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| Question |
| **Should ECPR vs. no ECPR be used for pediatric cardiac arrest ?** |
| **Population:** | pediatric cardiac arrest  |
| **Intervention:** | ECPR |
| **Comparison:** | no ECPR |
| **Main outcomes:** | Survival to hospital discharge; Survival to hospital discharge; Survival to 12 months; Survival to 12 months with VABS II >=70; Survival to 12 months with VABS II >=70. |
| **Setting:** | in hospital setting |
| **Perspective:** | In the pediatric cardiac population and other select physiologic conditions, conventional CPR may not provide the most optimal means of providing oxygenated perfusion to the cerebral and systemic circulations. |
| **Background:** | The evidence update in pediatric ECPR conducted from 2018 and 2021 included two systematic reviews {Esangbedo, 2020, e-934; Farhat, 2021, 682} and 15 published studies. Considering the evidence becoming available on this topic both in pediatrics and in adults, the decision was made to update the adult and pediatrics systematic review {Holmberg, 2022 – PROSPERO CRD42022341077}. |
| **Conflict of interests:** | None declared. |

# Assessment

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| ProblemIs the problem a priority? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know | Survival and neurologic outcomes from refractory in-hospital cardiac arrest in pediatrics remain poor.  |  |
| Desirable EffectsHow substantial are the desirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial○ Small○ Moderate● Large○ Varies○ Don't know | Given the favorable results reported in selected pediatric populations and in institutions with significant resources, there are promising outcomes that deserve to be better understood in order to be replicated. In some physiologic conditions or diseases, conventional CPR with chest compressions may not provide the most optimal means of providing oxygenated perfusion to the cerebral and systemic circulations. |  |
| Undesirable EffectsHow substantial are the undesirable anticipated effects? |
| Judgement | Research evidence | Additional considerations |
| ○ Large○ Moderate○ Small○ Trivial● Varies○ Don't know | The transition from delivering CPR to ECPR may alter the quality of resuscitation measures; moreover, the patient transport that may be necessary to move the patient with ongoing CPR to a cannulation-suited location may decrease the quality of CPR measures.  | The resources allocated to maintain the system performance (people, equipment) may redirect efforts away from other valuable and necessary care practices and interventions in the organization.  |
| Certainty of evidenceWhat is the overall certainty of the evidence of effects? |
| Judgement | Research evidence | Additional considerations |
| ● Very low○ Low○ Moderate○ High○ No included studies | Very low certainty of evidence in-hospital cardiac arrest.Insufficient evidence for out-of-hospital cardiac arrest. |  |
| ValuesIs there important uncertainty about or variability in how much people value the main outcomes? |
| Judgement | Research evidence | Additional considerations |
| ○ Important uncertainty or variability○ Possibly important uncertainty or variability● Probably no important uncertainty or variability○ No important uncertainty or variability | The field of pediatric resuscitation values survival with good (or favorable) neurological outcome. There is not much variability about its importance. There is variability on how studies analyze or dichotomize categorical neurological outcomes. | There are no comparative studies evaluating health related quality of life outcomes or patient-oriented outcomes. |
| Balance of effectsDoes the balance between desirable and undesirable effects favor the intervention or the comparison? |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention● Varies○ Don't know | See published updated systematic review. |  |
| Resources requiredHow large are the resource requirements (costs)? |
| ○ Judgement | Research evidence | Additional considerations |
| ● Large costs○ Moderate costs ○ Negligible costs and savings○ Moderate savings○ Large savings○ Varies○ Don't know | The resources required to deliver ECPR are higher than conventional CPR. There are no cost effectiveness studies published in pediatrics. The cost comparison published {Hamzah, 2021, 2523} reported as secondary outcomes longer lengths of stay and higher inpatient hospital costs in the ECPR group compared to the no ECPR group.  | The institutional resources needed to develop and sustain an ECPR system are substantial; these may represent significant incremental additional resources in institutions without cardiac surgery programs. |
| Certainty of evidence of required resourcesWhat is the certainty of the evidence of resource requirements (costs)? |
| Judgement | Research evidence | Additional considerations |
| ● Very low○ Low○ Moderate○ High○ No included studies | Limited information on cost comparisons is available from a single country (USA) which may or may not be generalizable to other regions. |  |
| Cost effectivenessDoes the cost-effectiveness of the intervention favor the intervention or the comparison? |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison○ Probably favors the comparison○ Does not favor either the intervention or the comparison○ Probably favors the intervention○ Favors the intervention○ Varies● No included studies | No included studies in pediatrics. |  |
| EquityWhat would be the impact on health equity? |
| Judgement | Research evidence | Additional considerations |
| ○ Reduced● Probably reduced○ Probably no impact○ Probably increased○ Increased○ Varies○ Don't know |  | There is insufficient published evidence to understand if there is equitable access within an institution or between institutions across a system (e.g., either regional or national). However, we speculate that there are wide differences in access in this complex and expensive intervention. |
| AcceptabilityIs the intervention acceptable to key stakeholders? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no● Probably yes○ Yes○ Varies○ Don't know | ECMO and ECPR has been adopted by some institutions. The acceptability has not been formally evaluated but quality networks (e.g., PC4) and registries (e.g., ELSO) report an increasing use of this technology for IHCA resuscitation in pediatrics. |  |
| FeasibilityIs the intervention feasible to implement? |
| Judgement | Research evidence | Additional considerations |
| ○ No○ Probably no○ Probably yes● Yes○ Varies○ Don't know | Systems with adequate and committed resources (people, expertise, equipment) have shown this intervention to be feasible to implement in the in-hospital setting. |  |

# Summary of judgements

|  | **Judgement** |
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| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | Moderate | **Large** |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | Trivial |  | **Varies** | Don't know |
| **Certainty of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | **Varies** | Don't know |
| **Resources required** | Large costs | **Moderate costs** | Negligible costs and savings | Moderate savings | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | Probably favors the intervention | Favors the intervention | Varies | **No included studies** |
| **Equity** | Reduced | **Probably reduced** | Probably no impact | Probably increased | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |

# Type of recommendation

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| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | **Conditional recommendation for the intervention** | Strong recommendation for the intervention |
| ○  | ○  | ○  | **●**  | ○  |

# Conclusions

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| Recommendation |
| We suggest there is insufficient evidence to change the treatment recommendation from the 2020 & 2021 Pediatric CoSTR (Maconochie 2020 A120, Maconochie 2021 147 Sup 1).We suggest that ECPR may be considered as an intervention for selected infants and children (e.g., 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-quality evidence). There is insufficient evidence in pediatric OHCA to formulate a treatment recommendation for the use of ECPR. |
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| Justification |
| In making this weak recommendation, we note that in select pediatric patient populations (i.e., cardiac arrest with cardiac disease) the practice of using ECPR has become widespread across some institutions with systems that support post operative cardiac surgical ecosystems. We acknowledge that ECPR is a complex system intervention that requires considerable resources and sustained training that may not be universally available. |

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| Subgroup considerations |
| The majority of the published literature includes in-hospital pediatric cardiac patients. There is a need to understand which out-of-hospital selected pediatric populations and in-hospital pediatric non-cardiac populations may benefit from ECPR compared to high quality CPR alone. |

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| Implementation considerations |
| The investment required to implement and sustain a high-quality ECPR program compared to a high-quality CPR program is significant. A high quality ECPR program is more likely to be feasible in organizations that build on the infrastructure and expertise necessary for cardiac surgery or trauma programs. Given the low frequency event and the high performing system required to sustain an ECPR program, organizations must be able to commit significant additional resources for training, simulation, and performance improvement processes to ensure the quality and the expertise are adequate. If these resources are not available, it may be reasonable to consider not using ECPR, as this intervention is not suitable to ad-hoc deployments. |

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| Monitoring and evaluation |
| The evaluations of processes and patient outcomes are necessary to continue to better understand the impact of ECPR compared to high-quality CPR alone.  |

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| Research priorities |
| The knowledge gaps remain numerous when it comes to comparing the application of ECPR (which involves a first period of conventional CPR) to conventional CPR alone in pediatrics. * There are no comparative prospective studies nor randomized trials.
* There are insufficient studies in selected IHCA (e.g., non-cardiac) or in OHCA populations.
* It remains unknown how the transition from conventional CPR to ECPR alters the quality of resuscitation measures.
* It remains unknown how best to provide closed chest CPR and transition to a peripheral or to central ECPR cannulation (with or without a sternotomy) or how to best perform open chest CPR in the context of surgical instrumentation for central ECPR.
* It remains unknown how best to provide immediate and early post cardiac arrest care with ECPR (E-PCAC) (temperature targeted management, oxygenation, decarboxylation, perfusion pressure, transfusion therapies).
* Reporting of studies using ECPR is heterogeneous and not standardized; this domain of resuscitation research would benefit from applying core definitions from the Utstein reporting standards and from incorporating pediatric core outcomes for cardiac arrest (P-COSCA) {Topjian 2020 e-246}. Moreover, an update in Utstein reporting definitions would serve to enhance the reporting of resuscitation measures applied during this technique (e.g., temperature applied on reperfusion; total duration of cardiac arrest deconstructed with intervals of conventional compressions, open chest compressions, and interruptions…).
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# References Summary