	Pediatric IHCA > 20 min with ECPR	191 ECPR Epinephrine was not evenly distributed throughout ECPR, with 66% of doses being given during the first half. Mean number of epinephrine doses was similar between survivors and non-survivors the first 10 minutes (2.7 doses). After 10 minutes, survivors received fewer doses than non-survivors during each subsequent 10-minute interval. Adjusted survival was not different between strategy groups [OR of survival for frequent epinephrine strategy: 0.78 (95% CI 0.36–1.69), p = 0.53]. Favorable neurologic outcome rates were similar between frequent and limited epinephrine dosing.	Survivors received fewer epinephrine doses than non-survivors after the first 10 minutes of resuscitation, and continued epinephrine dosing after 10 minutes did not improve survival.
Remy 2024[23] PDF ordered	ELSO registry	Sickle cell disease 5 neonates, 95 children, 110 adults.	No pediatric survivors among the ECPR group.	NA
Schwartz 2024[24]	Secondary analysis of a 2 center prospective observational study	Pediatric ECMO, with Cardiac arrest or ECPR	Biomarker levels (Tau) were higher in patients with cardiac arrest. Higher Tau levels were associated with increased risk of death or unfavorable neurologic outcomes.	Biomarkers show promising results for neuroprognostication.
Turner 2024[25] Pdf ordered	Retrospective observational study of ECMO Survivors	Long term neurologic outcomes among 41 survivors		

Varrica 2024[26] Pdf ordered	Retrospective single center observational study 2014-2021	Post cardiotomy ECMO (N90) 21 ECPR.	Survival rate 48% ECPR and brain injury 33% in overall cohort with ECPR being a risk factor.	ECPR primary risk factor for brain injury.
Yoo 2023[27]	Retrospective single center observational study 2010-2021 in Korea	51 ECPR < 1 year age	Survival 29%. Duration of CPR before cannulation 77 minutes (IQR, 61–103 minutes) Multivariate analysis, single-ventricular physiology (odds ratio [OR], 5.05; p=0.048), open sternum status (OR, 8.69; p=0.013), and C-CPR time (OR, 1.47 per 10 minutes; p=0.021) were significant predictors of in-hospital mortality	NA
Zhao 2024[28]	Retrospective single center study in China 2007-2022	77 ECPR focused on complication rates	Smaller weight, longer CPR duration, and ECMO duration were associated with complications. Complications were associated with increased mortality.	NA

Reviewer Comments: *(including whether this PICOST should have a systematic or scoping review*)

Over the last 2 years, since the systematic review published in 2023 that supported the ILCOR recent guidelines,[4, 29] ECPR in the context of pediatric cardiac arrest has been studied in 4 systematic reviews and one narrative review (Table 1). There are 22 manuscripts published that studied pediatric ECPR; the great majority of children studied are children with cardiac disease and ICU cardiac arrest (Table 2). New in this recent set of literature are 2 publications studying non cardiac disease,[9, 19] and 2 publications studying pediatric OHCA from the ELSO registry.[10, 21] Special circumstances associated with pediatric cardiac arrest such as overdoses and drowning are showing emerging reports. The geographic diversity has increased with reports from Croatia, Korea, China. There are also publications on the quality of resuscitation measures and epinephrine dosing during ECPR. Neurologic outcomes are rarely reported among registry studies however single center studies are reporting emerging information on long-term neurologic outcomes.

It is likely that the adult resuscitation science will continue to move ahead with randomized controlled trials however, the field of pediatric resuscitation will likely remain informed from observational studies. It is urgently needed however to generate comparative studies between conventional CPR and ECPR in children, most importantly in non cardiac populations. Given the emerging evidence in non cardiac populations with IHCA and OHCA, it may be reasonable to consider a scoping review in non cardiac populations in the next 2 years.

References:

1. Holmberg MJ, Granfeldt A, Guerguerian AM, Sandroni C, Hsu CH, Gardner RM, et al. Extracorporeal cardiopulmonary resuscitation for cardiac arrest: An updated systematic review. Resuscitation. 2023;182:109665.
2. Andre MC, Vuille-Dit-Bille RN, Berset A, Hammer J. Rewarming Young Children After Drowning-Associated Hypothermia and Out-of-Hospital Cardiac Arrest: Analysis Using the CAse REport Guideline. Pediatr Crit Care Med. 2023;24(9):e417-e24.
3. Sperotto F, Gearhart A, Hoskote A, Alexander PMA, Barreto JA, Habet V, et al. Cardiac arrest and cardiopulmonary resuscitation in pediatric patients with cardiac disease: a narrative review. Eur J Pediatr. 2023;182(10):4289-308.
4. Berg KM, Bray JE, Ng KC, Liley HG, Greif R, Carlson JN, et al. 2023 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations: Summary From the Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; Education, Implementation, and Teams; and First Aid Task Forces. Circulation. 2023;148(24):e187-e280.

5. Sperotto F, Daverio M, Amigoni A, Gregori D, Dorste A, Allan C, et al. Trends in In-Hospital Cardiac Arrest and Mortality Among Children With Cardiac Disease in the Intensive Care Unit: A Systematic Review and Meta-analysis. JAMA Netw Open. 2023;6(2):e2256178.
6. Maier S, Rösner L, Saemann L, Sogl J, Beyersdorf F, Trummer G, et al. Extracorporeal Membrane Oxygenation in Intoxication and Overdoses: A Systematic Review. Thorac Cardiovasc Surg. 2024;72(4):288-95.
7. Sperotto F, Daverio M, Amigoni A, Gregori D, Dorste A, Kobayashi RL, et al. Extracorporeal Cardiopulmonary Resuscitation Use Among Children With Cardiac Disease in the ICU: A Meta-Analysis and Meta-Regression of Data Through March 2024. Pediatr Crit Care Med. 2024.
8. Bakoš M, Braovac D, Barić H, Belina D, Željko Đ, Dilber D, et al. Extracorporeal membrane oxygenation in children: An update of a single tertiary center 11-Year experience from Croatia. Perfusion. 2023;38(5):1002-11.
9. Beni CE, Rice-Townsend SE, Esangbedo ID, Jancelewicz T, Vogel AM, Newton C, et al. Outcome of Extracorporeal Cardiopulmonary Resuscitation in Pediatric Patients Without Congenital Cardiac Disease: Extracorporeal Life Support Organization Registry Study. Pediatr Crit Care Med. 2023.
10. Bilodeau KS, Gray KE, McMullan DM. Extracorporeal cardiopulmonary resuscitation outcomes for children with out-of-hospital and emergency department cardiac arrest. Am J Emerg Med. 2024;81:35-9.
11. Brunetti MA, Gaynor JW, Zhang W, Banerjee M, Domnina YA, Gaies M. Hospital variation in post-operative cardiac extracorporeal membrane oxygenation use and relationship to post-operative mortality. Cardiol Young. 2024:1-8.
12. Choi YH, Jhang WK, Park SJ, Choi HJ, Oh MS, Kwon JE, et al. Pediatric Extracorporeal Membrane Oxygenation in Korea: A Multicenter Retrospective Study on Utilization and Outcomes Spanning Over a Decade. J Korean Med Sci. 2024;39(3):e33.
13. Gottschalk U, Köhne M, Holst T, Hüners I, von Stumm M, Müller G, et al. Outcomes of extracorporeal membrane oxygenation and cardiopulmonary bypass in children after drowning-related resuscitation. Perfusion. 2023;38(1):109-14.
14. Gutiérrez-Soriano L, Becerra Zapata E, Maya Trujillo N, Franco Gruntorad GA, Hurtado Peña P. ECPR for prolonged Pediatric Cardiac Arrest, an outcome without major neurological compromise. J Extra Corpor Technol. 2023;55(4):197-200.
15. Han P, Rasmussen L, Su F, Dacre M, Knight L, Berg M, et al. High Variability in the Duration of Chest Compression Interruption is Associated With Poor Outcomes in Pediatric Extracorporeal Cardiopulmonary Resuscitation. Pediatr Crit Care Med. 2024.
16. Joye R, Cousin VL, Wacker J, Hoskote A, Gebistorf F, Tonna JE, et al. Death by Neurologic Criteria in Children Undergoing Extracorporeal Cardiopulmonary Resuscitation: Retrospective Extracorporeal Life Support Organization Registry Study, 2017–2021. Pediatric Critical Care Medicine. 2024;25(3):e149-e57.
17. Kaku N, Matsuoka W, Ide K, Totoki T, Hirai K, Mizuguchi S, et al. Survival trends of extracorporeal membrane oxygenation support for pediatric emergency patients in regional and metropolitan areas in Japan. Pediatr Neonatol. 2024.
18. Kamsheh AM, Edelson JB, Faerber J, Mondal A, Quarshie W, Edwards JJ, et al. Mechanical Circulatory Support in Pediatric Myocarditis: Support Strategies and Outcomes in a Nationally Representative Cohort. JHLT Open. 2024;3.
19. Loaec M, Himebauch AS, Reeder R, Alvey JS, Race JA, Su L, et al. Outcomes of Extracorporeal Cardiopulmonary Resuscitation for In-Hospital Cardiac Arrest Among Children With Noncardiac Illness Categories. Crit Care Med. 2024;52(4):551-62.
20. Mowrer MC, Lima L, Nair R, Li X, Sandhu H, Bridges B, et al. Pediatric Hematology and Oncology Patients on Extracorporeal Membrane Oxygenation: Outcomes in a Multicenter, Retrospective Cohort 2009-2021. Pediatr Crit Care Med. 2024.
21. Olson TL, Kilcoyne HW, Morales-Demori R, Rycus P, Barbaro RP, Alexander PMA, et al. Extracorporeal cardiopulmonary resuscitation for pediatric out-of-hospital cardiac arrest: A review of the Extracorporeal Life Support Organization Registry. Resuscitation. 2024;203:110380.
22. Ortmann LA, Reeder RW, Raymond TT, Brunetti MA, Himebauch A, Bhakta R, et al. Epinephrine dosing strategies during pediatric extracorporeal cardiopulmonary resuscitation reveal novel impacts on survival: A multicenter study utilizing time-stamped epinephrine dosing records. Resuscitation. 2023;188:109855.
23. Remy T, Jegard J, Chenouard A, Maminirina P, Liet JM, Couec ML, et al. Characteristics and outcomes of children and young adults with sickle cell disease supported with extracorporeal membrane oxygenation (ECMO): An updated analysis of the ELSO registry. Artif Organs. 2024.
24. Schwartz JM, Ng DK, Roem J, Padmanabhan N, Romero D, Joe J, et al. Higher levels of brain injury biomarker tau are associated with unfavorable outcomes in patients supported with ECMO following cardiac arrest. Resusc Plus. 2024;18:100609.
25. Turner AD, Streb MM, Ouyang A, Leonard SS, Hall TA, Bosworth CC, et al. Long-Term Neurobehavioral and Functional Outcomes of Pediatric Extracorporeal Membrane Oxygenation Survivors. Asaio j. 2024;70(5):409-16.
26. Varrica A, Cotza M, Rito ML, Satriano A, Carboni G, Saracino A, et al. Post cardiotomy extracorporeal membrane oxygenation in pediatric patients: Results and neurodevelopmental outcomes. Artif Organs. 2024.
27. Yoo BA, Yoo S, Choi ES, Kwon BS, Park CS, Yun TJ, et al. Extracorporeal Cardiopulmonary Resuscitation in Infants: Outcomes and Predictors of Mortality. J Chest Surg. 2023;56(3):162-70.
28. Zhao WT, He WL, Yang LJ, Lin R. Outcomes in pediatric extracorporeal cardiopulmonary resuscitation: A single-center retrospective study from 2007 to 2022 in China. Am J Emerg Med. 2024;83:25-31.

29. Berg KM, Bray JE, Ng KC, Liley HG, Greif R, Carlson JN, et al. 2023 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations: Summary From the Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; Education, Implementation, and Teams; and First Aid Task Forces. Resuscitation. 2024;195:109992.

Worksheet Author(s): Janice Tijssen
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:

Population: Infants and children in cardiac arrest (in or out of hospital) (excluding resuscitation at birth)

Intervention: 1) Administration of the initial dose of epinephrine earlier or later than current guideline recommendations. 2) Administration of epinephrine more or less frequently than every 3-5 minutes following the initial dose.

Comparators: Timing of administration of epinephrine in line with current guideline recommendations.

Outcomes: Clinical outcomes, including short-term survival and neurological outcomes (e.g. hospital discharge, 28-days, 30-days, and 1-month), and long-term survival and neurological outcomes (e.g. 3-months, 6-months, and 1-year).

Study designs: Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Unpublished studies (e.g., conference abstracts, trial protocols) were excluded.

Timeframe: All years and all languages were included as long as there was an English abstract

Year of last full review: 2020

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

We suggest the initial dose of epinephrine in pediatric patients with both non-shockable IHCA and OHCA be administered as early in the resuscitation as possible (weak recommendation, very-low-certainty evidence).

We cannot make a recommendation for the timing of the initial epinephrine dose in shockable pediatric cardiac arrest.

The confidence of the effect estimates is so low that we cannot make a recommendation regarding the optimal epinephrine interval for subsequent epinephrine doses in pediatric patients with IHCA or OHCA.

Current Search Strategy (for an existing PICOST) included in the attached approved PICOST

1 exp Heart Arrest/

2 Ventricular Fibrillation/

3 Tachycardia, Ventricular/

4 exp Cardiopulmonary Resuscitation/

5 heart arrest*.tw,kf.

6 cardi* arrest*.tw,kw.

7 asystole*.tw,kf.

8 ventric* fibrillation*.tw,kf.

9 ventric* tachycardia*.tw,kf.

10 pulseless electrical activity.tw,kf.

11 advanced cardi* life support.tw,kf.

12 ACLS.tw,kf.

13 resuscitat*.tw,kf.

14 CPR.tw,kf.

15 or/1-14

16 Epinephrine/

17 epinephrine.tw,kf.

18 adrenaline.tw,kf.

19 or/16-18

20 Adolescent/ or exp Child/ or exp Infant/ or (child* or p?ediatric* or kid or kids or girl or girls or boy or boys or infant or infants or baby or babies or toddler* or youth* or young or youngster* or juvenile* or minors* or teen* or adolescent* or adolescence or puber* or pubescen* or pre?school* or kindergarten* or school* or highschool* or PICU).tw,kf.

21 15 and 19 and 20

22 limit 21 to ed=19460101-20200311

23 21 not 22

Database searched: Medline

Time Frame: (existing PICOST) – updated from end of last search (please specify) March 11, 2020 to May 31, 2022

Date Search Completed: 2021-April 25, 2024

Search Results (Number of articles identified and number identified as relevant): 166/5

Summary of Evidence Update:

Relevant Guidelines or Systematic Reviews

RCT: none

Nonrandomized Trials, Observational Studies

Study Acronym; Author; Year Published	Study Type/Design; Study Size (N)	Patient Population	Primary Endpoint and Results (include P value; OR or RR; & 95% CI)	Summary/Conclusion Comment(s)
TIMING FIRST DOSE EPI- OHCA				
Amoako, 2023	1032	OHCA, North America (2011-2015)	Received epinephrine PS to at-risk of receiving epinephrine (but not yet received) for each minute: receiving epinephrine was associated with survival to hospital discharge (6.3%vs 4.1%; RR, 2.09; 95%CI, 1.29-3.40) and prehospital ROSC (17.0%vs 11.9%; RR, 1.44; 95%CI 1.09-1.91), compared with those at risk of receiving epinephrine. Epinephrine	Getting epinephrine better than not getting epinephrine for same time point (for survival), but earlier not necessarily better… and not better functional outcomes. Data 10+ years old now.

			administration was not associated with favorable functional outcome at hospital discharge (4.9%vs 3.3%; RR, 1.61; 95%CI, 0.87-2.97). Treating the timing of epinephrine administration as a continuous variable, the interaction between epinephrine administration **and time to matching was not significant** (*P* for interaction = 0.34). The median (IQR) time interval between ALS arrival and epinephrine administration was 9 (6.2-12.1) minutes.	
TIMING FIRST DOSE EPI- IHCA				
Best, 2022	25, 1 centre,	Infants only, >1min CPR	19 before 4 mins and 6 after 4 minutes; ROSC rate similar between groups. Survivors had 1 or more epinephrine doses less frequently than non-survivors (p=0.003), n= 36	Too small a sample and no adjusted analyses.
EPI DOSING INTERVAL				
Ortmann, 2023	191, 5 centres	E-CPR	the cohort was divided into <3, 3–5, and >5 min/-dose average epinephrine dosing intervals: Number of doses was similar between survivors and non-survivors during the first 10 minutes of the event at 2.7 doses. After the first 10 minutes survivors consistently received fewer epinephrine doses than non-survivors throughout all 10 min periods. There was no difference in AKI incidence or favorable neurologic outcome in survivors between the frequent and limited epinephrine groups. average interval for the total cohort was <3 min/dose in 10% of patients, 3–5 min/dose in 23%, and >5 min/dose in 67%. There was a significant variation in dosing practice between hospitals, with a range of 7–38% in the 3–5	skewed distribution of epinephrine doses given across ECPR events, suggesting that the use of average dosing interval in previous resuscitation studies may result in an incomplete understanding of how epinephrine dosing impacts outcomes, at least in longer resuscitations. No difference between groups but most in >5min group.

			min/dose group (p < 0.001). There was no statistically significant difference in survival between the three dosing interval groups, although survival for patients receiving <3 min/dose epinephrine was 25% compared to 44% and 46% respectively for the 3–5 min/dose and >5 min/dose groups.	
Kienzle, 2024	382, 18 PICUs and CICUs	0-18y IHCA	epinephrine dosing interval of less than 3 vs. greater than or equal to 3 minutes; groups were balanced on baseline and other interventions. not associated with survival with favorable neurologic outcome (adjusted relative risk [aRR], 1.10; 95% CI, 0.84–1.46; *p* = 0.48) but were associated with improved sustained return of spontaneous circulation (ROSC) (aRR, 1.21; 95% CI, 1.07–1.37; *p* < 0.01) and shorter CPR duration (adjusted effect estimate, –9.5 min; 95% CI, –14.4 to –4.84 min; *p* < 0.01). In patients administered a vasoactive infusion at the time of arrest (*n* = 200), estimated dosing intervals less than 3 minutes were associated with improved survival to hospital discharge with favorable neurologic outcome (aRR, 1.48; 95% CI, 1.0–2.1; *p* = 0.035), as well as ROSC (aRR, 1.27; 95% CI, 1.06–1.53; *p* = 0.011), shorter CPR duration (adjusted effect estimate, –11.6 min; 95% CI, –17.9 to –5.3; *p* < 0.001). The rest of the cohort had no significant outcomes. estimated intervals of 3–5 and greater than 5 minutes compared to <3 minutes	Interval of <3 minutes appears to be significantly associated with survival with FNO for children in ICU setting who are on vasoactive at start of arrest.

			were associated with longer CPR duration in the full cohort and after stratification by vasoactive infusion. intervals less than or equal to 2 minutes were associated with higher relative risk of ROSC (aRR, 1.34; 95% CI, 1.20–1.49; $p < 0.001$) and shorter Ninety-six patients (25%) had estimated dosing intervals of less than 3 minutes. Two hundred seventy-three (71%) achieved ROSC, 167 (44%) survived to hospital discharge, and 143 (37%) survived with a favorable neurologic outcome	
EPI DOSE (added for this EvUp)				
Recher, 2022	755	Prepubescent OHCA	Standard dose epinephrine vs high dose epinephrine (>20% larger SDE)- propensity score matched: There were no between-group differences in D30 survival or hospital discharge (1.7% vs. 4.2%; OR: 2.4, 95% CI: 0.84–6.81), in ROSC (21.9% vs. 23.6%; OR: 1.1, 95% CI: 0.75–1.60), and D0 survival (22.6% vs. 26.4%; OR: 1.2, 95% CI: 0.84–1.76)	The only study from the last 20 years looking at epinephrine dose.

Reviewer Comments:

As we currently don't have a recommendation for epinephrine dosing interval, it is worth considering doing a systematic review for this question.

There is still no evidence for time to first dose epinephrine for shockable rhythms and thus an SR is not justified.

Time to first dose epi- OHCA

There was one study (Amoako) which propensity-score matched 1032 patients- 716 who received epinephrine vs those at risk of receiving epinephrine for the same time point. Groups were balanced. The group receiving epinephrine was associated with survival to hospital discharge (6.3%vs 4.1%; RR, 2.09; 95%CI, 1.29-3.40) and prehospital ROSC (17.0%vs 11.9%; RR, 1.44; 95%CI

1.09-1.91), but not with favorable functional outcome at hospital discharge (4.9% vs 3.3%; RR, 1.61; 95%CI, 0.87-2.97) compared with those at risk of receiving epinephrine. Treating the timing of epinephrine administration as a continuous variable, the interaction between epinephrine administration and time to matching was not significant (*P* for interaction = 0.34). The median (IQR) time interval between ALS arrival and epinephrine administration was 9 (6.2-12.1) minutes. Data was from more than 10 years ago.

Time to first dose epi- IHCA

The only evidence was in infants from 1 centre (Best), but the sample was too small to show a difference between groups or for adjusted analyses.

Epinephrine dosing Interval

One new study (Ortmann) for IHCA patients who underwent ECPR and successful cannulation were evaluated for epinephrine dosing interval. There was no statistically significant difference in survival between the three dosing interval groups, although survival for patients receiving <3 min/dose epinephrine was 25% compared to 44% and 46% respectively for the 3–5 min/dose and >5 min/dose groups. Number of doses was similar between survivors and non-survivors during the first 10 minutes of the event at 2.7 doses. After the first 10 minutes survivors consistently received fewer epinephrine doses than non-survivors throughout all 10 min periods. There was no difference in AKI incidence or favorable neurologic outcome in survivors between the frequent and limited epinephrine groups. The average interval for the total cohort was <3 min/dose in 10% of patients, 3–5 min/dose in 23%, and >5 min/dose in 67%.

A second study (Kienzle) for IHCA in patients in a PICU or CICU evaluated average epinephrine dosing interval of less or greater than 3 minutes. Groups were balanced on pre-arrest and arrest characteristics. The group that received epinephrine at an average interval of <3 minutes had no difference in survival to hospital discharge with favorable neurological outcome. This group did a higher rate of sustained ROSC and shorter duration of CPR. In the subgroup of those who were on vasoactives at the time of the IHCA, the survival to hospital discharge with neurological favorable outcome was improved for those who received epinephrine at an interval of <3 minutes.

Reference list:

Amoako, 2023, 10.1001/jamanetworkopen.2023.5187

Ortmann, 2023, 10.1016/j.resuscitation.2023.109855

Best, 2022, https://doi.org/10.1038/s41372-022-01349-x

Kienzle, 2024, 10.1097/CCM.0000000000006334

Recher, 2022, 10.3389/fped.2022.978742

2025 Evidence Update
PLS 4090.01 – Calcium During Cardiac Arrest

Worksheet Author(s): Monica Kleinman
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question: ***(Attach SAC representative approved completed PICOST template)***

Among infants and children who are in cardiac arrest in any setting (P), does calcium administration (I), compared with no calcium administration (C), change outcome (O)? S: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion; T: All years and languages were included if there was an English abstract. The literature search was updated from November 2019 to October 2024 to cover the time period since the last systematic review.

Year of last full review: 2020

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

Routine use of calcium for infants and children with cardiopulmonary arrest is not recommended in the absence of hypocalcemia, calcium channel blocker overdose, hypermagnesemia, or hyperkalemia.

Current Search Strategy

((("calcium*" OR "calcium chloride*" OR "calcium gluconate*") AND ("cardiac arrest" OR "heart arrest" OR "Cardiopulmonary Arrest*" OR asystole*)) AND ("Cardiopulmonary Resuscitation" OR "Cardio-pulmonary Resuscitation" OR CPR)

Database searched: PubMed

Time Frame: (existing PICOST) –November 2019 – October 2024

Date Search Completed: October 26, 2024

Search Results (Number of articles identified and number identified as relevant): 339 results, 3 relevant

Summary of Evidence Update:

An ILCOR led, systematic review, including adults, children and infants on the use of calcium using cardiac arrest was conducted in 2023.[1] This systematic review did not identify beneficial effects of routine calcium administration during cardiac arrest for adult OHCA and IHCA or pediatric IHCA patients. Since the 2023 review, two additional studies non-randomized observational studies, including 5656 children both identified a significant lower rate of sustained return of spontaneous circulation, lower survival rate to hospital discharge and lower survival to discharge with favorable neurologic outcome (Table 1).[2, 3] The evidence update supports the current recommendation against routine use of calcium for infants and children during cardiac arrest. However, the systematic review in 2023 and this evidence update did not examine the use of calcium in special circumstances (eg hypocalcemia, calcium channel blocker overdose, hypermagnesemia, or hyperkalemia during cardiac arrest).

Relevant Guidelines or Systematic Reviews

Organization (if relevant); **Author;** **Year Published**	**Guideline or systematic review**	**Topic addressed or PICO(S)T**	**Number of articles identified**	**Key findings**	**Treatment recommendations**
ILCOR; Hsu CH; 2023[1]	SR	Calcium use during cardiac arrest (adults, children, infants)	Adult: 4 RCTs (OHCA), 8 observational; Pediatric: 3 observational (IHCA)	Routine calcium administration during cardiac arrest did not improve the outcome of adult OHCA or IHCA or pediatric IHCA	This systematic review did not identify beneficial effects of routine calcium administration during cardiac arrest for adult OHCA and IHCA or pediatric IHCA patients

RCT: (NONE)

Nonrandomized Trials, Observational Studies

Study Acronym; **Author;**	**Study Type/Design; Study Size (N)**	**Patient Population**	**Primary Endpoint and Results (include P value; OR or RR; & 95% CI)**	**Summary/Conclusion Comment(s)**

Year Published				
Cashen; 2023[3]	Prospective observational (secondary analysis) using propensity-weighted cohort analysis N = 1100	1) Age: PCA >/=37 weeks up to 18 yrs 2) chest compressions in one of 18 ICUs	Sustained ROSC (aOR, 0.87; CI95 0.61–1.24; p=0.445) Survival to hospital discharge (aOR, 0.68; CI95 0.52–0.89; p=0.005) Survival with favorable neurologic outcome (aOR, 0.75; CI95 0.57–0.98; p=0.038)	Use of calcium during cardiac arrest was not associated with sustained ROSC, and was associated with lower survival to discharge and lower survival to discharge with favorable neurologic outcome.
Dhillon; 2022[2]	Retrospective observational (registry database) using propensity scoring matching N = 4556	Children <18 years of age with cardiac disease Index IHCA	Survival to hospital discharge Matched cohort: 39% vs 46%; p = 0.02 Entire cohort: odds ratio [OR], 0.78 [CI, 0.64–0.95]; p = 0.01)	Calcium administration during CPR for children with cardiac disease experiencing IHCA is common and is associated with worse survival to hospital discharge.

Reviewer Comments:

The current studies confirm the existing CoSTR treatment recommendations for calcium use in pediatric cardiac arrest. Given there is no new evidence to support a change in treatment recommendation, a scoping or systematic review is not indicated.

It should be noted that the use of calcium for documented hypocalcemia, hypermagnesemia, or suspected calcium channel blocker overdose was not included in this evidence review. Further evaluation of the use of calcium in these special circumstances are required.

The use of calcium in hyperkalemia has been reviewed by the PLS Task Force separately - PLS 4160.17.

Reference list:

1. Hsu CH, Couper K, Nix T, Drennan I, Reynolds J, Kleinman M, et al. Calcium during cardiac arrest: A systematic review. Resusc Plus. 2023;14:100379.
2. Dhillon GS, Kleinman ME, Staffa SJ, Teele SA, Thiagarajan RR. Calcium Administration During Cardiopulmonary Resuscitation for In-Hospital Cardiac Arrest in Children With Heart Disease Is Associated With Worse Survival-A Report From the American Heart Association's Get With The Guidelines-Resuscitation (GWTG-R) Registry. Pediatr Crit Care Med. 2022;23(11):860-71.
3. Cashen K, Sutton RM, Reeder RW, Ahmed T, Bell MJ, Berg RA, et al. Calcium use during paediatric in-hospital cardiac arrest is associated with worse outcomes. Resuscitation. 2023;185:109673.

PLS 4080.15 – IO vs. IV

Worksheet Author(s): Janice Tijssen
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:

Population: Pediatric patients in any setting (in-hospital or out-of-hospital) with cardiac arrest

Intervention: Placement of an intraosseous (IO) cannula and drug administration through this IO during cardiac arrest

Comparator: Placement of an intravenous (IV) cannula and drug administration through this IV during cardiac arrest

Outcome: Return of spontaneous circulation, survival to hospital discharge, and survival to hospital discharge with a favorable neurological outcome

Study design: Randomized trials, non-RCTs, and observational studies (cohort studies and case-control studies) comparing IO with IV administration of drugs included; randomized trials assessing the effect of specific drugs (eg, epinephrine, amiodarone/lidocaine) in subgroups related to IO versus IV administration also included

Time frame: All years and languages were included if there was an, English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded.

Year of last full review: 2020

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

Intraosseous cannulation is an acceptable route of vascular access in infants and children with cardiac arrest. It should be considered early in the care of critically ill children whenever venous access is not readily available.

Current Search Strategy

All Ovid Medline <1946 - present>
1 exp Heart Arrest/
2 Ventricular Fibrillation/
3 Resuscitation/
4 Heart Massage/
5 exp Cardiopulmonary Resuscitation/
6 cardi* arrest*.tw,kf.
7 heart arrest*.tw,kf.
8 OHCA.tw,kf.
9 IHCA.tw,kf.
10 CPR.tw,kf.
11 advanced cardiac life support.tw,kf.
12 ACLS.tw,kf.
13 basic life support.tw,kf.
14 BLS.tw,kf.
15 asystol*.tw,kf.
16 pulseless electrical activity.tw,kf.
17 pulseless ventricular tachycardia.tw,kf.
18 (return of circulation or return of spontaneous circulation or ROSC).tw,kf.
19 resuscitat*.tw,kf.
20 ventricular fibrillation*.tw,kf.
21 chest compression*.tw,kf.
22 or/1-21

23 Infusions, Intraosseous/
24 Intraosseous.tw,kf.
25 Intra-osseous.tw,kf.
26 or/23-25
27 Infusions, Intravenous/
28 Intravenous.tw,kf.
29 Intra-venous.tw,kf.
30 Umbilical Veins/
31 (umbilical vein or umbilical veins or umbilical venous).tw,kf.
32 (venous adj3 catheter*).tw,kf.
33 (vascular adj3 catheter*).tw,kf.
34 catheterization/ or catheterization, central venous/ or catheterization, peripheral/
35 catheters/ or catheters, indwelling/ or exp vascular access devices/
36 central venous.tw,kf.
37 vascular access.tw,kf.
38 or/27-37
39 (IO adj15 IV).tw,kf.
40 (26 and 38) or 39
41 22 and 40
42 41 not (animals/ not humans/)
43 limit 42 to (case reports or comment or editorial or letter)
44 42 not 43
45 remove duplicates from 44

Database searched: Medline

Time Frame: (existing PICOST) –January 1, 2021-May 10, 2024

Date Search Completed: May 10, 2024

Search Results (Number of articles identified and number identified as relevant):

75/0

Summary of Evidence Update:

Insufficient new evidence to justify a new SR.

Relevant Guidelines or Systematic Reviews

Reviewer Comments:

No new studies since 2021. For the last EvUp in 2021, there were 2 observational studies on this topic with significant limitations. The TF feels that there is insufficient evidence to justify performing a new SR at this stage. The adults have conducted a SR for this PICOST but the PLS TF feels that the adult evidence is too indirect to be considered relevant to the infant and child population due to unique anatomical differences that make obtaining IV access more challenging in infants and children. The adult evidence may have some relevance to the adolescent population, and may be explored by the TF in the future.

2025 Evidence Update
PLS 4160.05 – Intra CA Monitoring Echocardiography POCUS

Worksheet Author(s): Andrea Christoff, Barney Scholefield

Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:

Population: Infants & Children in any setting (in-hospital or out-of-hospital) with cardiac arrest

Intervention: the presence of variables -images, cut-off values or trends- during CPR (intra-arrest) that can provide physiologic feedback to guide resuscitation efforts, namely: Echocardiography / Point of care cardiac ultrasound

Comparators: the absence of such factors -images, cut-off values or trends.

Outcomes: Any clinical outcome.

Study Designs: STEP 1: Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) that concern directly the population and intervention described above are eligible for inclusion. If it is anticipated that there will be insufficient studies from which to draw a conclusion, case series may be included in the initial search. The minimum number of cases for a case series to be included was set by the taskforce at 5 cases. Unpublished studies (e.g., conference abstracts, trial protocols) are excluded.
STEP 2: the same study designs and/or existing systematic or scoping reviews not directly concerning the population or intervention defined above but considered informative as additional evidence for the development of the final taskforce insights.

Timeframe: For STEP 1, all languages are included, as long as there is an English abstract. We searched articles from 2020 onwards. For STEP 2, if a systematic or scoping review of high quality (as per AMSTAR 2 tool) is identified, search can be limited to beyond data and/or scope of that review.

Year of last full review: *2020*

Scoping review last searched July 2020

Kool M, Atkins DL, Van de Voorde P, Maconochie IK, Scholefield BR; PLS ILCOR Task Force. Focused echocardiography, end-tidal carbon dioxide, arterial blood pressure or near-infrared spectroscopy monitoring during paediatric cardiopulmonary resuscitation: A scoping review. Resusc Plus. 2021 Mar 30;6:100109. doi: 10.1016/j.resplu.2021.100109. PMID: 34228034; PMCID: PMC8244529.

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST

Task Force insights

The PLS Task Force agreed that they would not accept direct extrapolation from adult studies as a result of substantial differences between adult and pediatric cardiac arrest in terms of causes, anatomy and technical matters that could affect the usefulness and accuracy of the bedside echocardiography. While the technology is widely used within the pediatric critical care, emergency and resuscitation communities, more data detailing its advantages, pitfalls and characteristics of performance are needed so its usefulness and limitations in pediatric cardiac arrest can be fully defined.

In addition, there is inadequate pediatric literature regarding its intra-arrest prognostic utility and the Task Force urges great caution until more literature is available.

Treatment Recommendations 2020

There is insufficient evidence to recommend for or against the routine use of echocardiography during a pediatric arrest. Echocardiography may be considered to identify potentially treatable causes of an arrest when appropriately skilled personnel are available, but the benefits must be carefully weighed against the known deleterious consequences of interrupting chest compressions.[1,2]

Current Search Strategy (for an	**Query**	**Results from 25 Jun 2024**

existing PICOST) included in the attached approved PICOST

1	exp Echocardiography, Three-Dimensional/ or exp Echocardiography/	613,392
2	exp Point-of-Care Systems/ or exp Ultrasonography/ or exp Point-of-Care Testing/	1,603,671
3	exp Pulmonary Embolism/di, dg [Diagnosis, Diagnostic Imaging]	37,428
4	*Heart Rate/de or ventricular fibrillation/ or ("ventricular fibrillation" or "heart ventricle fibrillation" or "pulseless electrical activit*" or pulselessness).tw,kf.	83,996
5	exp Heart arrest/ or (((heart* or cardiac* or cardiopulmonary or cardiovascular) adj2 arrest*) or asystol*).tw,kf.	240,585
6	exp adolescent/ or exp child/ or exp infant/ or (infant disease* or childhood disease*).ti,ab,kf. or (adolescen* or babies or baby or boy? or boyhood or girlhood or child* or girl? or infan* or juvenil* or kid? or minors or minors* or neonat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).jn,jw. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).in.	12,960,230
7	1 or 2 or 3	1,632,146
8	4 or 5	298,600
9	7 and 8 and 6	4,922
10	("28045844" or "29261563").ui.	4
11	9 and 10	2
12	limit 9 to yr="2020 -Current" [Limit not valid in DARE; records were retained]	1,929

exp Echocardiography, Three-Dimensional/ or exp Echocardiography/
exp Point-of-Care Systems/ or exp Ultrasonography/ or exp Point-of-Care Testing/
exp Pulmonary Embolism/di, dg [Diagnosis, Diagnostic Imaging]

1 or 2 or 3
4 or 5
7 and 8 and 6
("28045844" or "29261563").ui.
9 and 10
limit 9 to yr="2020 -Current"

New Search strategy: (for a new PICOST should be outlined here as per Evidence Update Process)

n/a

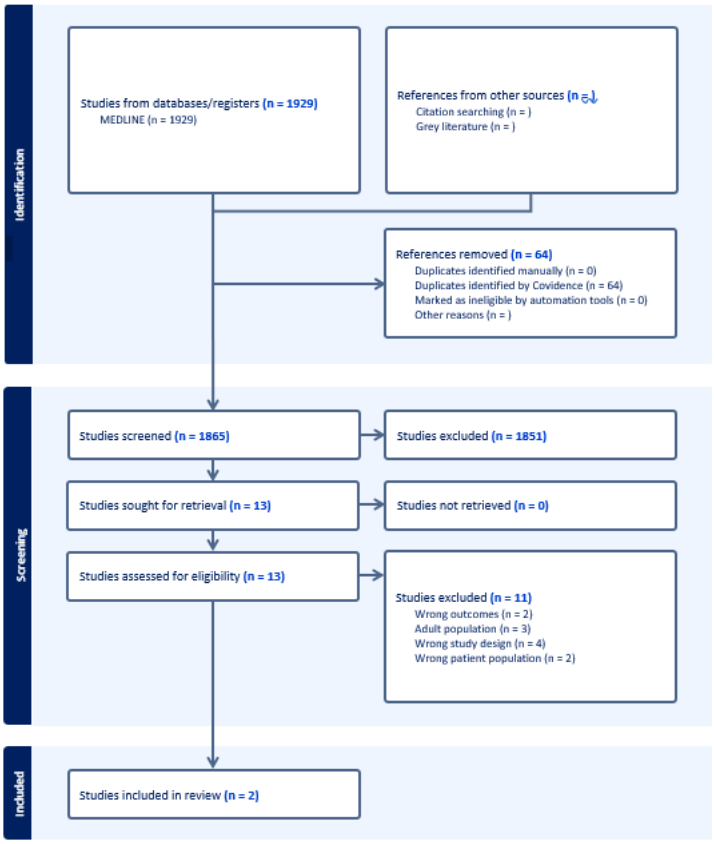
Database searched: eg Medline Embase Cochrane	Medline, Embase, Central
Time Frame: (existing PICOST) – updated from end of last search (please specify)	Last updated 25th July 2022 New Search July 2020 to 26th June 2024
Time Frame: (new PICOST) – at the discretion of the Task Force (please specify)	n/a
Date Search Completed:	26th June 2024
Search Results (Number of articles identified and number identified as relevant):	**1929 in search – 2 identified as relevant*** 

***Figure created COVIDENCE**

Summary of Evidence Update:

In the 2020 scoping review of intra-arrest monitoring[3], 2 studies were identified describing POCUS/Echo use during pediatric cardiac arrest[4,5] adding to previous case series of 14 cases in 2008[6]

The Evidence Update in 2022 identified only 1 small case series[7,8] which did not address minimizing intra-arrest compressions and focused on utility for confirming pulse checks and cardiac standstill to facilitate decision making to cease resuscitation efforts.

The Evidence Update in 2024 identified 2 studies.[9,10] The first study[9] was a retrospective review use of POCUS in the emergency department evaluating sensitivity and specificity for detecting left ventricular systolic dysfunction and pericardial effusion. Only 4 (0.9%) patients in cohort had a cardiac arrest. The POCUS exam details and patient outcomes were not reported. The second study[10] was a small case series with 3 pediatric patients describing feasibility of using echocardiography during cardiac arrest to assess ventricular contractility and pericardial effusion.

Relevant Guidelines or Systematic Reviews

Organization (if relevant); **Author;** **Year Published**	**Guideline or systematic review**	**Topic addressed or PICO(S)T**	**Number of articles identified**	**Key findings**	**Treatment recommendations**
European Resuscitation Council Guidelines 2021: Paediatric Life Support Van de Voorde P, 2021 [11]	Guideline		**2**	In their 2020 scoping review PLS 814 the ILCOR paediatric Taskforce warned against rapid implementation of POCUS in paediatric practice without sufficient evidence, despite its great potential and widespread acceptance. Acquisition and interpretation of images in children is more complex, especially in children with pre-existing heart disease. Furthermore, there are significant material and training costs which might be important in low-resource setting	We suggest the use of POCUS by competent healthcare providers, when feasible, to identify reversible causes of cardiac arrest (4H/4T). POCUS may also have role in identifying the presence of perfusion, but currently this should be only in the context of research. POCUS should currently not be used for prognostication.
American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Topjian AA et al 2020 [12]	Guideline		**3**	Several case series evaluated the use of bedside echocardiography to identify reversible causes of cardiac arrest, including pulmonary embolism. One prospective observational study of children (without cardiac arrest) admitted to an ICU reported good agreement of estimates of shortening fraction and inferior vena cava volume between emergency physicians using bedside limited echocardiography and cardiologists performing formal echocardiography.	When appropriately trained personnel are available, echocardiography may be considered to identify potential treatable causes of arrest, such as pericardial tamponade and inadequate ventricular filling, but the potential benefits should be weighed against the known deleterious consequences for

					interrupting chest compressions.

RCT: none

Nonrandomized Trials, Observational Studies

Study Acronym; Author; Year Published	**Study Type/Design; Study Size (N)**	**Patient Population**	**Primary Endpoint and Results (include P value; OR or RR; & 95% CI)**	**Summary/Conclusion Comment(s)**
Miller et al 2022[9]	Retrospective review	Pediatric N=456 POCUS exams performed 4/456 (.9%) cardiac arrest POCUS	To describe the test characteristics for POCUS performed by pediatric emergency physicians after structured training Detection of pericardiac effusion or LVSD > 90 % sensitivity and >98% specificity	Cardiac POCUS is feasible and can rapidly identify significant cardiac pathology. Not specific for intra-arrest use, only 4 arrest events reviewed and details and outcome not reported for cardiac arrest events
Azzopardi et al 2023[10]	Case study	Pediatric N=3 4yo IHCA 12 yo OHCA, no ROSC 6 yo, OHCA, no ROSC	Used to confirm cardiac standstill in 2 cases and support futility of ongoing resuscitation	Echocardiography during resuscitation is feasible and can be used for detection of contractility and pericardial effusion

Reviewer Comments:

There remains little pediatric evidence examining the use of the POCUS/echocardiography during pediatric cardiac arrest. Our evidence update only identified 2 small studies that described feasibility. Therefore, a systematic review of pediatric cardiac arrest patients is not justified at this time.

This limited evidence in pediatrics is different to the expanded body of evidence for POCUS use during cardiac arrest in adult cardiac arrest with international recommendations on practice[13].

We excluded two studies that reviewed use of POCUS in the delivery room during newborn resuscitation after birth. Both were small case series that concluded the use of ultrasound in the delivery room is feasible to detect reversible causes for cardiac arrest in the newborn infant. There was a systematic review to evaluate characteristics of POCUS in predicting poor outcomes in adult and pediatric traumatic cardiac arrest, 3 small pediatric studies were included in meta-analysis. Use of POCUS/echocardiography during delivery room resuscitation is a developing body of evidence they may contribute to future recommendations.

The Treatment Recommendation of 2020 has been downgraded to a GPS based on a rigorous scoping review in 2020 and evidence updates in 2022 and 2024

Good Practice Statement

For children in cardiac arrest, echocardiography may be considered to identify potentially treatable causes when appropriately skilled personnel are available, but the benefits must be carefully weighed against the known deleterious consequences of interrupting chest compressions

References

1. de Caen AR, Kleinman ME, Chameides L, Atkins DL, Berg RA, Berg MD, et al. Part 10: Paediatric basic and advanced life support: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. Resuscitation. 2010;81 Suppl 1:e213-59.
2. Kleinman ME, Chameides L, Schexnayder SM, Samson RA, Hazinski MF, Atkins DL, et al. Part 14: pediatric advanced life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010;122(18 Suppl 3):S876-908.
3. Haddaway NR, Page MJ, Pritchard CC, McGuinness LA. PRISMA2020: An R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and Open Synthesis. Campbell Systematic Reviews. 2022;18(2):e1230.
4. Kool M, Atkins DL, Van de Voorde P, Maconochie IK, Scholefield BR, Force PIT. Focused echocardiography, end-tidal carbon dioxide, arterial blood pressure or near-infrared spectroscopy monitoring during paediatric cardiopulmonary resuscitation: A scoping review. Resusc Plus. 2021;6:100109.
5. Morgan RW, Stinson HR, Wolfe H, Lindell RB, Topjian AA, Nadkarni VM, et al. Pediatric In-Hospital Cardiac Arrest Secondary to Acute Pulmonary Embolism. Crit Care Med. 2018;46(3):e229-e34.
6. Tsung JW, Blaivas M. Feasibility of correlating the pulse check with focused point-of-care echocardiography during pediatric cardiac arrest: a case series. Resuscitation. 2008;77(2):264-9.
7. Leviter JI, Chen L, O'Marr J, Riera A. The Feasibility of Using Point-of-Care Ultrasound During Cardiac Arrest in Children: Rapid Apical Contractility Evaluation. Pediatr Emerg Care. 2022.
8. Leviter JI, Walsh S, Riera A. Point-of-Care Ultrasound for Pulse Checks in Pediatric Cardiac Arrest: Two Illustrative Cases. Pediatr Emerg Care. 2022.
9. Miller AF, Piyawat A, Gravel CA, Viera RL, et al. Use of Cardiac Point-of Care Ultrasound in the Pediatric Emergency Department. Pediatr Emerg Care. 2022
10. Azzopardi E, Grech E, Grech V. Point of Care cardiac Ultrasonography in Three Paediatric Arrests.Malta Med J. 2023
11. Van de Voorde P, Turner NM, Djakow J, de Lucas N, Martinez-Mejias A, Biarent D, et al. European Resuscitation Council Guidelines 2021: Paediatric Life Support. Resuscitation. 2021;161:327-87.
12. Topjian AA, Raymond TT, Atkins D, Chan M, Duff JP, Joyner BL, Jr., et al. Part 4: Pediatric Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020;142(16_suppl_2):S469-s523.
13. Avila-Reyes D, Acevedo-cardona AO, Gomez-Gonzalez JF, Echeverry-Piedrahita DR, Aguirre-Florez M, Giraldo-Diaconeasa A. Point-of-care ultrasound in cardiorespiratory arrest (POCUS-CA): narrative review article. Ultrasound J. 2021;13(1):46.

2025 Evidence Update
PLS 4160.07 – Intra Cardiac Arrest Monitor – ETCO2

Worksheet Author(s): Andrea Christoff, Barney Scholefield
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:

Population: Infants & Children in any setting (in-hospital or out-of-hospital) with cardiac arrest

Intervention: the presence of variables -images, cut-off values or trends- during CPR (intra-arrest) that can provide physiologic feedback to guide resuscitation efforts, namely:

End-tidal carbon dioxide (CO2)

Comparators: the absence of such factors -images, cut-off values or trends.

Outcomes: Any outcome as defined in the Pediatric Core Outcome Set for Cardiac Arrest

Study Designs: STEP 1: Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) that concern directly the population and intervention described above are eligible for inclusion. If it is anticipated that there will be insufficient studies from which to draw a conclusion, case series may be included in the initial search. The minimum number of cases for a case series to be included was set by the taskforce at 5 cases. Unpublished studies (e.g., conference abstracts, trial protocols) are excluded.

STEP 2: the same study designs and/or existing systematic or scoping reviews not directly concerning the population or intervention defined above but considered informative as additional evidence for the development of the final taskforce insights.

Timeframe: For STEP 1, all languages are included, as long as there is an English abstract. We searched articles from 2020 onwards. For STEP 2, if a systematic or scoping review of high quality (as per AMSTAR 2 tool) is identified, search can be limited to beyond data and/or scope of that review.

Scoping review last searched September 2020

Kool M, Atkins DL, Van de Voorde P, Maconochie IK, Scholefield BR; PLS ILCOR Task Force. Focused echocardiography, end-tidal carbon dioxide, arterial blood pressure or near-infrared spectroscopy monitoring during paediatric cardiopulmonary resuscitation: A scoping review. Resusc Plus. 2021 Mar 30;6:100109. doi: 10.1016/j.resplu.2021.100109. PMID: 34228034; PMCID: PMC8244529.[1]

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

Task Force insights

Use of ETCO2 monitor for intubation and airway management is established. The Task Force therefore focused on the role of ETCO2 measurement on quality of CPR and impact on patient level outcome (ROSC, survival, favorable neurological outcome). There is available pediatric data that suggests monitoring end tidal CO2 contributes to improved quality of CPR and to the adherence of current guidelines. However, more evidence is required to assess the association between intra-arrest end tidal CO2 monitoring and outcomes in children and the Task Force cannot make a recommendation for or against targeting end tidal CO2 during pediatric cardiac arrest. Specific ETCO2 values to guide therapy have not been established in children[1]

Current Treatment Recommendations Based on 2015 TR – Non GRADE systematic review

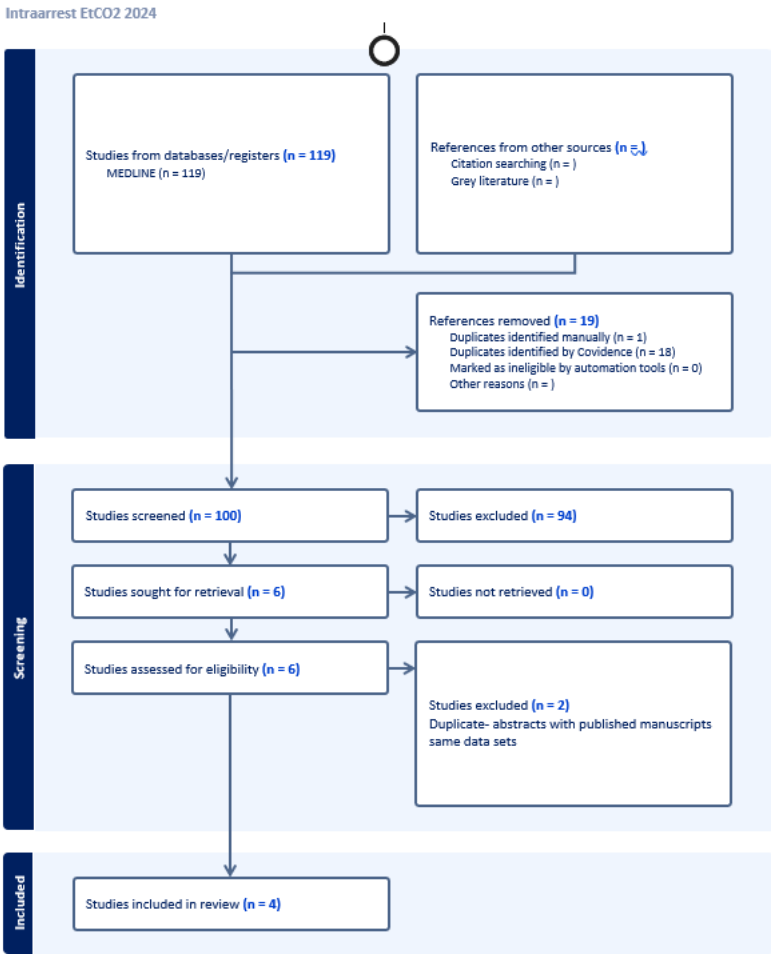
The PLS Task Force agreed that the evidence for or against the use of ETCO2 to guide resuscitation efforts and improve pediatric cardiac arrest outcomes is insufficient to recommend consideration of a SysRev. As a result, the 2015 treatment recommendation remain[1-3]

Current Search Strategy (for an existing PICOST) included in the attached approved PICOST	**Query**	**Results from 25 Jun 2024**	
	1	exp capnography Capnography/ or Carbon Dioxide/an	22,394
	2	(end-tidal or end-tidal carbon dioxide or etco2 or end-tidal CO2 or end tidal).mp. [mp=ti, bt, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, sy, ux, mx, tn, dm, mf, dv, dq, tx, kw, ct]	32,464
	3	*Heart Rate/de or ventricular fibrillation/ or ("ventricular fibrillation" or "heart ventricle fibrillation" or "pulseless electrical activit*" or pulselessness).tw,kf.	83,996
	4	exp Heart arrest/ or (((heart* or cardiac* or cardiopulmonary or cardiovascular) adj2 arrest*) or asystol*).tw,kf.	240,585
	5	exp adolescent/ or exp child/ or exp infant/ or (infant disease* or childhood disease*).ti,ab,kf. or (adolescen* or babies or baby or boy? or boyhood or girlhood or child* or girl? or infan* or juvenil* or kid? or minors or minors* or neonat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).jn,jw. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).in.	12,960,230
	6	1 or 2	53,837

	7	3 or 4	298,600
	8	6 and 7 and 5	428
	9	("38088765" or "37929615").ui.	3
	10	8 and 9	2
	11	limit 8 to yr="2020 -Current" [Limit not valid in DARE; records were retained]	119

exp capnography Capnography/ or Carbon Dioxide/an
(end-tidal or end-tidal carbon dioxide or etco2 or end-tidal CO2 or end tidal).mp. [mp=ti, bt, ab, ot, nm, hw, fx, kf, ox, px, rx, ui, sy, ux, mx, tn, dm, mf, dv, dq, tx, kw, ct]
Heart Rate/de or ventricular fibrillation/ or ("ventricular fibrillation" or "heart ventricle fibrillation" or "pulseless electrical activit" or pulselessness).tw,kf.
exp Heart arrest/ or (((heart* or cardiac* or cardiopulmonary or cardiovascular) adj2 arrest*) or asystol*).tw,kf.
exp adolescent/ or exp child/ or exp infant/ or (infant disease* or childhood disease*).ti,ab,kf. or (adolescen* or babies or baby or boy? or boyhood or girlhood or child* or girl? or infan* or juvenil* or kid? or minors or minors* or neonat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).jn,jw. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).in.
1 or 2
3 or 4
6 and 7 and 5
("38088765" or "37929615").ui.
8 and 9
limit 8 to yr="2020 -Current"

New Search strategy: (for a new PICOST should be outlined here as per Evidence Update Process)	n/a
Database searched: eg Medline Embase Cochrane	Medline, Embase, Central
Time Frame: (existing PICOST) – updated from end of last search (please specify)	Prior Scoping Review published March 2021 This search covered Jan 2020 to 26th June 2024

Time Frame: (new PICOST) – at the discretion of the Task Force (please specify)	n/a
Date Search Completed:	26th June 2024
Search Results (Number of articles identified and number identified as relevant):	

Summary of Evidence Update:

Evidence Update in 2022 identified one randomized clinical trial[4] four observational studies[5-8] and one systematic review of pediatric extracorporeal resuscitation[9] that reported end-tidal CO2 monitoring during CPR and/or patient outcomes. One observational study demonstrated an association between end tidal CO2 monitoring and ROSC in adolescents. Overall, the evidence did not support an association between monitoring end tidal CO2 with ROSC, survival to hospital discharge or survival with favorable neurologic outcome. However, the evidence did support an association with chest compression depth and adherence to resuscitation guidelines for metric targets for CPR quality.

Evidence Update in 2024 included the observational study[5] published in 2022 which demonstrated an association between end tidal CO2 monitoring and ROSC in adolescents. A propensity weighted cohort study[12] concluded pediatric patients with clinician reported

use of end tidal CO2 intra-arrest was not associated with ROSC. The ICU-RESUS was a large multicenter prospective observational cohort study. A secondary analysis study of ICU-RESUS ECPR found no association between end tidal CO2 in first 10 min CPR event and survival with favorable neurologic outcome.[14] However, Morgan et al [13] conducted an ancillary study of children in ICU-RESUS trial (CPR-NOVA) and found a higher incidence of ROSC and survival to hospital discharge in patients with end tidal CO2 target >20 mmHg. It is the first pediatric study to support use of end tidal CO2 monitoring intra-arrest and defines an intra-arrest ETCO2 target.

Relevant Guidelines or Systematic Reviews

Organization (if relevant); **Author;** **Year Published**	**Guideline or systematic review**	**Topic addressed or PICO(S)T**	**Number of articles identified**	**Key findings**	**Treatment recommendations**
European Resuscitation Council Guidelines 2021: Paediatric Life Support Van de Voorde P, 2021[10]	Guideline		2	ETCO2 is correlated with pulmonary blood flow and cardiac output. ETCO2 is also affected by minute ventilation and ventilation: perfusion matching	The level of certainty of the available paediatric evidence is too low to make nay recommendation for or against the use of ETCO2 to guide resuscitation efforts in children with cardiac arrest. More specifically, there is no single ETCO2 value that can be used as a target during CPR or as an indicator to continue or discontinue CPR.
American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Topjian AA et al 2020[11]	Guideline		2	End-tidal CO2 reflects both the cardiac output produced and ventilation efficacy and may provide feedback on the quality of CPR. A sudden rise in ETCO2 may be an early sign of ROSC.	ETCO2 monitoring may be considered to assess the quality of chest compressions, but specified values to guide therapy have not been established in children.

RCT: none

Nonrandomized Trials, Observational Studies

Study Acronym; Author; Year Published	**Study Type/Design; Study Size (N)**	**Patient Population**	**Primary Endpoint and Results (include P value; OR or RR; & 95% CI)**	**Summary/Conclusion Comment(s)**
Sorcher et al[5] 2022	**EVuP 2022** Single center cohort study N =143 CPR events	Children and adolescents	The median event ETCO2 for all 143 events was 16.8 [9.3-26.3] mmHg. There was a significant difference in median event ETCO2 between events that achieved ROSC and those that did not (ROSC: 19.3 [14.4-26.6] vs. NO ROSC: 13.9 [6.6-25.5] mmHg; $p < 0.05$).	This collection of ETCO2 and chest compression data in pediatric patients with unadjusted analyses suggests an association between ETCO2 and ROSC in adolescents.
Yu et al [6] 2020	**Abstract EVuP 2022** Multicenter in-hospital CPR cohort N= 44 events 4 centers pediRES-Q collaborative	<18yo and >37 weeks Chest compressions > 1min Intra-arrest ETCO2 data available	44 CPR events ETCO2>20 mmHg cutoff was associated with CC depth [RR 1.55 (95%CI: 1.20,2.00) p=0.0007], and age-specific AHA depth quality target compliance [RR 1.01 (95%CI: 1.00,1.02) p=0.02. ETCO2 >20mmHg cutoff was not significantly associated with survival: ROSC [RR 1.08 (95%CI: 0.71, 1.65), p=0.72)] nor survival to hospital discharge [RR 1.10 (95%CI: 0.33, 3.65), p=0.87].	ETCO2>20mmHg cutoff averaged during the first 10-min of recorded CPR was significantly associated with CC depth and age-specific AHA depth quality target compliance, but not with ROSC or survival to hospital discharge.
Kienzle et al [12] 2022	Retrospective cohort study N=2886 with IABP monitoring N= 6829 with invasive airway	Inclusion:<18 yo with IHCA and either an invasive airway in situ or arterial line in place at time of arrest event Clinician reported monitoring ETCO2 during arrest event	Primary outcome Sustained ROSC > 20 min Secondary outcome 24-hour survival, survival to hospital discharge (SHD) and survival to hospital discharge with favorable neurologic outcome (FNO)	Patients with advanced airway at time of arrest, clinician reported monitoring on ETC02 was not associated with ROSC, SHD, SHD with FNO Association ETCO2 monitoring with improved return of circulation with ECMO

		Exclusion < 1 min CPR Arrest event outside PICU	ETCO2 monitoring used in 1335/8829 (21%) CPR events clinician reported monitoring with ETCO2 was not associated with ROSC (aOR 1.03, CI95 [0.9,1.18]; p=0.66) Post hoc analysis event outcomes in ETCO2 monitored group higher rate ECPR than those without monitoring (11.2% vs 6.5%) ETCO2 monitoring associated with improved odds of ROC with ECMO (CI 95%, OR 1.22 [1.04 – 1.43])	Clinician reported CPR quality monitoring using ETCO2 and DBP increased over time
Morgan et al[13] 2024	Prospective observational cohort study, ancillary study of ICU-RESUS called CPR-NOVA N= 234 events included in final analysis cohort 18% before CPR-NOVA and 47% during CPR-NOVA 18 intensive care units in United States	Inclusion: <18 yo and > 37 weeks IHCA chest compressions any duration advanced airway or tracheostomy intra-arrest evaluable ETCO2 data Exclusion: terminal illness, documented limitations of ICU interventions, determined brain dead, or had OHCA	Primary outcome: survival to hospital discharge Secondary outcome: sustained ROS, SHD with FNO and new morbidity in survivors Outcome exposure event leveled average ETCO2 in first 10 min CPR (>20 mmHg or < 20 mmHg) 133/234 (57%) had event leveled ETCO2 >20 mmHg and average ETCO2 > 20mmHg was associated with higher incidence SHD (86/133 [65%] vs 48/101 [48%] adjusted RR 1.33 [95% CI, 1.04 – 1.69]; p=0.023) and ROSC (95/133 [71%] vs 59/101 [58%] adjusted RR 1.22[95%CI, 1-1.49]; p=0.046) Events with event-level average ETCO2 >20 mmHg intra-arrest SBP and DBP were	First pediatric study to support monitoring ETCO2 during arrest event Patients with advanced airway in situ at beginning CPR with and average ETCO2 >20 mmHg during first 10 min associated with higher incidence and aRR of survival to hospital discharge and ROSC ETCO2 >20 mmHg during CPR associated with higher intra-arrest systolic and diastolic BP targets Chest compression characteristics (rate depth and fraction) did not differ between ETCO2 > 20 mmHg or <20 mmHg Confounder is relationship to ventilation rate during CPR event

			higher than events with ETCO2 < 20 mmHg P<0.001	Evaluation limited to association ETCO2 in first 10 min of CPR event
Yates et al[14] 2024	Secondary analysis ICU-RESUS study a prospective observational cohort study N= 97 ECPR events	Inclusion < 18 yo and > 37 weeks gestation IHCA Any duration chest compressions Exclusion: OHCA Limitation of ICU interventions pre-arrest, determination brain death Secondary analysis only included patients achieved ROC with ECMO	Primary outcome: survival with FNO ETCO2 available for analysis 35/97 patients (36%) and IQR of average level was 18 mmHg. Average ETCO2 <10 mmHg in 4/17(24%) patients who survived	No association between end tidal CO2 in first 10 min CPR event and survival with FNO Candidates for ECPR with ETCO2 <10 mmHg may survive with FNO and therefore low ETCO2 levels should not preclude from cannulating for ECMO

Reviewer Comments:

The available data supports that monitoring of ETCO2 intra-arrest in children with advanced airways contributes to improve the quality of CPR and to the adherence of resuscitation guidelines. There is one recent study that demonstrates an association with an ETCO2 intra-arrest target >20 mmHg and survival to hospital discharge and higher systolic blood pressure values in first 10 min of arrest event; but fails to demonstrate an association with ETCO2 target and quality of CPR metrics[13]

Therefore, in children ETCO2 monitoring may be considered to assess the quality of chest compressions, but specified values to guide intra-arrest therapies have not been well established. There is recent data from a large multicenter study to suggest targeting an intra-arrest ETCO2 >20 mmHg is associated with higher blood pressure and survival to hospital discharge. A task force led systematic review may be justified following future publications that support similar findings.

The level of certainty of the available pediatric evidence is too low to make any recommendation for or against the use of ETCO2 to guide resuscitation efforts in children with cardiac arrest. Furthermore, there is no single ETCO2 value that can be used as a target during CPR or as an indicator to continue or discontinue resuscitation.

The Treatment Recommendation of 2015 has been downgraded to a GPS based on a rigorous scoping review in 2020 and evidence updates in 2022 and 2024

- There is insufficient evidence to support or advise against a treatment recommendation related to intra-cardiac arrest end tidal CO2 monitoring

Good Practice Statement

For children in cardiac arrest monitoring ETCO2 may be considered to encourage adherence to resuscitation guidelines for metric targets for CPR quality; however, specified values to guide intra-arrest interventions have not been well established.

References

1. Kool M, Atkins DL, Van de Voorde P, Maconochie IK, Scholefield BR, Force PIT. Focused echocardiography, end-tidal carbon dioxide, arterial blood pressure or near-infrared spectroscopy monitoring during paediatric cardiopulmonary resuscitation: A scoping review. Resusc Plus. 2021;6:100109.

212. Kienzle MF, Morgan RW, Alvey JS, Reeder R, Berg RA, Nadkarni V, Topijan AA et al. Clinician reported physiologic monitoring of cardiopulmonary Resuscitation quality during pediatric in-hospital cardiac arrest: a propensity weighted cohort study. Circulation.2022;146(Supplement 1):

13 Morgan RW, Reeder RW, Bender D, Cooper KK, Friess SH, Graham, K et al. Associations Between End- Tidal Carbon Dioxide During Pediatric Cardiopulmonary Resuscitation, Cardiopulmonary Resuscitation Quality and Survival.Circulation.2024;149:367-378.

14. Yates AR, Naim MY, Reeder RW, Banks RK, Bell MJ, Berg RA et al. Early Cardiac Arrest Hemodynamics, End-Tidal CO2, and Outcome in Pediatric Extracorporeal Cardiopulmonary Resuscitation: Secondary Analysis of the ICU-RESUScitation Project Dataset (2016-2021). Ped Crit Care Med.2024;25(4):312-322.

2025 Evidence Update
PLS 4160.09 – Intra Arrest NIRS

Worksheet Author(s): Andrea Christoff, Barney Scholefield
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:

Population: Infants & Children in any setting (in-hospital or out-of-hospital) with cardiac arrest

Intervention: the presence of variables -images, cut-off values or trends- during CPR (intra-arrest) that can provide physiologic feedback to guide resuscitation efforts, namely: Near Infrared Spectroscopy

Comparators: the absence of such factors -images, cut-off values or trends.

Outcomes: Any clinical outcome.

Study Designs: STEP 1: Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) that concern directly the population and intervention described above are eligible for inclusion. If it is anticipated that there will be insufficient studies from which to draw a conclusion, case series may be included in the initial search. The minimum number of cases for a case series to be included was set by the taskforce at 5 cases. Unpublished studies (e.g., conference abstracts, trial protocols) are excluded.
STEP 2: the same study designs and/or existing systematic or scoping reviews not directly concerning the population or intervention defined above but considered informative as additional evidence for the development of the final taskforce insights.

Timeframe: For STEP 1, all languages are included, as long as there is an English abstract. We searched articles from 2022 onwards. For STEP 2, if a systematic or scoping review of high quality (as per AMSTAR 2 tool) is identified, search can be limited to beyond data and/or scope of that review.

Year of last full review: 2020 EvUp 2022

Scoping review last searched September 2020

Kool M, Atkins DL, Van de Voorde P, Maconochie IK, Scholefield BR; PLS ILCOR Task Force. Focused echocardiography, end-tidal carbon dioxide, arterial blood pressure or near-infrared spectroscopy monitoring during paediatric cardiopulmonary resuscitation: A scoping review. Resusc Plus. 2021 Mar 30;6:100109. doi: 10.1016/j.resplu.2021.100109. PMID: 34228034; PMCID: PMC8244529.[1]

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

Treatment Recommendations 2020

There is insufficient quality evidence to support or advise against a treatment recommendation related to intra-cardiac arrest NIRS monitoring

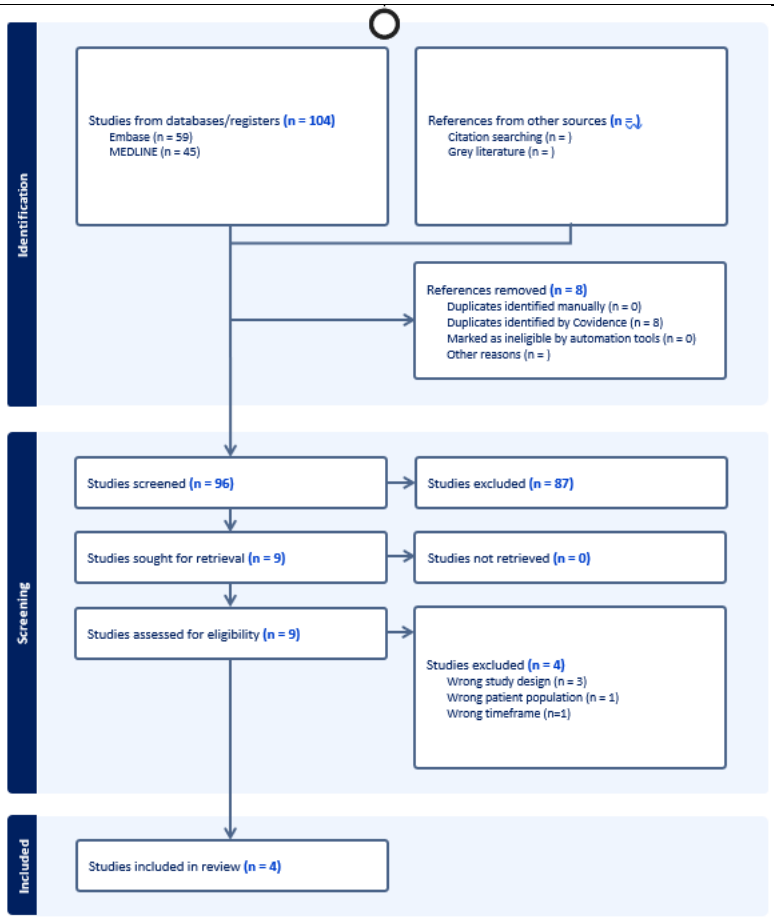
Current Search Strategy (for an existing PICOST)	1	exp Spectroscopy, Near-Infrared/	32,723
	2	(cerebral oximetry or regional cerebral oxygenation or regional cerebral oxygen saturation).mp. [mp=title, abstract, heading word,	2,322

included in the attached approved PICOST

	drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]	
3	1 or 2	34,035
4	*Heart Rate/de or ventricular fibrillation/ or ("ventricular fibrillation" or "heart ventricle fibrillation" or "pulseless electrical activit*" or pulselessness).tw,kf.	43,801
5	exp Heart arrest/ or (((heart* or cardiac* or cardiopulmonary or cardiovascular) adj2 arrest*) or asystol*).tw,kf.	156,737
6	4 or 5	184,106
7	exp adolescent/ or exp child/ or exp infant/ or (infant disease* or childhood disease*).ti,ab,kf. or (adolescen* or babies or baby or boy? or boyhood or girlhood or child* or girl? or infan* or juvenil* or kid? or minors or minors* or neonat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).jn,jw. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).in.	7,037,674
8	3 and 6 and 7	174
9	("38180092" or "35314211").ui.	0
10	8 and 9	0
11	limit 8 to yr="2020 -Current"	68
12	limit 11 to (comment or editorial or letter) [Limit not valid in Embase; records were retained]	5
13	limit 11 to animal	4
14	11 not (12 or 13)	59

exp Spectroscopy, Near-Infrared/
(cerebral oximetry or regional cerebral oxygenation or regional cerebral oxygen saturation).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
1 or 2
Heart Rate/de or ventricular fibrillation/ or ("ventricular fibrillation" or "heart ventricle fibrillation" or "pulseless electrical activit" or pulselessness).tw,kf.
exp Heart arrest/ or (((heart* or cardiac* or cardiopulmonary or cardiovascular) adj2 arrest*) or asystol*).tw,kf.
4 or 5
exp adolescent/ or exp child/ or exp infant/ or (infant disease* or childhood disease*).ti,ab,kf. or (adolescen* or babies or baby or boy? or boyhood or girlhood or child* or girl? or infan* or juvenil* or kid? or minors or minors* or neonat* or neo-nat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or

	perinat* or preschool* or puber* or pubescen* or school* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).jn,jw. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).in. 3 and 6 and 7 ("38180092" or "35314211").ui. limit 11 to (comment or editorial or letter) limit 11 to animal 11 not (12 or 13)
New Search strategy: (for a new PICOST should be outlined here as per Evidence Update Process)	n/a
Database searched: eg Medline Embase Cochrane	Medline, Embase, Central
Time Frame: (existing PICOST) – updated from end of last search (please specify)	Last updated 25 July 2022. New Search 25th July 2020 to 26th June 2024
Time Frame: (new PICOST) – at the discretion of the Task Force (please specify)	n/a
Date Search Completed:	26th June 2024

Search Results (Number of articles identified and number identified as relevant):	

Summary of Evidence Update:

The Evidence Update in 2022 identified one observational study that reported near infrared monitoring during CPR and/or outcomes.[2] and one abstract[3].

The single center study[2] evaluated 21 patients with 23 events and found an association between higher crSO2 with NIRS measurements during the entire monitored event and last 5 minutes of the event with ROSC. The abstract[3] reviewed a small cohort of patients including children with congenital heart disease from three centers. The data did not demonstrate an association with outcomes with multivariable analysis.

The Evidence Update in 2024 identified 1 additional abstract[4] and a single center observational study by the same authors utilizing data from three hospitals in the Pediatric Resuscitation Quality Collaborative (pediRES-Q)[5]

Both studies concluded that higher median crSo2 measured with cerebral NIRS intra-arrest during IHCA in children was associated with increased rate of ROSC and survival to hospital discharge. The multicenter observational study[4] reviewed 123 IHCA events which included infants and children with congenital heart disease. It is the first pediatric study to report a significant association between intra-arrest crSO2 NIRS with survival to hospital discharge and survival with favorable neurological outcome.

Nonrandomized Trials, Observational Studies

Study Acronym; Author;	Study Type/Design; Study Size (N)	Patient Population	Primary Endpoint and Results (include P value; OR or RR; & 95% CI)	Summary/Conclusion Comment(s)

Year Published				
Francoeur[2]	**Study Type:** Single center observational study N= 23	**Inclusion Criteria:** Children with cardiac arrest in PICU, CICU, or ED with at least 30 seconds of NIRS monitoring	**1° endpoint:** Sustained ROSC > 20 min The median rSO2 was higher for events with ROSC compared to no ROSC for the overall event (62% [56,70] vs. 45% [35,51], p = 0.025) and for the final five minutes of the event (66% [55,72] vs. 43% [35,44], p = 0.01). Patients who achieved ROSC had more rSO2 epochs above 50% during the final 5 minutes of the event (100% [100,100] vs. 0% [0,29], p = 0.01).	Higher crSO2 with NIRS during CPR for pediatric cardiac arrest was associated with higher rates of ROSC but not with survival to discharge. 23 cardiac arrest events in 21 patients' limitation low power to demonstrate association between crSo2 with NIRS and survival
Esangbedo [3] 2020	**Abstract** Multicenter observational N= 36 3 sites pediRES-Q	Children < 18, > 2 min CPR Intra-arrest NIRS monitoring at time of arrest Exclusion: ECMO/ECPR	Sustained ROSC >20 min Mean intra-arrest cerebral rSo2 was 44.2% (+/-19.5) for ROSC vs. 37.4% (+/-15) for non-ROSC group (p=0.267). Using mean crSo2 cutoffs >25, >30, >35, >40, and>50%, we found no significant association with ROSC.	There was no significant association between cerebral NIRS crSo2 during pediatric cardiac arrest and ROSC, even after controlling for important confounders of age and SV physiology.
Esangbedo[4] 2022	**Abstract** Multicenter observational N= 106 In 81 patients 3 sites pediRES-Q	Children <18 yo, >=1 min CPR, included cyanotic heart disease Intra-arrest NIRS monitoring at time of arrest excluded ECMO	Sustained ROSC >20 min and SHD CPR events with ROSC median intra-arrest crSO2 (IQR) 46% (30,60) vs 25% (15,46) in non-ROSC group p = 0.001 Entire event with ROSC median crSO2 >30% 100% vs 35% non-ROSC (p<0.001) Entire event with ROSC median crSO2 >40% 79% vs 17% in non-ROSC (p=0.022)	Higher median crSo2 measured with cerebral NIRS intra-arrest during IHCA in children was associated with increased rate of ROSC and SHD.

			Entire events with SHD crSO2 >30% 100% vs non-SHD 35% (p=0.001) Entire evens with SHD median crSO2 >40% 73% vs non-SHD 14% (p=0.002). multivariant analysis controlling for age (aOR 1.02 p=0.012) and cyanotic heart disease (aOR 1.03 p=0.008) showed median crSO2 was independently associated with ROSC	
Raymond [5]	Multicenter, observational N= 123 arrest events in 93 patients	Children ,18 yo arrest event >=1 min includes cyanotic heart disease Intra-arrest NIRS monitoring Exclusion: ECMO/ECPR	Sustained ROSC >20 min, SHD, favorable neurologic outcome (PCPC 1-2) Median intra- arrest crSo2 during the 91 index CPR events 38% Median intra-arrest crSo2 44% (33,59) in SHD group vs 26% (18,43) in non-SHD group (p <= 0.001) Median intra-arrest crSo2 in favorable neurologic outcome group 50% (36,60) vs 26% (18,46) in poor neurologic outcome group (p<0.001). patients with FNO all had crSo2 measurements about 30% throughout entire CPR event. Multivariant logistic regression all infants < 1yo to assess association between median crSo2 and all outcomes controlling for cyanotic heart disease. After controlling for cyanotic heart disease Median crSo2 associated with ROSC (OR 1.06 p<0.001), SHD (OR 1.04 p=0.01), FNO (OR 1.05, p=0.003)	Higher crSO2 with NIRS during pediatric IHCA was associated with increased rate of ROSC, SHD and favorable neurological outcome (FNO). Intra-arrest crSo2 with NIRS may have a role as a real-time non-invasive predictor of ROSC First study in children to report a significant association between intra-arrest cerebral NIRS monitoring with SHD and survival with FNO.

Reviewer Comments:

There remains little pediatric specific evidence examining the use of cerebral NIRS during cardiac arrest. Our evidence up-date identified one observational study and one abstract. The observational study is the largest pediatric cohort to date and is the first study in children to report a significant association between intra-arrest cerebral NIRS monitoring with survival to hospital discharge and survival with favorable neurologic outcome. However, a systematic review of cerebral monitoring with NIRS of pediatric cardiac arrest events is not justified at this time.

The Treatment Recommendation of 2020 has been downgraded to a GPS based on a rigorous scoping review in 2020 and evidence updates in 2022 and 2024

Good Practice statement

Monitoring cerebral oxygenation during cardiopulmonary resuscitation is a non-invasive metric that does not require pulsatile signal and may be beneficial to monitor. However, there is no consensus about a cut-off threshold for cerebral oxygenation that can be used to guide or terminate resuscitation during in hospital cardiac arrest in children.

References

1. Kool M, Atkins DL, Van de Voorde P, Maconochie IK, Scholefield BR; PLS ILCOR Task Force. Focused echocardiography, end-tidal carbon dioxide, arterial blood pressure or near-infrared spectroscopy monitoring during paediatric cardiopulmonary resuscitation: A scoping review. Resusc Plus. 2021 Mar 30;6:100109. doi: 10.1016/j.resplu.2021.100109. PMID: 34228034; PMCID: PMC8244529
2. Francoeur C, Landis WP, Winters M, Naim MY, Donoghue A, Dominick CL, Huh JW, MacDonald JM, Lang SS, Yuan I, Berg RA, Nadkarni VM, Kilbaugh TJ, Sutton RM, Kirschen MP, Morgan RW, Topjian AA. https://pubmed.ncbi.nlm.nih.gov/35314211/ Resuscitation. 2022 May; 174:35-41.
3. Esangbedo I, Rajapreyar P, Kirschen M, Hanna R, Niles DE, Zhang X, Griffis HM, Francoeur C, Wakeham MK, Petersen T, Topjian AA, Nadkarni VM, Raymond TT. Cerebral oximetry during pediatric in-hospital cardiac arrest. Circulation Conference, American Heart Association Resuscitation Science Symposium, ReSS- Volume 142, Issue 0, published 2020
4. Esangbedo L, Rajapreyar P, Kirschen M, Niles D, Je S, Topijan AA, Nadkarni, VM, Raymond TT. Cerebral Near-infrared spectroscopy During Pediatric In-hospital Cardiac Arrest: A multicenter, Observational Study. Circulation 2022;146 (Supplement 1)
5. Raymond TT, Esangbedo ID, Rajapreyar P, Je S, Zhang X, Griffs HM, Wakeman MK, Petersen TL, Kirschen MP, Topjian AA, Lasa JJ, Francoeur CI, Nadkarni VM. Cerebral Oximetry during pediatric in-hospital cardiac arrest: A multicenter study or survival and neurologic outcome. Crit Care Med 2024; 52(5) 775-785. doi:10.1097/CCM.0000000000006186.

2025 Evidence Update
PLS 4060.01 – Advanced Airway Interventions in Pediatric Cardiac Arrest

Worksheet Author(s): Jason Acworth, Elliot Acworth
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:

Population	Infants and children (excluding newborn children) who had received CPR after out-of-hospital or in-hospital cardiac arrest
Intervention	Placement of an advanced airway device
Comparison	BMV alone or with non–advanced airway interventions (Primary); or another advanced airway device (Secondary)
Outcomes	Any clinical outcome including but not limited to: ▪ survival to hospital discharge with good neurologic outcome ▪ survival to hospital discharge ▪ survival to hospital admission ▪ return of circulation (ROC) The PLS TF prefers outcomes defined in the P-COSCA publication (Topjian 2021 162)
Study Design	Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion. Unpublished studies (e.g., conference abstracts, trial protocols) are excluded. All relevant publications in any language are included as long as there is an English abstract.
Timeframe	As this is an update to a previously published ILCOR systematic review, all studies published since most recent search date (August 15, 2023) will be included. The search will include publication dates from August 1, 2023 onwards to ensure no articles are missed.

Year of last full review: 2023

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

We suggest the use of BMV rather than TI or SGA in the management of children during cardiac arrest in the out-of-hospital setting (weak recommendation, very low certainty evidence).

There is insufficient quality evidence to make a recommendation for or against the use of the BMV compared to TI or SGA for in-hospital cardiac arrest.

The main goal of cardiopulmonary resuscitation is effective ventilation and oxygenation, by whatever means, without compromising quality of chest compressions. We suggest that clinicians consider transitioning to an advanced airway intervention (SGA or TI) when the team has sufficient expertise, resources, and equipment to allow TI/SGA placement to occur with minimal interruptions to chest compressions or when BMV is not providing adequate oxygenation/ventilation [Good Practice Statement].

(Greif 2024)

Database searched: PubMed

Time Frame: Last search updated 15 August 2023. New search 1 August 2023 to 22 May 2024 to include date of previous search.

Date Search Completed: 22 May 2024

Search Strategies:

PUBMED.ncbi.nlm.nih.gov

((((("supraglottic"[Title/Abstract] OR "laryngeal mask"[Title/Abstract] OR "LMA"[Title/Abstract] OR "combitube"[Title/Abstract] OR "EasyTube"[Title/Abstract] OR "king airway"[Title/Abstract] OR "I-Gel"[Title/Abstract] OR "ProSeal"[Title/Abstract] OR "CTrach"[Title/Abstract] OR "esophageal obturator"[Title/Abstract] OR "bag-mask"[Title/Abstract] OR "bag-valve-mask"[Title/Abstract] OR "bag-mask"[Title/Abstract] OR "bag-valve-mask"[Title/Abstract] OR "advanced airway"[Title/Abstract] OR ("intubation"[Title/Abstract] OR "intratracheal tube"[Title/Abstract] OR "endotracheal tube"[Title/Abstract] OR "ETT"[Title/Abstract])) AND ("infan*"[Text Word] OR "child*"[Text Word] OR "adolescen*"[Text Word] OR "pediatric*"[Text Word] OR "paediatric*"[Text Word] OR "pube*"[Text Word] OR "juvenil*"[Text Word] OR "school*"[Text Word] OR "newborn*"[Title/Abstract] OR "newborn*"[Title/Abstract] OR "neonat*"[Title/Abstract] OR "neonat*"[Title/Abstract] OR "premature*"[Title/Abstract] OR "postmature*"[Title/Abstract] OR "premature*"[Title/Abstract] OR "post mature*"[Title/Abstract] OR "preterm*"[Title/Abstract] OR "preterm*"[Title/Abstract] OR "baby"[Title/Abstract] OR "babies"[Title/Abstract] OR "toddler*"[Title/Abstract] OR "youngster*"[Title/Abstract] OR "preschool*"[Title/Abstract] OR "kindergart*"[Title/Abstract] OR "kid"[Title/Abstract] OR "kids"[Title/Abstract] OR "playgroup*"[Title/Abstract] OR "play group*"[Title/Abstract] OR "playschool*"[Title/Abstract] OR "prepube*"[Title/Abstract] OR "preadolescen*"[Title/Abstract] OR "junior high*"[Title/Abstract] OR "highschool*"[Title/Abstract] OR "senior high"[Title/Abstract] OR "young people*"[Title/Abstract] OR "minors"[Title/Abstract]) AND ("life support care"[MeSH Terms] OR "life support"[Title/Abstract] OR "cardiopulmonary resuscitation"[MeSH Terms] OR "cardiopulmonary resuscitation"[Title/Abstract] OR "ROSC"[Title/Abstract] OR "return of spontaneous circulation"[Title/Abstract] OR "heart arrest"[MeSH Terms] OR "cardiac arrest"[Title/Abstract])) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])) NOT ("Letter"[Publication Type] OR "Editorial"[Publication Type] OR "Comment"[Publication Type])) AND 2018/07/01:2023/12/31[Date - Publication]

Search Results (Number of articles identified and number identified as relevant):

56 articles after limit search August 2023 to current

3 articles after 53 excluded upon title and abstract screening

No articles suitable for inclusion in analysis after full text review

Summary of Evidence Update:

Our Evidence Update in 2024 identified no new pediatric studies on this subject.

Reviewer Comments: *(including whether this PICOST should have a systematic or scoping review*)

As our evidence update failed to identify any new publications since the updated systematic review was conducted in 2023, a new systematic review of advanced airway interventions in pediatric cardiac arrest patients is not warranted at this time. The PLS Task Force is aware of an ongoing RCT on advanced airway management being conducted by the PECARN research network which my provide useful data on this question in the near future.

Reference list:

Topjian 2021 162 [https://pubmed.ncbi.nlm.nih.gov/32967446/]

Greif R, 2024 e1 [https://pubmed.ncbi.nlm.nih.gov/39540293/]

2025 Evidence Update
PLS 4080.01 – Lay Rescuer use of AED Defibrillators in Infants, Children, and Adolescents

Worksheet Author(s): Jason Acworth, Elliot Acworth
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:

Population	Infants and children (excluding newborn children) with non-traumatic out-of-hospital cardiac arrest (OHCA)
Intervention	Application of or shock delivery from an automated external defibrillator (AED) by lay rescuers
Comparison	Standard care by lay rescuer without AED application
Outcomes	Any clinical outcome including but not limited to: ▪ survival to hospital discharge with good neurologic outcome ▪ survival to hospital discharge ▪ survival to hospital admission ▪ return of circulation (ROC) The PLS TF prefers outcomes defined in the P-COSCA publication (Topjian 2021 162)
Study Design	Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion. Unpublished studies (e.g., conference abstracts, trial protocols) are excluded. All relevant publications in any language are included as long as there is an English abstract.
Timeframe	As this is an update to a previously published ILCOR systematic review, all studies published since most recent search date (March 11, 2021) will be included. The search will include publication dates from January 1, 2021 onwards to ensure no articles are missed.

Year of last full review: 2021

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

We suggest the use of an AED by lay rescuers for all children >1 year of age who have nontraumatic OHCA (weak recommendation, very low–certainty evidence).

We cannot make a recommendation for or against the use of an AED by lay rescuers for all children <1 year of age with nontraumatic OHCA. (Wyckoff 2022 208)

Database searched: PubMed

Time Frame: Last search updated 11 March 2021. New search 1 January 2021 to 22 May 2024 to include date of previous search.

Date Search Completed: 22 May 2024

Search Strategies:

PUBMED.ncbi.nlm.nih.gov

(((((("Out-of-Hospital Cardiac Arrest"[Mesh] OR "Out of Hospital Cardiac Arrest" [TIAB] OR "Out-of- Hospital Cardiac Arrest" [TIAB] OR "Out of Hospital Cardiac Arrests" [TIAB] OR "Out-of-Hospital Cardiac Arrests" [TIAB] OR (("out-of-hospital"[TIAB] OR "out of hospital"[TIAB] OR "outside of hospital"[TIAB]) AND cardiac[TIAB] AND arrest*[TIAB]) OR "Heart Arrest"[Mesh:NoExp] OR "heart arrest"[TIAB] OR "heart arrests"[TIAB] OR "cardiac arrest"[TIAB] OR "cardiac arrests"[TIAB] OR "cardiovascular arrest"[TIAB] OR "asystole"[TIAB] OR "Heart Failure"[Mesh] OR "heart failure"[TIAB] OR "cardiopulmonary arrest"[TIAB] OR "cardiopulmonary arrests"[TIAB] OR "cardio-pulmonary arrest"[TIAB] OR "cardio-pulmonary arrests"[TIAB] OR "Ventricular Fibrillation"[Mesh] OR "Ventricular Fibrillation"[TIAB] OR "Tachycardia, Ventricular"[Mesh] OR "pulseless ventricular tachycardia"[TIAB] OR (Pulseless[TIAB] AND (V-tach[TIAB] OR VT[TIAB])) OR "Cardiopulmonary Resuscitation"[Mesh] OR "cardiopulmonary resuscitation"[TIAB] OR CPR[TIAB] OR "Resuscitation"[Mesh] OR resuscitat*[TIAB])) AND (("early defibrillation"[TIAB] OR "automatic external defibrillator"[TIAB] OR "automatic external defibrillators"[TIAB] OR "automated external defibrillator"[TIAB] OR "automated external defibrillators"[TIAB] OR AED[TIAB] OR AEDs[TIAB] OR "automatic external defibrillation"[TIAB] OR "public access defibrillation program"[TIAB] OR "public access defibrillation programs"[TIAB] OR (("Electric Countershock"[Mesh] OR "electric countershock"[TIAB] OR countershock*[TIAB] OR electroversion*[TIAB] OR cardioversion*[TIAB] OR "Defibrillators"[Mesh] OR defibrillator*[TIAB] OR defibrillation*[TIAB]) AND (public[TIAB] OR bystander*[TIAB] OR "first responder"[TIAB] OR "first responders"[TIAB] OR "firstresponder"[TIAB] OR "first-responders"[TIAB] OR Layperson*[TIAB] OR "lay people"[TIAB] OR "lay rescuer"[TIAB] OR "lay rescuers"[TIAB] OR witness*[TIAB] OR Firefighter*[TIAB] OR "fire fighter" OR "fire fighters" OR "Firefighters"[Mesh] OR "Police"[Mesh] OR Police[TIAB] OR "non- healthcare professionals"[TIAB] OR "Emergency Medical Technicians"[Mesh] OR "emergency medical"[TIAB] OR "EMS"[TIAB] OR "EMT"[TIAB] OR paramedic*[TIAB])))))) AND (Infan* OR newborn* OR new-born* OR perinat* OR neonat* OR baby OR baby* OR babies OR toddler* OR minors OR minors* OR boy OR boys OR boyfriend OR boyhood OR girl* OR kid OR kids OR child OR child* OR children* OR schoolchild* OR schoolchild OR school child[tiab] OR school child*[tiab] OR adolescen* OR juvenil* OR youth* OR teen* OR under*age* OR pubescen* OR pediatrics[mh] OR pediatric* OR paediatric* OR peadiatric* OR school [tiab] OR school*[tiab] OR prematur* OR preterm*)) NOT (implantable[TIAB])) Filters: from 2021/1/1 - 2024/12/31

Search Results (Number of articles identified and number identified as relevant):

193 articles after limit search 1 January 2021 to current

14 articles after 179 excluded upon title and abstract screening

6 articles included in analysis after full text review

Summary of Evidence Update:

The ILCOR PLS Task Force systematic review performed in 2021 on lay rescuer use of automated external defibrillators in infants, children and adolescents (Atkins 2022 100283) analyzed data from 4 studies and found that AED application by lay rescuers was associated with survival to hospital discharge and improved survival with a CPC of 1–2 at 30 days for children >1 year. There was limited data on AED use in infants.

Our Evidence Update in 2024 identified 5 additional registry-based pediatric cohort studies on this subject. All of these studies had findings that supported the benefits of lay rescuer use of automated external defibrillators in infants, children and adolescents. None of these provided data that would potentially allow a specific recommendation to be made on lay rescuer use of automated external defibrillators in infants.

Relevant Guidelines or Systematic Reviews:

Organization (if relevant); **Author;** **Year Published**	**Guideline or systematic review**	**Topic addressed or PICO(S)T**	**Number of articles identified**	**Key findings**	**Treatment recommendations**

ILCOR PLS Task Force; Atkins 2022	Systematic Review		4 articles included in analysis	Lay rescuer AED application resulted in improved survival with CPC 1–2 at hospital discharge or 30 days to hospital discharge in age groups 1–12 and 13–18 years (RR 3.84 [95 % CI 2.69–5.5], RR 3.75 [95 %CI 2.97–4.72]), respectively and hospital discharge in both groups (RR 3.04 [95 % CI 2.18–4.25], RR 3.38 [95 % CI 2.17–4.16]), respectively. AED use with CPR improved CPC 1–2 at hospital discharge and hospital discharge (RR 1.49 [95 % CI 1.11–1.97], RR 1.55[1.12–2.12]). AED application by lay rescuers is associated with survival to hospital discharge and improved survival with a CPC of 1–2 at 30 days for children > 1 year. This association persists even when CPR is provided. There is limited data on use in children < 1 year.	

RCT: none

Nonrandomized Trials, Observational Studies:

Study Acronym; Author; Year Published	**Study Type/Design; Study Size (N)**	**Patient Population**	**Primary Endpoint and Results (include P value; OR or RR; & 95% CI)**	**Summary/Conclusion Comment(s)**
Banerjee 2020	Prospective observational study N=109	Pediatric patients (0-9 years) in OHCA attended to by a single county EMS service in USA	Children who had AED placement compared to no AED placement had higher incidence of ROSC [OR 9.39, 95%CI 1.42-62.12, p=0.0073] and higher rate of survival to hospital [OR 10.19, 95%CI 1.41-73.71, p=0.0062].	AED placement was associated with significantly higher rates of ROSC and survival to hospital in this population.
Goto 2022	Propensity matched registry-based cohort study	Children (<18 years) with OHCA who received dispatcher-assisted	Children who accessed public access defibrillation (PAD) had a higher rate of 1-month survival	Access to PAD was associated with better outcomes.

	N=8172 (5236 in propensity-matched cohort)	bystander CPR entered onto national cardiac arrest registry in Japan	compared to no PAD [92/275 (33%) v 512/4961 (10%)]. Children who accessed public access defibrillation (PAD) had a higher rate of 1-month survival with favorable neurological outcome compared to no PAD [75/275 (27%) v 150/4991 (3%)].	
Holgersen 2022	Registry-based cohort study N=173	Pediatric patients (0-16 years) in OHCA entered onto national cardiac arrest registry in Denmark	Children who survived to 30 days were more likely to have received defibrillation by bystander compared to those who died [15.7% compared to 1.9%, p<0.001].	This study only included data on AED shocks rather than placement and also included trauma-related deaths (10%)
Kim 2022	Registry-based cohort study N=4561	Children (<18 years) with OHCA who entered onto national cardiac arrest registry in Korea	Children who had pre-hospital AED shock compared to no AED had higher incidence of ROSC [OR 2.74, 95%CI 1.99-3.78], higher rate of survival to hospital discharge [OR 5.86, 95%CI 4.09-8.39] and higher rate of survival with good neurological outcome [OR 7.96, 95%CI 5.09-12.43]	Pre-hospital delivery of AED shock to children aged 6-12 years and 13-17 years correlated with good survival to discharge and good neurologic outcomes.
Kiyohara 2024	Registry-based cohort study N=318	School-age children (6-19 years) with non-traumatic OHCA during school sport activity entered onto national cardiac arrest registry in Japan	Children who received AED+CPR had a higher rate of 1-month survival with favorable neurological outcome compared to no bystander intervention (CPR or AED) [aOR 3.97, 95%CI 1.32-11.9, p=0.014].	The combination of CPR and AED use as basic life support performed by bystanders for non-traumatic OHCA during school-supervised sports activities improved outcomes.

Reviewer Comments: *(including whether this PICOST should have a systematic or scoping review*)

As our evidence update failed to identify any new evidence since the systematic review was conducted in 2022 that would potentially alter the current ILCOR Treatment Recommendation on this topic, a new systematic review of lay rescuer use of automated external defibrillators in infants, children and adolescents is not warranted at this time.

With respect to the use of AEDs in infants, the PLS Task Force recognizes that:

i) Interruptions to CPR related to AED use in infants with non-shockable rhythms may be detrimental
ii) Shockable rhythms do occur in infancy (though less commonly than other ages)
iii) AEDs can accurately define shockable rhythms in this age group
iv) The risk of injury from shocks is low with biphasic defibrillation
v) The risk of delaying treatment of shockable rhythms is high

Reference list:

Topjian 2021 162 [https://pubmed.ncbi.nlm.nih.gov/32967446/]

Wyckoff 2022 208 [https://pubmed.ncbi.nlm.nih.gov/36325905/]

Atkins 2022 100283 [https://pubmed.ncbi.nlm.nih.gov/35992959/]

Banerjee 2020 100062 [https://pubmed.ncbi.nlm.nih.gov/34223334/]

Goto 2022 106 [https://pubmed.ncbi.nlm.nih.gov/34648920/]

Holgersen 2022 58 [https://pubmed.ncbi.nlm.nih.gov/36397074/]

Kim 2022 e317 [https://pubmed.ncbi.nlm.nih.gov/36377293/]

Kiyohara 2024 100531 [https://pubmed.ncbi.nlm.nih.gov/38155977/]

2025 Evidence Update
PLS 4080.04 – Anti-arrhythmic in CA with Shockable Rhythms at anytime during CPR or immediately after ROSC

Worksheet Author(s): Thomaz Bittencourt Couto
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:

Population: Patients of all ages (neonates, children and adolescents <18) in any setting with cardiac arrest and a shockable rhythm at any time during CPR or immediately after ROSC

Intervention: Administration (IV or IO) of an anti-arrhythmic drug

Comparator: Another anti-arrhythmic or placebo

Outcome: Survival to hospital discharge with good neurologic outcome, survival to hospital discharge, ROSC and re-arrest after ROSC

Study Design: Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion.

Year of last full review: 2022

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST: We suggest that amiodarone or lidocaine may be used for the treatment of pediatric shock–resistant VF/pVT (weak recommendation, very-low-quality evidence). [1,2]

Current Search Strategy:

1 exp Heart Arrest OR

2 exp Cardiopulmonary Resuscitation OR

3 "cardiac arrest".tw OR

4 "cpr".tw OR

5 "resuscitation".tw OR

6 "heart arrest".tw) AND

(8 ("Antiarrhythmic agent" OR "antiarrhythmic drug" OR "antiarrhythmic medication").tw OR

9 ("Anti-arrhythmic agent" OR "anti-arrhythmic drug" OR "anti-arrhythmic medication").tw OR

10 (Dysrhythmic agent OR dysrhythmic drug OR dysrhythmic medication).tw OR

11 exp Anti-Arrhythmia Agents OR

12 "lidocaine".tw OR

13 "amiodarone".tw OR

14 Lidocaine OR

15 Amiodarone OR

16 "lignocaine".tw OR

17 "procainamide".tw OR

18 Procainamide OR

19 Bretylium Tosylate OR

20 "bretylium".tw OR

21 "nifekalant".mp OR

22 "quinidine".mp OR Quinidine OR

23 "ajmaline".mp OR

24 "disopyramide".mp OR

25 "phenytoin".mp OR

26 "mexiletine".mp OR

27 "tocainide".mp OR

28 "flecainide".mp OR

29 "encainide".mp OR

30 "propafenone".mp OR

31 "moricizine".mp OR

32 "carvedilol".mp OR

33 "propranolol".mp OR

34 "esmolol".mp OR

35 "timolol".mp OR

36 "metoprolol".mp OR

37 "atenolol".mp OR

38 "sotalol".mp OR

39 "bisoprolol".mp OR

40 "nebivolol".mp OR

41 "ibutilide".mp OR

42 "dofetilide".mp OR

43 "dronedarone".mp OR

44 "verapamil".mp OR

45 "diltiazem".mp OR

46 "adenosine".mp OR

47 "digoxin".mp OR

48 exp Adrenergic beta-Antagonists OR

49 "beta blocker".mp OR

50 exp Calcium Channel Blockers OR

51 "magnesium sulfate”

52. or/8-51

53. 7 and 52

54. limit 53 to "therapy"

55. limit 53 to "reviews"

56. 54 or 55

57. 56 not (exp Adult/ not (exp Infant/ OR exp Child/ OR Adolescent/ OR (child* OR pediatric* OR kid OR kids OR girl OR girls OR boy OR boys OR infant OR infants OR baby OR babies OR toddler* OR youth* OR young OR youngster* OR juvenile* OR minors* OR teen* OR adolescent* OR adolescence OR puber* OR pubescen* OR preschool* OR kindergarten* OR school* OR highschool* OR PICU).tw,kf.))

58. limit 57 to ed=2022/07/05-2024/10/01

New Search strategy:

exp Heart Arrest/ OR exp Cardiopulmonary Resuscitation/ OR "cardiac arrest" OR "CPR" OR "resuscitation" OR "heart arrest") AND ("Antiarrhythmic agent" OR "Antiarrhythmic drug" OR "Antiarrhythmic medication" OR exp Anti-Arrhythmia Agents/ OR lidocaine OR amiodarone OR lignocaine OR procainamide OR Bretylium Tosylate OR bretylium OR nifekalant OR quinidine OR ajmaline OR disopyramide OR phenytoin OR mexiletine OR tocainide OR flecainide OR encainide OR propafenone OR moricizine OR carvedilol OR propranolol OR esmolol OR timolol OR metoprolol OR atenolol OR sotalol OR bisoprolol OR nebivolol OR ibutilide OR dofetilide OR dronedarone OR verapamil OR diltiazem OR adenosine OR digoxin OR exp Adrenergic beta-Antagonists/ OR "beta blocker" OR exp Calcium Channel Blockers/ OR "fast channel blocker" OR magnesium sulfate) AND (therapy OR reviews)

limit to 2022/07/05-2024/10/04

Database searched: Medline

Time Frame: July 5, 2022-Oct 1, 2024

Date Search Completed: Oct 1, 2024

Search Results (Number of articles identified and number identified as relevant): Original search revealed 0 papers, so new search not limiting to children got 190 papers, 9 remained for full reading, 0 relevant.

Summary of Evidence Update: No new paper found. There is insufficient new evidence to trigger a systematic or scoping review.

Reviewer Comments:

There was no new evidence found since the last Evup, in 2022.[1] There are only two papers directly assessing antiarrhythmics for pediatric refractory shockable rhythms; Valdez 2014,[3] an observational study derived from the AHA Get With The Guidelines Resuscitation registry. It evaluated a cohort of children enrolled from 2000 to 2008 who had an in-hospital cardiac arrest requiring CPR for at least 2 minutes, with a rhythm of VF/pVT at any time during the cardiac arrest, with 889 patients. Patients receiving lidocaine had statistically higher rates of ROSC compared with patients receiving amiodarone or no antiarrhythmic medication. There was no significant difference in ROSC for patients receiving amiodarone compared with those receiving no antiarrhythmic medication. There was no difference in survival to hospital discharge across the 3 groups. On multivariate analysis, lidocaine was independently associated with ROSC (odds ratio, 2.02; 95% CI, 1.36–3.00). Neither lidocaine nor amiodarone was found to have a significant independent association with survival to hospital discharge, and Holmberg 2020,[4] observational study also using GWTG database, which found no significant difference in outcomes when propensity matched scores were used to compare children who received lidocaine vs children who received amiodarone for shockable rhythm during cardiac arrest.

During taskforce discussions concerns were presented on the wording of the PICOST, which includes a second research question, related to patients immediately post arrest, although there is current no pediatric recommendation for this population, nor there is evidence found in our literature search.

The PLS task force considered the use of downgraded adult data for this question as there are no new pediatric studies. This will be considered for the next review, as the current COSTR is based solely on pediatric studies and did not include evidence extrapolated from adult studies. However, it is likely that most developments and trials in this area will come from adult data. The taskforce also discussed whether pediatric patients with VF/pVT cardiac arrest have significant differences from adult patients that could affect their presentation, treatment, and response to antiarrhythmic drugs.

There is insufficient evidence to trigger a new systematic review.

Reference list:

1. Berg KM, 2023, 201. https://doi.org/10.1016/j.resuscitation.2023.109992
2. Duff JP, 218, e731 2018. https://doi.org/10.1161/cir.0000000000000612
3. Valdes SO, 2014, 381. https://doi.org/10.1016/j.resuscitation.2013.12.008
4. Holmberg MJ, 2020, 149. https://doi.org/10.1016/j.resuscitation.2019.12.033

2025 Evidence Update
PLS 4120.02 – Ventilation Rate with Advanced Airway During Pediatric Cardiac Arrest

Worksheet Author(s): Jimena del Castillo, Jesús López-Herce
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:

PICOST	
Population	Infants and children (excluding newborn infants) with out-of-hospital or in-hospital cardiac arrest (asphyxial or arrhythmic origin) and an advanced airway
Intervention	Use of a any specific respiratory rate
Comparison	Compared with ventilation rate of 8-10 per minute
Outcomes	Any clinical outcome
Study Design	Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion. Unpublished studies (e.g., conference abstracts, trial protocols) are excluded. If it is anticipated that there will be insufficient studies from which to draw a conclusion, case series may be included in the initial search. The minimum number of cases for a case series to be included was set by the taskforce at 5. All relevant publications in any language are included as long as there is an English abstract. The PLS TF prefers outcomes defined in the P-COSCA publication (Topjian 2021 162)
Timeframe	All years

Year of last full review: 2023

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

There is currently no supporting evidence to recommend a specific ventilatory rate in pediatric cardiopulmonary resuscitation with an advanced airway.

There is insufficient data to recommend a specific respiratory rate in the on out-of-hospital setting.

For in-hospital cardiac arrest with and advanced airway (tracheal intubation), the use of higher ventilation rates greater than 10 breaths per minute is reasonable (Good Practice Statement).

For in-hospital cardiac arrest with an advanced airway (tracheal intubation) we suggest:

1) avoid hyperventilation

2) might be reasonable to consider age-appropriate low normal or normal ventilatory rates during paediatric cardiac arrest

3) await further studies before we can make specific rate recommendations in paediatric cardiac arrest in general

4) unknown if modifications could be needed in specific paediatric (special) populations with known cardiac/respiration conditions in the in-hospital setting.

Current Search Strategy (for an existing PICOST) included in the attached approved PICOST

PUBMED.ncbi.nlm.nih.gov

((("ventilation"[Title/Abstract] OR "breath"[Title/Abstract] OR "respirat*"[Title/Abstract] OR "positive pressure respiration"[MeSH Terms]) AND ("rate"[Title/Abstract]) AND ("life support care"[MeSH Terms] OR "life support"[Title/Abstract] OR "cardiopulmonary resuscitation"[MeSH Terms] OR "cardiopulmonary resuscitation"[Title/Abstract] OR "heart arrest"[MeSH Terms] OR "cardiac arrest"[Title/Abstract]) AND ("Adolescent"[MeSH Terms] OR "Child"[MeSH Terms] OR "Infant"[MeSH Terms] OR "Pediatrics"[MeSH Terms] OR "infan*"[Title/Abstract] OR "child*"[Title/Abstract] OR "adolescen*"[Title/Abstract] OR "pediatric*"[Title/Abstract] OR "paediatric*"[Title/Abstract] OR "pube*"[Title/Abstract] OR "juvenil*"[Title/Abstract] OR "school*"[Title/Abstract] OR "newborn*"[Title/Abstract] OR "new born*"[Title/Abstract] OR "neonat*"[Title/Abstract] OR "premature*"[Title/Abstract] OR

"postmature*"[Title/Abstract] OR "pre mature*"[Title/Abstract] OR "post mature*"[Title/Abstract] OR "preterm*"[Title/Abstract] OR "pre term*"[Title/Abstract] OR "baby"[Title/Abstract] OR "babies"[Title/Abstract] OR "toddler*"[Title/Abstract] OR "youngster*"[Title/Abstract] OR "preschool*"[Title/Abstract] OR "kindergart*"[Title/Abstract] OR "kid"[Title/Abstract] OR "kids"[Title/Abstract] OR "playgroup*"[Title/Abstract] OR "play group*"[Title/Abstract] OR "playschool*"[Title/Abstract] OR "prepube*"[Title/Abstract] OR "preadolescen*"[Title/Abstract] OR "junior high*"[Title/Abstract] OR "highschool*"[Title/Abstract] OR "senior high"[Title/Abstract] OR "young people*"[Title/Abstract] OR "minors"[Title/Abstract])) NOT ("Letter"[Publication Type] OR "Editorial"[Publication Type] OR "Comment"[Publication Type])) NOT ("animals"[MeSH Terms] NOT "humans"[MeSH Terms])

Database searched: Pubmed

Time Frame: May 2023-October 2024 (updated from previous search)

Date Search Completed: 30 September 2024

Search Results (Number of articles identified and number identified as relevant): 68 articles identified. 2 selected after title and abstract screening, 0 found relevant.

68 articles after limit search 1 May 2023 to 1 October 2024

2 articles after 66 excluded upon title and abstract screening

0 articles included in analysis after full text review

Summary of Evidence Update:

The ILCOR PLS Task Force systematic review performed in 2023 on ventilation rates during pediatric cardiac arrest didn't find any publication that could support new treatment recommendations. Our Evidence Update in 2024 identified no new pediatric studies on this subject.

Relevant Guidelines or Systematic Reviews

Organization (if relevant); **Author;** **Year Published**	**Guideline or systematic review**	**Topic addressed or PICO(S)T**	**Number of articles identified**	**Key findings**	**Treatment recommendations**
ILCOR PLS Task Force; (no ref yet)	Systematic review		0		There is currently no supporting evidence to recommend a specific ventilatory rate in pediatric cardiopulmonary resuscitation with an advanced airway. There is insufficient data to recommend a specific respiratory rate in the on out-of-hospital setting.

Reviewer Comments:

As our evidence update failed to identify any new publications since the updated systematic review was conducted in 2023, a new systematic review of ventilation rates in pediatric cardiac arrest patients is not warranted at this time.

2025 Evidence Update
PLS 4160.11 – Management of Pulmonary Hypertension with CA in Infants and Children in the Hospital Setting

Worksheet Author(s): Anne-Marie Guerguerian
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:

Year of last full review: (*insert year where this PICOST was most recently reviewed)* 2023

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

Good practice statement following Scoping Review:

In children including neonates with pulmonary hypertension hospitalized for a clinical worsening event, we suggest avoiding factors that may increase pulmonary vascular resistance while treating the aggravating condition to decrease the risk of cardiac arrest. There is insufficient evidence to suggest using specific interventions over others. Management strategies include avoiding hypoxia, hypercapnia, acidosis, stressors such as pain, agitation, dehydration or fluid overload, anemia, infection, or arrhythmias. Pulmonary hypertension specific treatments e.g., iNO, L-Arginine, phosphodiesterase inhibitors (e.g., Milrinone, Sildenafil) or endothelin-1 inhibitors (e.g., Bosentan) may be considered.

In children who develop signs of pulmonary hypertensive crisis, of low cardiac output or of right ventricular failure despite optimal medical therapy, ECMO may be considered before cardiac arrest or for refractory cardiac arrest, as a bridge to recovery, or as a bridge to the evaluation for organ replacement and transplantation in very selected cases.

Current Search Strategy:

Database searched: Medline October 17, 2024

Time Frame: (existing PICOST) – updated from end of last search (please specify)

Date Search Completed: December 22, 2023 in Medline, Embase, and Cochrane for previous CoSTR and run in May 22 2024 and October 17, 2024 in Medline only

Search Results (Number of articles identified and number identified as relevant): None

Summary of Evidence Update: There is no new published evidence since December 2023 informing the PICOST that was evaluated with a scoping review. 0

Reviewer Comments:

There is insufficient evidence to support the conduct of a systematic review. There were many reviews and consensus statements on the treatment of pulmonary hypertension in neonates and in children published prior to 2024, however these collectively do not address resuscitation measures applied the context of cardiac arrest.

2025 Evidence Update
PLS 4180.01 and 4180.02– Post-ROSC Oxygenation and POST-ROSC Ventilation

Worksheet Author(s): Joseph, Rossano, Gabrielle Nuthall, Andrea Christoff, Steve Schexnayder, Michelle Myburgh, Barney Scholefield, Raffo Escalante
Task Force: Pediatric Life Support
Conflicts of Interest: None

PICOST / Research Question:

PICOST	Description
Population	Paediatric patients (>28 days to 18 years of age) who achieve return of circulation (ROC) after out-of-hospital or in-hospital cardiac arrest.
Intervention	a ventilation and oxygenation strategy targeting a specific oxygen saturation as measured by a pulse oximeter (SpO2), partial pressure of oxygen in arterial blood (PaO2), and/or partial pressure of carbon dioxide in arterial blood (Pa CO2)
Comparison	compared to treatment without specific targets or with an alternate target to the intervention
Outcomes	Any outcome as defined in the Pediatric Core Outcome Set for Cardiac Arrest
Study Design	Randomized controlled trials (RCTs) and non-randomized studies (non-randomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) and case series >10 cases are eligible for inclusion. Unpublished studies (e.g., conference abstracts, trial protocols) are excluded. All relevant publications in any language are included as long as there is an English abstract**.**
Timeframe	***July 1, 2019 to June 20, 2024 – Evidence Update Search timeframe (update from the Holmberg previous SR on adult and children 2019)***

Year of last full review: SR in 2019

Current ILCOR Consensus on Science and Treatment Recommendation for this PICOST:

We suggest that rescuers measure PaO2 after ROSC and target a value appropriate to the specific patient condition. In the absence of specific patient data, we suggest rescuers target normoxemia after ROSC (weak recommendation, very-low-quality evidence).
Given the availability of continuous pulse oximetry, targeting an oxygen saturation of 94-99% may be a reasonable alternative to measuring PaO2 and titrating oxygen when feasible to achieve normoxia.(based on expert opinion)
We suggest that rescuers measure PaCO2 after ROSC and target normocapnia (weak recommendation, very-low-certainty evidence).
Consider adjustments to the target paCO2 for specific patient populations where normocapnia may not desirable (e.g. chronic lung disease with chronic hypercapnia, congenital heart disease with single ventricle physiology, increased intracranial pressure with impending herniation) (based on expert opinion)

Current Search Strategy

MEDLINE
1 exp Heart Arrest/
2 ((heart or cardi* or cardiovascular) adj1 arrest*).ab,kf,ti.
3 code 99.ab,kf,ti.
4 asystole.ab,kf,ti.
5 ((cardiopulmonary or cardio-pulmonary) adj1 arrest*).ab,kf,ti.
6 code blue.ab,kf,ti.
7 respiratory arrest*.ab,kf,ti.
8 pulseless electrical activity.ab,kf,ti.
9 Advanced Cardiac Life Support/
10 Advanced Cardi* Life Support.ab,kf,ti.
11 ACLS.ab,kf,ti.
12 exp Cardiopulmonary Resuscitation/
13 ventricular fibrillation/ or Tachycardia, Ventricular/
14 resuscitation/
15 ((cardiopulmonary or cardio-pulmonary) adj1 resuscitation).ab,kf,ti.
16 CPR.ab,kf,ti.
17 Resuscitation.jw.
18 or/1-17
19 (spontaneous circulation or Return of circulation).ab,kf,ti.
20 ROSC.ab,kf,ti.
21 (re-animat* or reanimate* or reanimation).ab,kf,ti.

22 (post resuscitat* or post-resuscitat* or postresuscitat*).ab,kf,ti.
23 postarrest*.ab,kf,ti.
24 (post adj2 (heart or cardiac or cardiovascular) adj1 arrest*).ab,kf,ti.
25 Intensive Care Units/
26 (Intensive Care or ICU or ICUs).ab,kf,ti.
27 or/19-26
28 Oxygen/bl [Blood]
29 Carbon Dioxide/bl [Blood]
30 hypoxia/ or hypercapnia/ or hyperoxia/ or hypocapnia/
31 exp Oxygen Inhalation Therapy/
O2 and CO2 Systematic Review Protocol
Page **6** of **13**
32 Respiration, Artificial/
33 exp Ventilators, Mechanical/
34
((blood or arterial or peripheral or titrated or inspired or high flow or supplement* or concentration or saturat*) adj2 (oxygen or oxygenation or reoxygenation or Carbon Dioxide or CO2 or O2)).ab,kf,ti.
35 (hypoxia or hyperoxia or normoxia or normocarbia or hypercapnia or hypocapnia or hyperoxic or supranormal or normoxic or titrated).ab,kf,ti.
36 Mechanical ventilat*.ab,kf,ti.
37 ventilation strateg*.ab,kf,ti.
38 (PaO2 or SpO2 or PaCO2).ab,kf,ti.
39 or/28-38
40 18 and 27 and 39
41 Animals/ not (Animals/ and Humans/)
42 40 not 41
43 (case reports or comment or editorial).pt.
44 42 not 43
45 ("30430209" or "29437118" or "24892265" or "27697606" or "27060535").ui.
46 44 and 45
47 ("26415731" or "25600183" or "24557423" or "24210887" or "23613256" or "23454258" or "17101205").ui.
48 44 and 47

EMBASE
1 heart arrest/ or cardiopulmonary arrest/ or "out of hospital cardiac arrest"/
2 ((heart or cardi* or cardiovascular) adj1 arrest*).ab,kw,ti.
3 (code 99 or code blue).ab,kw,ti.
4 asystole.ab,kw,ti.
5 ((cardiopulmonary or cardio-pulmonary) adj1 arrest*).ab,kw,ti.
6 respiratory arrest/
7 "respiratory arrest*".ab,kw,ti.
8 pulseless electrical activity.ab,kw,ti.
9 *resuscitation/
10 "Advanced Cardi* Life Support".ab,kw,ti.
11 ACLS.ab,kw,ti.
12 heart ventricle fibrillation/ or heart fibrillation/
13 heart ventricle tachycardia/
O2 and CO2 Systematic Review Protocol
Page **7** of **13**
14 ((cardiopulmonary or cardio-pulmonary) adj1 resuscitation).ab,kw,ti.
15 CPR.ab,kw,ti.
16 Resuscitation.jx.
17 or/1-16
18 "return of spontaneous circulation"/

19 (spontaneous circulation or Return of circulation).ab,kw,ti.
20 ROSC.ab,kw,ti.
21 (re-animat* or reanimate* or reanimation).ab,kw,ti.
22 (post resuscitat* or post-resuscitat* or postresuscitat*).ab,kw,ti.
23 "postarrest*".ab,kw,ti.
24 (post adj2 (heart or cardi* or cardiovascular) adj1 arrest*).ab,kw,ti.
25
intensive care unit/ or exp coronary care unit/ or medical intensive care unit/ or pediatric intensive care unit/
26 (Intensive Care or ICU or ICUs).ab,kw,ti.
27 or/18-26
28 *oxygen/
29 oxygen therapy/
30 oxygen blood level/
31 *carbon dioxide/
32 carbon dioxide blood level/
33 *hypoxia/ or *hypercapnia/ or *hyperoxia/ or *hypocapnia/
34 artificial ventilation/
35 mechanical ventilator/
36
((blood or arterial or peripheral or titrated or inspired or high flow or supplement* or concentration or saturat*) adj2 (oxygen or oxygenation or reoxygenation or Carbon Dioxide or CO2 or O2)).ab,kw,ti.
37
(hypoxia or hyperoxia or normoxia or normocarbia or hypercapnia or hypocapnia or hyperoxic or supranormal or normoxic or titrated).ab,kw,ti.
38 "Mechanical ventilat*".ab,kw,ti.
39 "ventilation strateg*".ab,kw,ti.
40 (PaO2 or SpO2 or PaCO2).ab,kw,ti.
41 oxygen saturation/
42 blood oxygenation/
43 arterial oxygen tension/
44 arterial carbon dioxide tension/
45 *oxygen concentration/
46 or/28-45
47 17 and 27 and 46
48 47 not ((exp animal/ or nonhuman/) not exp human/)
49 (books or conference abstract or conference paper or conference review or editorial).pt.
50 "case report"/
51 case study/
52 case series.ti.
53 49 or 50 or 51 or 52
54 48 not 53
55 remove duplicates from 54

EBM Reviews
1 ((heart or cardi* or cardiovascular) adj1 arrest*).mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
2 ((cardiopulmonary or cardio-pulmonary) adj1 arrest*).mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
3 respiratory arrest*.mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
4
(asystole or code blue or code 99 or Advanced Cardiac Life Support or pulseless electrical activity).mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
5 ((cardiopulmonary or cardio-pulmonary) adj1 resuscitation).mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
6 (ventricular fibrillation or Ventricular Tachycardia).mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
7 1 or 2 or 3 or 4 or 5 or 6
8 ((spontaneous or Return) adj2 circulation).mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
9 (ROSC or re-animat* or reanimate* or reanimation).mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]

10
(post resuscitat* or post-resuscitat* or postresuscitat* or postarrest*).mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
11 (post adj2 (heart or cardi* or cardiovascular) adj1 arrest*).mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
12 (Intensive Care or ICU or ICUs).mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
13 8 or 9 or 10 or 11 or 12
14
((blood or arterial or peripheral or titrated or inspired or high flow or supplement* or concentration or saturat*) adj2 (oxygen or oxygenation or reoxygenation or Carbon Dioxide or CO2 or O2)).mp. [mp=ti, O2 and CO2 Systematic Review Protocol
Page **9** of **13**
ot, ab, tx, kw, ct, sh, hw]
15
((hypoxia or hyperoxia or normoxia or normocarbia or hypercapnia or hypocapnia or hyperoxic or supranormal or normoxic) adj2 (oxygen or oxygenation or reoxygenation or Carbon Dioxide or CO2 or O2)).ab,kf,ti.
16 Mechanical ventilat*.mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
17 ventilation strateg*.mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
18 (PaO2 or SpO2 or PaCO2).mp. [mp=ti, ot, ab, tx, kw, ct, sh, hw]
19 14 or 15 or 16 or 17 or 18
20 7 and 13 and 19

Database searched: Medline, Embase, Cochrane
Time Frame: (existing PICOST) –July 1, 2019 to June 20, 2024

Date Search Completed: 9/12/2024
Search Results
2,230 studies identified and 3 included as relevant. One additional relevant study was identified from discussion with the co-authors that is currently in press.

Summary of Evidence Update:

Relevant Guidelines or Systematic Reviews

Organization (if relevant); Author; Year Published	**Guideline or systematic review**	**Topic addressed or PICO(S)T**	**Number of articles identified**	**Key findings**	**Treatment recommendations**
Holmberg, 2020, 107 (ILCOR)[1]	Systematic review that formed basis of ILCOR CoSTR	(P), does a ventilation strategy targeting a specific oxygen saturation as measured by a pulse oximeter (SpO2), partial pressure of oxygen in arterial blood (PaO2), and/or partial pressure of carbon dioxide in arterial blood (PaCO2) (I), as	3	Three observational studies assessed found no association of hypoxemia on favorable neurologic outcome or survival to hospital discharge. One observational study found an association of hypercapnia and hypocapnia and	From ILCOR CoSTR: Suggest that rescuers measure PaO2 after ROSC and target a value appropriate to the specific patient condition. In the absence of specific patient data, we suggest rescuers target normoxemia after ROSC (weak recommendation, very-low-quality evidence). Given the availability of continuous pulse oximetry, targeting an oxygen saturation of 94-99% may be a reasonable alternative to measuring PaO2 and titrating oxygen

		compared to treatment without specific targets or with an alternate target to the intervention, improve clinical outcomes (O).		worse survival to hospital discharge.	when feasible to achieve normoxia. Suggest that rescuers measure PaCO2 after ROSC and target normocapnia (weak recommendation, very-low-certainty evidence). Consider adjustments to the target paCO2 for specific patient populations where normocapnia may not desirable (e.g. chronic lung disease with chronic hypercapnia, congenital heart disease with single ventricle physiology, increased intracranial pressure with impending herniation).

Nonrandomized Trials, Observational Studies

Study Acronym; Author; Year Published	**Study Type/Design; Study Size (N)**	**Patient Population**	**Primary Endpoint and Results (include P value; OR or RR; & 95% CI)**	**Summary/Conclusion Comment(s)**
Frazier, 2024, 895[2]	**<u>Study Type:</u>** Retrospective, observational study N=284 Secondary analysis of the ICU-Resuscitation Project which was a multi-center randomized trial of quality improvement measures to improve CPR outcomes in children with IHCA. Study conducted at 18 pediatric and cardiac intensive care units in the United States. Definitions for oxygenation groups were as follows: hypoxemia (lowest arterial oxygen tension/pressure	**<u>Inclusion Criteria:</u>** Patients <18 years and with a corrected gestational age of >37 weeks who received chest compressions of any duration for IHCAs in participating ICUs Index IHCA events with arterial blood gas data during the first 24 hours post–cardiac arrest were included. Patients were excluded with any of the following: 1. were not expected to survive hospitalization because of terminal illness or documented lack of commitment to	**<u>1° endpoint:</u>** Survival to hospital discharge Hypoxemia vs Normoxemia 48/80 (60%) vs 72/85 (85%) Adjusted risk: RR 0.71 (0.58 – 0.87) Survival to hospital discharge Hyperoxemia vs Normoxemia 70/87 (81%) vs 72/85 (85%) Adjusted risk: RR 1.00 (0.87 to 1.15) Survival to hospital discharge Hypercapnia vs Normocapnia 96/147 (65%) vs 71/78 (91%) Adjusted risk: RR 0.74 (0.64 to 0.84) Survival to hospital discharge Hypocapnia vs Normocapnia 22/29 (76%) vs 71/78 (91%) Adjusted risk: RR 0.91 (0.74 to 1.12) **<u>2° endpoints:</u>** Favorable neurologic outome (PCPC 1,2, or 3 or no worse than baseline PCPC) Hypoxemia vs Normoxemia 42/80 (53%) vs 66/85 (78%) Adjusted risk: RR 0.67 (0.52 to 0.85)	Both hypoxemia and hypercapnia groups had worse survival to hospital discharge and neurologically favorable survival on unadjusted and adjusted analyses. These was no association of hyperoxia and hypocapnia on outcomes.

	[PaO2] ,60 mm Hg), normoxemia (all PaO2 measurements, 60–199 mm Hg), and hyperoxemia (highest PaO2, >200 mm Hg).	aggressive ICU therapies 2. were brain dead 3. had an out-of-hospital cardiac arrest (OHCA) associated with current hospitalization 4. cyanotic congenital heart defects or receiving extracorporeal membrane oxygenator (ECMO) therapy were excluded	Favorable neurologic outcome (PCPC 1,2, or 3 or no worse than baseline PCPC) Hyperoxemia vs Normoxemia 67/87 (77%) vs 66/85 (78%) Adjusted risk: RR 1.04 (0.78 – 1.23) Favorable neurologic outcome (PCPC 1,2, or 3 or no worse than baseline PCPC) Hypercapnia vs Normocapnia 89/147 (61%) vs 66/78 (85%) Adjusted risk: RR 0.74 (0.63 to 0.86) Favorable neurologic outcome (PCPC 1,2, or 3 or no worse than baseline PCPC) Hypocapnia vs Normocapnia 22/29 (76%) vs 66/78 (85%) Adjusted risk: RR 0.98 (0.78 to 1.23) Favorable neurologic outcome (PCPC 1 or 2 or no worse than baseline PCPC) Hypoxemia vs Normoxemia 39/80 (49%) vs 62/85 (73%) Adjusted risk: RR 0.66 (0.51 to 0.87) Favorable neurologic outcome (PCPC 1 or 2 or no worse than baseline PCPC) Hyperoxemia vs Normoxemia 60/87 (69%) vs 62/85 (73%) Adjusted risk: RR 0.99 (0.82 to 1.20) Favorable neurologic outcome (PCPC 1 or 2 or no worse than baseline PCPC) Hypercapnia vs Normocapnia 79/147 (54%) vs 63/78 (81%) Adjusted risk: RR 0.68 (0.56 to 0.82) Favorable neurologic outcome (PCPC 1 or 2 or no worse than baseline PCPC) Hypocapnia vs Normocapnia 22/29 (76%) vs 63/78 (81%) Adjusted risk: RR 0.99 (0.79 to 1.26)	
Baretto, 2022, 8[3]	**<u>Study Type:</u>** Retrospective observational study from a single center. N= 187 Hyperoxia was defined as follows: During the first 24 hours after cardiac arrest, using four different definitions: a single PaO2 above 150, 200, or 300 mmHg in the first 24	**<u>Inclusion Criteria</u>** Patients younger than 18 years of age with in-hospital cardiac arrest (receiving at least one minute of chest compressions) between December 2012 and December 2019, who achieved return of circulation (ROC)	**<u>1° endpoint:</u>** Survival to hospital discharge Hyperoxia vs No Hyperoxia 40/89 (45%0 vs 37/98 (38%) OR 1.1 (0.6 to 2.1) **<u>2° endpoint:</u>** Death or poor neurologic outcome (PCPC 3 or more or an increase between hospital admission and discharge for those with an abnormal pre-arrest PCPC score) Hyperoxia vs No Hyperoxia 46/89 (52%) vs 44/98 (45%) OR 1.2 (0.5 to 2.8)	There was no association found with hyperoxia and survival to hospital discharge or with the outcome of death or poor neurologic outcome.

<table>
<tr>
<td></td>
<td>hours after cardiac arrest, or time spent with SpO2 > 99% in the first 24 hours after cardiac arrest.</td>
<td>for longer than 20 minutes, survived at least 24 hours after cardiac arrest, and had documented partial pressure of oxygen (PaO2) or SpO2 during
the first 24 hours after ROC

Exclusion criteria: Missing data on survival to hospital discharge and/or Pediatric Cerebral Performance Category (PCPC) scores. For patients with more than one cardiac arrest during the study period, only the first arrest event was included in the analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holton, 2023, e362[4]</td>
<td><u>Study Type:</u>
Retrospective, observational study. The cohort was from Virtual Pediatric Systems (VPS) that is a clinical pediatric critical care database with over 135 participating hospitals in North America.
N=1500 (post-cardiac arrest patients). The cardiac arrest patients were a subgroup of the 13,071 were included in the overall study.

The PaO2 levels were assessed on admission to the ICU.</td>
<td><u>Inclusion Criteria</u>
Patients 18 years old or younger and admitted between 2015 and 2019 with a documented admission PaO2

Exclusion criteria: Cardiac patients and those admitted to a cardiac ICU</td>
<td><u>1° endpoint:</u>
Hospital mortality

<table>
<tr><th>PaO2</th><th>n</th><th>mortality (%)</th></tr>
<tr><td>0-49</td><td>161</td><td>68.94%</td></tr>
<tr><td>50-99</td><td>494</td><td>62.15%</td></tr>
<tr><td>100-149</td><td>244</td><td>63.93%</td></tr>
<tr><td>150-199</td><td>169</td><td>62.72%</td></tr>
<tr><td>200-249</td><td>112</td><td>50.00%</td></tr>
<tr><td>250-299</td><td>103</td><td>65.05%</td></tr>
<tr><td>300+</td><td>217</td><td>65.90%</td></tr>
<tr><td>Total</td><td>1500</td><td>63.07%</td></tr>
</table>
</td>
<td>There was no clear relationship between admission PaO2 and hospital mortality</td>
</tr>
</table>

<table>
<tr>
<td>Albrecht, 2024 (In Press)[5]</td>
<td><u>Study Type:</u>
Retrospective observational study of data collected from five hospitals that participated in the Pediatric Resuscitation Quality partnership (pediRES-Q).

N=292 (four were lost to follow-up and six had neurologic functioning at discharge was missing)

Cumulative exposure to PaO_2 and $PaCO_2$ was calculated. All available ABGs per child were divided into two time intervals: 0–6h and 7–24h post-ROC. Prior to analysis, cumulative PaO2 and PaCO2 values were rescaled by dividing by 100 in order to keep them in a similar range to other variables in the multivariable analysis.</td>
<td><u>Inclusion Criteria</u>
Children with ROC after IHCA or OHCA aged > 1 day and < 18 years admitted to one of the study hospital paediatric intensive care units (PICUs) between January 2019 and February 2022 were eligible.

Exclusion criteria: Arrests in neonates <24h old (perinatal asphyxia), children with congenital cyanotic heart disease and events with <4 arterial blood gas (ABG) samples taken within the first 24h post-ROC or any number of ABGs spanning less than 12h were excluded.</td>
<td><u>1° endpoint:</u>
The primary outcome measure was survival to hospital discharge with favorable neurologic outcome defined as a PCPC of 1 to 3, or no pre-arrest baseline difference.

<table>
<tr><td></td><td colspan="4">Survival with post-arrest PCPC 1-3 or ΔPCPC 0 at hospital discharge</td></tr>
<tr><td rowspan="2">AUC Variable</td><td colspan="2">Crude</td><td colspan="2">Adjusted[a]</td></tr>
<tr><td>OR (95% CI)</td><td>p-value</td><td>OR (95% CI)</td><td>p-value</td></tr>
<tr><td>AUC PaO_2 0 - 6 h mm Hg[b]</td><td>1.039 (0.958-1.096)</td><td>0.162</td><td>1.038 (0.974-1.105)</td><td>0.255</td></tr>
<tr><td>AUC PaO_2 6 - 24 h mm Hg[b]</td><td>0.989 (0.961-1.017)</td><td>0.425</td><td>0.989 (0.958-1.021)</td><td>0.508</td></tr>
<tr><td>AUC PaO_2 0 - 24 h mm Hg[b]</td><td>1.000 (0.980-1.021)</td><td>0.976</td><td>1.000 (0.977-1.023)</td><td>0.995</td></tr>
<tr><td>AUC $PaCO_2$ 0 - 6 h mm Hg[b]</td><td>1.011 (0.760-1.344)</td><td>0.94</td><td>1.017 (0.687-1.504)</td><td>0.934</td></tr>
<tr><td>AUC $PaCO_2$ 7 - 24 h mm Hg[b]</td><td>1.025 (0.904-1.161)</td><td>0.703</td><td>0.942 (0.818-1.085)</td><td>0.409</td></tr>
<tr><td>AUC $PaCO_2$ 0 - 24 h mm Hg[b]</td><td>1.025 (0.934-1.126)</td><td>0.598</td><td>0.974 (0.872-1.088)</td><td>0.643</td></tr>
</table>

<u>2° endpoint:</u>
The secondary outcome measures were 1. survival to hospital discharge and 2.</td>
<td>Cumulative PaO2 and PaCO2 exposure was not associated with survival to hospital discharge with a favorable neurologic outcome or survival to hospital discharge. In a subgroup analysis of infants, cumulative PaCO2 was associated with survival to hospital discharge.</td>
</tr>
</table>

favorable neurologic outcome only in the survivors (i.e. excluding PCPC 6).

	Survival to hospital discharge			
AUC Variable	Crude		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
AUC PaO_2 0 - 6 h mm Hg[b]	1.027 (0.973–1.084)	1.084	1.032(0.967-1.102)	0.339
AUC PaO_2 6 - 24 h mm Hg[b]	0.986 (0.959-1.013)	1.013	0.989(0.958-1.021)	0.492
AUC PaO_2 0 - 24 h mm Hg[b]	0.996 (0.977-1.017)	1.017	0.998(0.975-1.022)	0.889
AUC $PaCO_2$ 0 - 6 h mm Hg[b]	0.946 (0.712-1.258)	1.258	0.924(0.615-1.387)	0.702
AUC $PaCO_2$ 7 - 24 h mm Hg[b]	1.007 (0.899-1.142)	1.142	0.907(0.785-1.048)	0.184
AUC $PaCO_2$ 0 - 24 h mm Hg[b]	1.007 (0.917-1.105)	1.105	0.943(0.843-1.055)	0.307

	Favorable neurologic outcome only in survivors (i.e. excluding PCPC 6)			
AUC Variable	Crude		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value

			AUC PaO_2 0 - 6 h mm Hg[b]	1.051 (0.935-1.182)	0.405	1.011(0.891-1.147)	0.865	
			AUC PaO_2 6 - 24 h mm Hg[b]	0.998 (0.948-1.050)	0.929	0.989(0.939-1.041)	0.670	
			AUC PaO_2 0 - 24 h mm Hg[b]	1.007 (0.966-1.050)	0.731	0.996(0.955-1.038)	0.846	
			AUC $PaCO_2$ 0 - 6 h mm Hg[b]	1.326 (0.687-2.558)	0.400	1.666(0.708-3.922)	0.243	
			AUC $PaCO_2$ 7 - 24 h mm Hg[b]	1.131 (0.791-1.617)	0.501	1.167(0.752-1.180)	0.490	
			AUC $PaCO_2$ 0 - 24 h mm Hg[b]	1.126 (0.862-1.470)	0.384	1.188(0.837-1.687)	0.334	
			Subgroup analysis: No significant associations in multivariable logistic regression were found for a different definition of favorable neurologic outcome or arrest location (OHCA or IHCA). In the infant age group (<1 year old), cumulative $PaCO_2$ exposure 0–24h post-ROC was associated after adjustment with survival to hospital discharge (OR 0.80, 95% CI 0.64–0.99).					

Reviewer Comments: ***(including whether this PICOST should have a systematic or scoping review*****)**

There were 4 studies identified in this update, published after the systematic review was published: all of which were retrospective, observational studies. One study found an association with hypoxemia and hypercapnia on the critical outcomes of favorable

neurologic outcome and survival to hospital discharge, while the other studies found no overall association. In the study by Albrecht et al., increased cumulative PaCO2 exposer was associated with survival to hospital discharge among infants.

Given the additional studies identified by our evidence update, we suggest an update of the systematic review is warranted.

Reference list:

1. Holmberg MJ, Nicholson T, Nolan JP, Schexnayder S, Reynolds J, Nation K, Welsford M, Morley P, Soar J, Berg KM. Oxygenation and ventilation targets after cardiac arrest: A systematic review and meta-analysis. Resuscitation. 2020;152:107-115.
2. Frazier AH, Topjian AA, Reeder RW, Morgan RW, Fink EL, Franzon D, Graham K, Harding ML, Mourani PM, Nadkarni VM, et al. Association of pediatric postcardiac arrest ventilation and oxygenation with survival outcomes. Ann Am Thorac Soc. 2024;21:895-906.
3. Barreto JA, Weiss NS, Nielsen KR, Farris R, Roberts JS. Hyperoxia after pediatric cardiac arrest: Association with survival and neurological outcomes. Resuscitation. 2022;171:8-14.
4. Holton C, Lee BR, Escobar H, Benton T, Bauer P. Admission pa o2 and mortality among picu patients and select diagnostic subgroups. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies. 2023;24:e362-e371.
5. Albrecht M, de Jonge RCJ, Del Castillo J, Christoff A, De Hoog M, Je S, Nadkarno VM, Niles DE, Tegg O, Wellnitz K, et al. Association of cumulative oxygen and carbon dioxide levels with neurologic outcome after pediatric cardiac arrest resuscitation: A multicenter study. Resuscitation. 2024 (In Press)