QUESTION

Should a specific blood pressure target (I) vs no blood pressure target or a different blood pressure target be used for infants and children in any setting (in-hospital or out-of-hospital cardiac arrest) after return of spontaneous circulation (ROSC) (P)?	
POPULATION:	infants and children after return of spontaneous circulation (ROSC) (P),
INTERVENTION:	A specific blood pressure target
COMPARISON:	No blood pressure target or a different blood pressure target
MAIN OUTCOMES:	Survival to hospital discharge; Survival with favourable neurological outcome;
SETTING:	in-hospital or out of hospital cardiac arrest (IHCA, OHCA)
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	A Topjian – Senior author on included studies was recused from Pediatric Task Force recommendations. However, did provide context and background information.

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Cardiac arrest In and out of hospital is a major cause of morbidity and mortality in infants and children. Once return of circulation (ROC) is achieved, the next phase is ensuring adequate organ perfusion and reducing the risk of further neurological injury during the post-resuscitation syndrome. Blood pressure control is among the critical factors influencing prognosis and outcome after cardiac arrest. Maintaining an adequate blood pressure may be linked to maintaining adequate tissue perfusion and optimizing patient outcomes. Determining the optimal blood pressure targets in infants and children after ROC poses a significant challenge due to lack of evidence. Clinical practice in this area is largely based upon a few pediatric studies, extrapolation from studies conducted in adult populations or expert consensus recommendations. While studies identified an association between hypotension post-ROC in infants and children, these studies are small and it is also difficult to know if the association is causal or is a surrogate marker of more severe cardiac arrest. Potential benefits include both more survivors to hospital discharge and also more survivors with favourable neurological outcomes. However, use of higher blood pressure targets may	This is the first systematic review on this topic for the pediatric task force

	have undesirable patient effects, such as longer length of hospital or intensive care stay and complications of requiring central intravenous access to deliver medication.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Six studies were included from the systematic review (Topjian 2014, 1518; Topjian 2018, 143; Topjian 2019a, 88; Topjian 2019b, 24, Laverriere 2020, 143; Gardner 2023, 388). All six were non-randomized observational cohort studies, with five being secondary analyses. The review identified significant variation in BP target definitions (e.g. systolic, mean and diastolic BP; and >5th, >10th and >50th centile for age) and time frames for measurement (<20 minutes, 0 to 6 hours, within 24 hours, and within 0-72 hours). In our final analysis, we included four studies (Topjian 2014, 1518; Topjian 2018, 143; Topjian 2019a, 88; Laverriere 2020, 143) examining the BP targets of systolic BP >5th centile for age compared with systolic BP ≤5th centile within the first six hours post return of circulation. The pooled sample included 463/930 (49.8%) patients following in-hospital cardiac arrest (IHCA), and 467/930 (50.2%) after out-of-hospital cardiac arrest). We also included one study (Gardiner 2023, 388) which enrolled 693 infants and children after IHCA (excluding patients requiring extra-corporeal life support). This study compared systolic BP >10th centile with systolic BP ≤10th centile within the first six hours post return of circulation. The systolic BP cut off at the 10th centile was generated from receiver operator characteristic curves and spline curves created from the study data. For the critically important outcome of survival, we identified very-low-certainty evidence (downgraded for inconsistency and indirectness) from four observational studies (Topjian 2014, 1518; Topjian 2018, 143; Topjian 2019a, 88; Laverriere 2020, 143) enrolling 931 children after in-hospital or out-of-hospital cardiac arrests, in the first six hours post return of circulation (ROC), that showed benefit from exposure to a systolic BP >5th centile when compared with systolic BP ≤5th centile (pooled adjusted Relative Risk (aRR), 1.34; 95%CI, 1.07 to 1.52); P = 0.01); 143 more patients/1000 survived with the intervention [95% CI, 30 more patients/1000 to 219 more patients/1000 survived with the intervention]). For the critically important outcome of survival with good neurological outcome, we identified very-low-certainty evidence (downgraded for inconsistency and indirectness) from two observational studies (Topjian 2014, 1518; Laverriere 2020, 143) enrolling 584 children after in-hospital or out-of-hospital cardiac arrests, in the first six hours post ROC, that showed benefit from exposure to a systolic BP >5th centile when compared with SBP ≤5th centile (pooled aRR, 1.30; 95%CI, 1.06 to 1.60); P = 0.01); 156 more patients/1000 survived with the intervention [95% CI, 31 more patients/1000 to 312 more patients/1000 survived with the intervention]).	Although the size effect from the combines studies is small, the value of the outcomes is of high value and the potential impact on infants and children globally who get ROSC following a CA is large. The three studies (Gardner 2023, 388; Topjian 2019a, 88; Topjian 2019b, 24) use BP norms adjusted for age, sex and height, Topjian (2018, 1518) uses age, and the other papers used BP norms adjusted for age and sex. The task force felt it was most appropriate to use BP norms adjusted for age, sex and height. Two studies (Topijan 2019b, 24; Topijan 2014, 143) targeted temperature management was applied. The SBP measurements were obtained during the 0-6 hour time frame from when the targeted temperature management was applied and not from the time of sustained ROC. In both studies targeted temperature management was initiated within the first 6 hours of sustained ROC. Two studies were excluded as the definition of hypotension could not be ascertained (Lin 2010, 410; Lin 2013, 439).

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Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk >5th SBP centile systolic blood pressure target within 6 hours compared with ≤5th	Risk difference with >5th centile systolic blood pressure target within 6 hours compared with ≤5th.
Survival to hospital discharge assessed with: survival	931 (4 non-randomised studies)[1,2,3,4]	⨁◯◯◯ Very low[a,b]	**RR 1.41** (1.20 to 1.60)	Study population	
				422 per 1,000	**173 more per 1,000** (84 more to 253 more)
Survival with favourable neurological outcome assessed with: PCPC 1-2 and 0-1 change from baseline, or 1-3 and no change from baseline	584 (2 non-randomised studies)[1,4]	⨁◯◯◯ Very low[c,d]	**RR 1.30** (1.06 to 1.60)	Study population	
				520 per 1,000	**156 more per 1,000** (31 more to 312 more)

1. Topjian, et al. Early postresuscitation hypotension is associated with increased mortality following pediatric cardiac arrest. Critical care medicine ; 2014.
2. Topjian, et al. Association of Early Postresuscitation Hypotension With Survival to Discharge After Targeted Temperature Management for Pediatric Out-of-Hospital Cardiac Arrest: Secondary Analysis of a Randomized Clinical Trial. JAMA pediatrics ; 2018.
3. Topjian, et al. Therapeutic Hypothermia after Pediatric Cardiac Arrest Trial, Investigators. The association of early post-resuscitation hypotension with discharge survival following targeted temperature management for pediatric in-hospital cardiac arrest.. Resuscitation; 2019.
4. Laverriere, et al.. Association of Duration of Hypotension With Survival After Pediatric Cardiac Arrest. Pediatric. Pediatric critical care medicine; 2020.

a. Combining OHCA and IHCA with different BP monitoring devices.
b. Secondary analysis of RCTs. BP assessment was not primary goal
c. Similar assessment of hypotension and burden of hypotension.

d. Only 2 studies available

For the critically important outcome of survival, we identified very-low-certainty evidence (downgraded for indirectness) from one study (Gardner 2023, 388), showing benefit from exposure to a systolic BP > 10th centile when compared with systolic BP ≤10th centile (aRR, 1.21; 95%CI, 1.00 to 1.33); P <0.01); 138 more patients/1000 survived with the intervention [95% CI, 66 more patients/1000 to 213 more patients/1000 survived with the intervention]).

For the critically important outcome of survival with good neurological outcome, we identified very-low-certainty evidence (downgraded for indirectness) from one study (Gardner 2023, 388), that showed benefit from exposure to a systolic BP >10th centile when compared with systolic BP ≤10th centile (aRR, 1.22; 95%CI, 1.10 to 1.35); P <0.01); 134 more patients/1000 survived with the intervention [95% CI, 61 more patients/1000 to 213 more patients/1000 survived with the intervention]).

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk >10th SBP centile systolic blood pressure target within 6 hours compared with ≤10th	Risk difference with >10th centile systolic blood pressure target within 6 hours compared with ≤10th.
Survival	693 (1 non-randomised study)[1]	⨁◯◯◯ Very low[a,b]	**RR 1.210** (1.100 to 1.333)	Study population	
				657 per 1,000	**138 more per 1,000** (66 more to 219 more)
Survival with favourable neurological outcome assessed with: PCPC 1-3 or no change from baseline	692 (1 non-randomised study)[1]	⨁◯◯◯ Very low[a,b]	**RR 1.22** (1.10 to 1.35)	Study population	
				610 per 1,000	**134 more per 1,000** (61 more to 213 more)

	5. Gardner, et al. Identification of post-cardiac arrest blood pressure thresholds associated with outcomes in children: an ICU-Resuscitation study.. Critical Care; 2023. a. Only contained IHCA. b. Only one study available.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	The undesirable effects of not surviving to hospital discharge and surviving with unfavourable neurological outcomes are significant. However, we did not look at reasons for non-survival as an *a priori* outcome, and the studies do not report value to families of survival with un-favourable neurological outcomes vs death.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Six studies were included in the systematic review. All studies were non-randomised cohort studies, with five out of the six being secondary analyses of other studies. Two of these (Topjian 2018, 1518; Topjian 2019b,24) were secondary analysis of multicentre RCT's (Therapeutic hypothermia after pediatric cardiac arrest (THAPCA) In Hospital Cardiac Arrest and out of Hospital Cardiac Arrest) (Moler 2015, 372; Moler 2017, 318). Topjian (2019a, 88), was a secondary analysis of a prospective multicentre cohort study, Topjian (2014, 143) was a retrospective cohort study from a multicentre database of cardiac arrest, the Pediatric Emergency Care Applied Research Network (PECARN). The only single centre study, (Laverriere 2020, 143), was a retrospective cohort study of both IHCA and OHCA from a prospectively collected database. The largest study, of 693 infants and children, (Gardiner 2023, 388), was a secondary analysis of prospectively collected data for the ICU-RESUS trial and involved 18 US centres (ICU-RESUS Groups 2022, 327). The blood pressure cut offs of	For the question of $\geq$ 5th centile blood pressure target within 6 hours, the 4 papers included were, Topjian 2019b (p 24), Laverriere 2020 (p 143), Topjian 2014 (p 143) and Topjian 2018 (p 1518) including a total of 933 patients with both IHCA and OHCA. The combined population in the studies included patients with IHCA and OHCA, (463/930 (49.8%) IHCA, and 467/930 (50.2%) OHCA).

	systolic blood pressure greater than 10th centile and diastolic blood pressure of greater than 50th centile were generated from receiver operator characteristic curves and spline curves.	For the question of ≥ 10th centile blood pressure target within 6 hours there was one paper, Gardner (2023; 388), with 693 patients included over 18 pediatric intensive care units, who all had IHCA.

Values

Is 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 ILCOR P-COSCA initiative developed a core outcome set specific for pediatric cardiac arrest studies. The design and methods of the initiative included use of a Delphi process to develop consensus on a core domain set. (Topjian 2020 e246) The P-COSCA outcomes of survival to discharge and survival to discharge with favourable neurological outcomes were chosen as critical outcomes for this review and are highly valued.	

Balance of effects

Does 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	Acknowledging the very low level of certainty the current available data suggest that exposure to a systolic blood pressure (SBP) target of > 5th centile for age and height within the first 6 hours post ROSC is better compared to exposure to ≤5th centile for the critical outcomes of both survival to hospital discharge and also favourable neurological outcomes at discharge. Evidence, with low level of certainty, also suggest that exposure to a systolic blood pressure (SBP) target of >10th centile for age and height within the first 6 hours post ROSC is better compared to exposure to ≤10th centile for the critical outcomes of both survival to hospital discharge and also favourable neurological outcomes at discharge. No studies compared 5th centile with 10th centile targets. The Task Force considered that the 5th centile target was included (overlapped) within the comparison group of the <10th centile target population. The 10th centile cut off was chosen after discussion on 1) the statistical methods to identify the 10th centile target (using receiver operator and cubic spline analysis), 2) evidence that patients exposed to systolic BP between 5th to 10th centile in the study by	It is unclear if 10th centile systolic BP targets are superior to 5th centile BP targets. In addition higher BP targets were not compared. Also, there was no comparison between systolic versus mean arterial BP or diastolic BP.

	Gardener (2023; 388) experience worse outcome (lower risk of survival, or survival with favourable neurological outcome).	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	There are no specific studies looking at this, but in settings where ICU level of care is available, measuring and managing blood pressure is standard of care. In all 4 studies information was provided around inotrope use, but this was not analysed as it was not an *a priori* question or subgroup. There was heterogeneity between the studies as to how they reported inotrope use.	In places where ICU level of care is not available for infants and children post cardiac arrest this will be more difficult to achieve, but the principle is likely to still be acceptable to stakeholders. It was felt by the task force that in infants and children who have cardiac arrest followed by ROC, blood pressure should be measured as part of their post cardiac arrest care.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	There is no specific research evidence to support the intervention being feasible to implement, but management of blood pressure is presently part of standard post cardiac arrest care.	In places where ICU level of care is not available for infants and children post cardiac arrest this will be more difficult to achieve, but the principle is likely to still be acceptable to stakeholders.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		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
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

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

Recommendation

We suggest in infants and children post return of circulation, following an in-hospital or out-of-hospital cardiac arrest, that a systolic blood pressure >10th centile for age should be targeted (weak recommendation, very low certainty evidence).

Justification

The Pediatric Task Force considered that the measurement and treatment of blood pressure is a standard component of the post-resuscitation bundle of care after cardiac arrest. However, current post-cardiac arrest blood pressure treatment targets and thresholds for treatment have been suggested through expert consensus and evidence extrapolated from individual studies. The Pediatric Task Force therefore undertook an ILCOR led systematic review of the current evidence.

Measurement of blood pressure is a low-cost intervention and available in nearly all resource settings. However, the taskforce did not review the cost-effectiveness of intermittent, non-invasive blood pressure measurement with invasive arterial or continuous BP measurement.

There were no randomized controlled studies comparing two treatment approaches, or two BP targets following cardiac arrest. The available evidence consisted of observational data demonstrating the impact of exposure to two different blood pressure thresholds on clinically important outcomes. However, the blood pressure thresholds were chosen either a-priori by investigators as a clinically important threshold (eg ≤5th centile), or the cut off value was derived statistically from the population data, as the most significant inflection point (≤10th centile). The Pediatric Task Force focused on the impact of hypotension on clinical outcome and did not include studies assessing normotension or hypertension on outcomes. This will form part of future assessments.

The Pediatric Task Force considered the exposure overlap of the two thresholds ≤5th centile and ≤10th centile. It was not statistically possible to perform meta-regression to compare the two treatment targets. The consensus of the Pediatric Task Force was that higher threshold cut off target (<10th centile) included the population included in the ≤5th centile group and felt that, accepting the low certainty of evidence, the target of >10th centile SBP was the more conservative systolic BP goal to suggest until more evidence is available.

The Task Force felt, that although the effect size from the pooled studies is small, the value of the outcome is high and the potential impact on infants and children survivors globally is therefore large.

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- In two papers (Topjian b p24) and Topjian p143) targeted temperature management was applied. The SBP measurements were obtained during the 0-6 hour time frame from when the targeted temperature management was applied and not from the time of sustained ROSC. In both studies targeted temperature management was initiated within the first 6 hours of sustained ROSC, but it was not an a priori sub group analysis.

Implementation considerations

Management of blood pressure is a component of standard pediatric care treatment.

Monitoring and evaluation

See research priorities below.

Research priorities

There are no interventional randomized controlled trials comparing benefit or harm of targeting specific BP targets.

Information on impact of pre-hospital BP measurement or treatment for OHCA is missing.

It is unclear if specific sub-groups of pediatric patients post return of circulation require different BP targets. Observational data demonstrate an association between exposure to lower BP targets and worse outcome; however, more data are required to demonstrate a causal relationship between treatment

interventions to achieve higher BP targets and improved outcomes. In addition, the TF was unable to assess the benefits or harm of exposure to hypertension in the period after cardiac arrest.

Commented [di3]: IS it just treatment interventions of does this include children who don't need additional support?

We encourage consistent reporting of BP monitoring definitions (e.g. site, repeated measurement, component of BP (systolic, diastolic, mean BP) and definitions of exposure to hypotension (e.g. single episode versus percentage of time).

Majority of included data report exposure to BP thresholds within six hours; impact of BP interventions outside this timeframe is important.

It is unclear which strategy is optimal to achieve a BP above the threshold level (e.g. fluids, vasopressor support, mechanical support), and interventions themselves may be associated with harm.

There is limited data if a BP target or another marker of end organ perfusion is the most appropriate target.

Optimal BP targets during extracorporeal life support (ECLS) post-cardiac arrest are unknown. Some patients on ECLS may have a lack of heart pulsatilty which also limits use of systolic BP targets in this patient group.

There is limited data available on the optimal strategy to use when cerebral autoregulation is impaired.

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QUESTION

Should one pharmacological strategy for seizure treatment vs. another pharmacological strategy or no seizure treatment be used for patients with ROSC after cardiac arrest?	
POPULATION:	Children with ROSC after cardiac arrest
INTERVENTION:	One strategy for prophylactic anti-seizure medication OR seizure treatment
COMPARISON:	Another strategy or no prophylactic anti-seizure medication OR seizure treatment
MAIN OUTCOMES:	Good neurological outcome or survival as per Pediatric Core Outcome Set for Cardiac Arrest (1)
SETTING:	In-hospital or out-of-hospital cardiac arrest
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	None declared

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Cardiac arrest in children, both in the out-of-hospital and in-hospital setting, is relatively common and has a very high mortality, with hypoxic-ischemic brain injury as a common cause of death. Seizures including suspected clinical seizures, electroclinical and electrographic seizures with EEG correlation are common manifestations of post-cardiac arrest brain injury in children with approximate incidence of 10-40% (Brooks and Park, 2018, 324, Fung et al., 2019, 349, Abend et al., 2011, 141). Seizures and abnormalities on EEG post cardiac arrest are associated with poor neurological outcome in children (Fung et al., 2019, 349, Lin et al., 2020, 534, Ostendorf et al., 2016, 667, Topjian et al., 2016, 547). It is unclear if prophylactic anti-seizure medication to prevent seizures and treatment of seizures when they are identified improves outcome. There are no existing ILCOR recommendations for children.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	***Prophylactic Anti-Seizure Medication*** For the critical outcome of survival with favourable neurological outcome at discharge/30 days or longer, no pediatric RCTs nor non-randomized comparative studies were identified. Indirect evidence from adult patients was identified. For the critical outcome of survival with favourable neurological outcome at discharge; Two prospective RCTs (BRCT Study Group 1986, 397; Longstreth 2002 506) involving a total of 562 comatose adults post-arrest provided very low-certainty evidence (downgraded for risk of bias, indirectness and imprecision) of no benefit from prophylactic anti-seizure medication administration. For the BRCT study, good neurological outcome for treatment with thiopentone vs standard care (no prophylactic anti-seizure medication) had a RR of 1.3 [95% CI 0.76 to 2.21; 46 more survivors per 1,000 patients [95% CI from 37 fewer to 185 more). For the Longstreth study: for treatment with intravenous magnesium versus placebo, RR for improved outcome was 1.37 [95% CI 0.83 to 2.25]; 94 more survivors per 1,000 patients [95% CI from 43 fewer to 317 more]; for treatment with intravenous diazepam versus placebo, RR for improved outcome was 0.68 [95% CI 0.36 to 1.28]; 81 fewer survivors per 1,000 patients [95% CI from 162 fewer to 71 more]; for treatment with intravenous magnesium *and* diazepam versus placebo, RR for improved outcome was 0.68 [95% CI 0.36 to 1.28]; 81 fewer survivors per 1,000 patients [95% CI from 162 fewer to 71 more]. One non-randomized prospective clinical trial (Monsalve 1987, 244) with 107 adults compared patients who received a bolus and continuous infusion of thiopentone and phenobarbital compared to historic controls, provided very low-certainty evidence (downgraded for risk of bias, indirectness, and imprecision) of no benefit (RR 1.41 [95% CI 0.88 to 2.27]; 137 more survivors per 1,000 adults [95% CI from 40 fewer to 423 more]). For the critical outcome of survival to hospital discharge/30 days or longer, one non-randomized prospective clinical trial (Monsalve 1987, 244) with 107 adults compared patients who received a bolus and continuous infusion of thiopentone and phenobarbital compared to historic controls, provided very low-certainty evidence (downgraded for risk of bias, indirectness, and imprecision) of no benefit (RR 1.40 [95% CI 0.83 to 2.36]; 119 more survivors per 1,000 patients [95% CI from 50 fewer to 403 more].	The TF also discussed that high seizure burden in children has been associated with poor neurological outcome (Payne 213, 1429, Srinivasakumar 2015, e1302). There are safe and effective anti-seizure medications that can reduce seizure burden which in turn is likely to benefit longer term outcomes (Lyttle, 2019, 2125). Therefore, the Task Force decided to make the Good Practice Statement suggesting for the treatment of seizures in children post-cardiac arrest.

	Treatment of Seizures For the critical outcome of survival with favourable neurological outcome at discharge/30 days or longer, no pediatric RCTs or non-randomized comparative studies were identified. Indirect evidence from adults were identified. For the critical outcome of survival with favourable neurological outcome at discharge/30 days or longer; One RCT (Ruijter 2022, 724) that addressed the effect of treatment of rhythmic and periodic discharges with anti-seizure medications in 172 comatose adults post-cardiac arrest, compared with no seizure treatment on the critical outcome of survival with favourable neurological outcome at 3 months (CPC score 1 or 2). This study provided low level certainty evidence (downgraded for imprecision and indirectness) of no significant difference for the intervention (administration of anti-seizure medications for rhythmic and periodic EEG patterns) compared with standard care (RR 1.21 [95% CI 0.47 to 3.10; 2 more survivors per 100 patients, [95% CI from 7 fewer to 11 more]). For the critical outcome of survival to 3 months, we identified low certainty evidence (downgraded for imprecision, indirectness) from one RCT (Ruijter 2022, 724) for no significant effect of treatment of rhythmic and periodic EEG patterns in 172 comatose adults post-cardiac arrest, compared with no seizure treatment (RR 0.14 [95% CI 0.62 to 2.12; 3 more survivors per 100 adults, [95% CI from 9 fewer to 14 more].	
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	There is no direct evidence of undesirable effects of anti-seizure medications in children post-cardiac arrest survivors. Treatment with sedatives and conventional antiseizure medications in high doses has the potential to delay awakening, prolong the need for mechanical ventilation, and increase critical care days. The task force also discussed the potential cost of delayed neurological prognostication and prolonged ICU care associated with active treatment of seizures because of the need to continue sedation.	
Certainty of evidence		

What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Overall evidence is of very low certainty. No evidence in the pediatric population was found. Indirect evidence for adults after cardiac arrest, both anti-seizure medication use and in treatment of seizures was identified but downgraded for indirectness, and imprecision.	
Values Is 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	Survival with favorable neurologic outcome at discharge/30 days or longer are generally accepted as critical outcomes (Topjian P-COSCA). Similar outcomes were identified in the adult studies.	
Balance of effects Does 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	No pediatric studies were identified The TELSTAR study suggests that there is little improvement in outcome with treatment compared with no treatment, of rhythmic and periodic EEG discharges in adult patients who are post- cardiac arrest.	Detecting seizures post cardiac arrest can be difficult unless the patient has continuous video EEG (cEEG)I monitoring. This is not available at many centres and is complicated, requiring availability of experts to interpret the recordings. Intermittent EEG recording has been shown to detect less episodes of seizure-like activity than cEEG - but if Rx of abnormal EEG activity doesn't alter patient outcome, there is less reason to do it, suggesting time and resources routinely invested in cEEG monitoring may not be worthwhile. However,

		research comparing testing modalities is warranted as there is no current evidence.

Resources required

How 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	We did not identify any studies evaluating the cost of a sedating agents and conventional anti-seizure medication in post-cardiac arrest patients. Cost is variable depending on type and number of agents used. Continuous EEG monitoring is used to assess prognosis and to diagnose seizures and monitor response to therapy. It is labor intensive and likely to add significant cost to patient care. The net cost-effectiveness of this approach is controversial and may depend substantially on the organization. There is also the potential cost of delayed neurologic prognostication and prolonged ICU care.	We need to understand the efficacy of continuous vs intermittent EEG monitoring in post arrest patients prior to calculating required resources and cost effectiveness metrics

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	We have not identified studies evaluating the cost of sedating agents and conventional anti-seizure medication in this patient population.	

Cost effectiveness

Does 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	We did not identify any studies addressing cost-effectiveness of post-cardiac arrest seizure treatment.	We need to understand the efficacy of continuous vs intermittent EEG monitoring in post arrest patients prior to calculating required resources and cost effectiveness metrics

Equity

What 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	We identified no studies that addressed health equity. Disparities in the availability of anti-seizure medication therapy in various settings was not investigated. However, it is likely that the availability of specific agents will vary with setting and region. The availability of conventional and continuous EEG monitoring is likely to be limited in low resourced environments.	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ● Don't know	We identified no research that assessed acceptability.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Feasibility was not specifically addressed by this review. However, treatment for seizures with anti-seizure medication is routine in pediatric practice.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	**Probably yes**	Yes		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		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

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

Recommendation

Prophylactic Anti-Seizure Medication

There is insufficient evidence to make a *treatment recommendation* for or against the use of prophylactic anti-seizure medication in children post-cardiac arrest.

We suggest against the routine use of prophylactic anti-seizure medications in children post-cardiac arrest (Good Practice Statement).

Seizure Treatment

There is insufficient evidence to make a *treatment recommendation* for or against the treatment of seizures in children post-cardiac arrest.

We suggest for the treatment of seizures in children post-cardiac arrest (Good Practice Statement).

Justification

Prophylactic Anti-Seizure Medication

Due to the lack of direct evidence in children post-cardiac arrest, and very low certainty of the indirect evidence from adults, the Task Force was unable to make a treatment recommendation. The Task Force decision to provide a Good Practice Statement suggesting against post-cardiac arrest prophylactic anti-seizure medication was based on the absence of in-direct evidence from adult comatose cardiac arrest survivors that prophylactic therapy with anti-seizure medication prevents seizures or improves important outcomes. However, the Task Force did recognize the very low certainty of the evidence from RCTs. The Task Force also considered that the administration of prophylactic anti-seizure medication in other forms of acute brain injury (e.g. neonatal hypoxic-ischemic encephalopathy) (Young 2016, 1) is not associated with improved long-term outcomes. Although prophylactic anti-seizure medication is recommended following traumatic brain injury in children (Kochanek 2019, 1172), the evidence of benefit for early seizure prevention is very-low certainty and there is no evidence of improved long-term outcomes (7) (Liesemer 2011, 755)

The medications used for anti-seizure prophylaxis in the included trials (e.g. barbiturates) can have significant side effects although the cardiac side-effects seen in adults may be less common in children. The Task Force acknowledged that newer anti-seizure medications have not been evaluated and their efficacy and side effect profile may differ. Further evaluation is encouraged.

Seizure Treatment

No direct pediatric evidence of the effects of treating seizures in children after cardiac arrest was identified and the Task Force was unable to make a treatment recommendation.

High seizure burden in children has been associated with poor neurological outcome (Payne 213, 1429, Srinivasakumar 2015, e1302). There are safe and effective anti-seizure medications that can reduce seizure burden which in turn is likely to benefit longer term outcomes (Lyttle, 2019, 2125). Therefore, the Task Force decided to make the Good Practice Statement suggesting for the treatment of seizures in children post-cardiac arrest.

There is insufficient evidence to suggest for or against the treatment of rhythmic and periodic EEG patterns in children post-cardiac arrest. One adult RCT (Ruijter 2022 724) did not find a difference in the primary outcome with one therapeutic approach to treatment of rhythmic and periodic EEG patterns. However, no significant harm was noted in the treatment or control arm. Further research is required in children to evaluate the impact on treating specific EEG patterns and electrographic seizures.

Medication for sedation (e.g. benzodiazepines and propofol) and targeted temperature management use after cardiac arrest may also affect seizure thresholds. Evaluation of the use of prophylactic anti-seizure medication and seizure treatment in the context of these therapies is important.

Subgroup considerations

No subgroups were considered due to lack of pediatric data.

Implementation considerations

The Task Force acknowledges the challenge of seizure diagnosis and the important role of confirmatory electroencephalographic (EEG) in addition to clinical signs of seizure to increase certainty of diagnosis. The potential risk of treating suspected seizures in settings without access to EEG confirmation needs to be balanced with potential harm of anti-seizure medications. EEG confirmation remains the gold-standard approach for seizure diagnosis; however, EEG may not be available in many clinical settings as it requires significant resources, including neuro-physiology equipment, training and expertise. Continuous EEG monitoring is labor intensive and likely to add significant cost to patient care. The cost-effectiveness of this approach is controversial and may depend on the setting. The relative benefit of continuous EEG compared with intermittent EEG monitoring was not reviewed.

Research priorities

There is no pediatric data for the use of prophylactic anti-seizure medication post-cardiac arrest. We encourage the assessment of newer anti-seizure medications and the role of sedative medications with anti-seizure properties used in the post-cardiac arrest period.

There is no pediatric data for the use of anti-seizure medications to treat seizures on important clinical outcomes post-cardiac arrest. We encourage research in this field.

EEG diagnosis remains the gold standard for seizure diagnosis. Risks and benefits of treating seizures without EEG and the importance of EEG monitoring post-cardiac arrest is a high priority with an important focus on cost effectiveness. This includes the role of continuous EEG, quantitative EEG and intermittent EEG.

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QUESTION

Advanced airway interventions in pediatric cardiac arrest	
POPULATION:	Infants (excluding newborns) and children in cardiac arrest
INTERVENTION:	A specific advanced airway intervention - tracheal intubation (TI) or supraglottic airway (SGA) during cardiac arrest
COMPARISON:	A different advanced airway intervention (eg. SGA) or no advanced airway management method [bag-mask ventilation (BMV) only] during cardiac arrest.
MAIN OUTCOMES:	Survival with Good Neurologic Function (SGNF); Survival to Hospital Discharge (SHD)
SETTING:	All study settings. Subgroup analysis was performed for (a) OHCA and (b) IHCA settings.
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	nil

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Airway management is vital in pediatric resuscitation, especially since respiratory conditions are frequently the primary cause of pediatric cardiac arrest. Maintaining an open airway and delivering sustained effective ventilations using a bag-mask device can be difficult (even in skilled hands). Advanced airway interventions, such as placement of a supraglottic airway (SGA) or tracheal intubation (TI), may facilitate more effective resuscitation than bag-mask ventilation (BMV) but require more skilled personnel. Also, the time taken to perform the procedure may interfere with other vital components of resuscitation eg. chest compressions. Potential benefits of advanced airway interventions include more effective ventilation; prevention of aspiration of gastric contents; delivery of continuous as opposed to interrupted chest compressions; and more effective monitoring of CPR effectiveness/ROSC detection via EtCO2.	A recent ILCOR PLS task force systematic review (Lavonas, 2019 114) identified that neither tracheal intubation (TI) nor supraglottic airway (SGA) placement were associated with better outcomes than bag-mask ventilation (BMV) in pediatric cardiac arrest. This resulted in a change in treatment recommendation to a preference for the use of BMV rather than TI or SGA in the management of children during cardiac arrest in the out-of-hospital setting. The current analysis represents an update to the previous systematic review (Lavonas, 2019 114) to explore more recently published studies, in both out-of-hospital and in-hospital arrest settings.

	Potential harms include incorrect tube placement or tube displacement leading to lack of lung ventilation or oxygenation; reduction in CPR quality secondary to prolonged interruption of chest compressions; and hyperventilation leading to respiratory alkalosis, reduced cerebral perfusion, or pneumothorax.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Overall, based on current evidence the updated systematic review results suggest with low to very low certainty that neither TI-based nor SGA-based interventions are superior to BMV-based resuscitation for cardiac arrest in children for the critically important outcomes of survival to hospital discharge (SHD) and survival to hospital discharge with good neurologic function (SGNF). Data from 5 propensity- adjusted cohort studies, including 4,093 children with cardiac arrest reported reduced survival with good neurologic outcome associated with the TI intervention (67 fewer survivors per 1,000 resuscitations; CI: 104 fewer to 0 fewer). Data from 2 other cohort studies, including 372 children with cardiac arrest also reported reduced SGNF associated with the TI intervention (131 fewer survivors per 1,000 resuscitations; CI: 212 fewer to 27 fewer). Data from 4 propensity- adjusted cohort studies, involving 3,123 patients showed no significant difference to SGNF associated with SGA ventilation (33 fewer survivors per 1,000 resuscitations; CI 95%: 56 fewer to 18 more). Data from these 4 propensity-adjusted cohort studies also showed no significant difference to SHD associated with SGA ventilation (14 fewer survivors per 1,000 resuscitations; CI 95%: 58 fewer to 58 more). Additional very low certainty evidence from two observational studies of 3,085 children found no significant effect on SHD associated with SGA placement (43 fewer survivors per 1,000 treated with SGA; CI 95%: 71 fewer to 31 more).	Although the size of effect from the studies is small, the potential impact on the number of survivors on a global scale, particularly in resource-limited environments, could be large.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Specific undesirable effects (outside of the lack of SGNF/SHD) were not consistently reported in the studies identified eg. regurgitation/aspiration, difficult airway management, CPR quality measures including compression fraction and interruptions to CPR. None of these outcomes were proposed *a priori* as important or critical by the PLS Task Force.	There might be specific subgroups where the presumed desired effects do not uphold and where an unidentified benefit of advanced airway management exists. For example, we might think about long distance transportation, prolonged resuscitation situations, with highly experienced airway operators, if advanced airway placement is only attempted in specific situations.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Twenty studies were included in the systematic review. Only 1 study provided clinical trial data. (Gausche 2000 783) This study provided low certainty evidence comparing TI to BMV for the critical outcomes of SGNF and SHD in pediatric cardiac arrest. The remaining 19 studies were all cohort studies and provided very low certainty evidence for the comparisons (TI-BMV, SGA-BMV, TI-SGA) with the critical outcomes described. Five studies provided propensity-adjusted cohort data amenable to meta-analysis. (Andersen 2016 1786) (Hansen 2017 51) (Ohashi-Fukuda 2017 66) (Okubo 2019 175) (Tham 2022 9) Ten other studies provided retrospective cohort data amenable to meta-analysis. (Abe 2012 612) (Aijian 1989 489) (Deasy 2010 1095) (del Castillo 2015 340) (Guay 2004 373) (Handley 2021 14) (Hansen 2020 53) (Pitetti 2002 283) (Sirbaugh 1999 174) Four studies provided retrospective cohort data in adjusted form only, not amenable to meta-analysis.(Fink 2016 121) (Tijssen 2015 1) (LeBastard 2021 191) (Cheng 2021 723327)	Most of the available data has been obtained from registries and an unknown proportion of events labelled as BMV resuscitation may have had failed TI and/or SGA attempts (which would bias against BMV). Conversely, most of the included studies are susceptible to resuscitation-time bias ie. the longer the child is in cardiac arrest, the more likely they will receive interventions but the less likely they will survive (which should bias against TI/SGA).

Values

Is 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 ILCOR P-COSCA initiative developed a core outcome set specific for pediatric cardiac arrest studies. The design and methods of the initiative included use of a Delphi process to develop consensus on a core domain set. (Topjian 2020 e246)	

	The P-COSCA outcomes of SGNF and SHD were chosen as critical outcomes for this review and are highly valued. We have not identified any airway studies that specifically addressed how patients valued the different outcomes.	

Balance of effects

Does 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	Acknowledging the very low level of certainty, the current available data suggest that the critical outcomes of SGNF and SHD are not significantly better or worse when resuscitation is performed with either TI or SGA, compared with BMV alone. Data from 5 propensity- adjusted cohort studies, including 4,093 children with cardiac arrest reported reduced survival with good neurologic outcome associated with the TI intervention (67 fewer survivors per 1,000 resuscitations; CI: 104 fewer to 0 fewer). Data from 2 other cohort studies, including 372 children with cardiac arrest also reported reduced SGNF associated with the TI intervention (131 fewer survivors per 1,000 resuscitations; CI: 212 fewer to 27 fewer). Separate analyses of studies of IHCA and OHCA produced similar results. However, the body of evidence for IHCA is particularly small (consisting of 1 propensity-matched cohort study and 3 other cohort studies) and provides very low certainty evidence. (Andersen 2016 1786) (del Castillo 2015 340) (Guay 2004 373) (Handley 2021 165) The studies are very heterogenous and showed inconsistent results.	The benefit or harm associated with advanced airway interventions resuscitation is likely to differ depending upon the context.

Resources required

How 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	While no studies evaluated this specifically (including cost effectiveness) BMV requires fewer resources because it is and always has been the default technique.	Paediatric advanced airway interventions require a moderate investment in equipment and a significant investment in training, skills maintenance, and quality control programs to be successful. While TI is supported in essentially all hospital settings in the developed world, and a standard component of care for respiratory arrest and in post-ROSC care, advanced life (ALS) support-capable emergency medical services agencies and IHCA teams will need to maintain this capability as well.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No studies regarding resource requirements were included in this systematic review.	

Cost effectiveness

Does 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	Cost effectiveness data was not identified in this systematic review.	

Equity

What 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		Varies, and is related to acceptability. Advanced airway interventions are currently offered in hospitals and in EMS systems with ALS capability. This varies by country and region. Paediatric advanced airway interventions require a moderate investment in equipment and a significant investment in training, skills maintenance, and quality control programs to be successful. While TI is supported in essentially all hospital settings in the developed world, and a standard component of care for respiratory arrest and in post-ROSC care, advanced life (ALS) support-capable emergency medical services agencies and IHCA teams will need to maintain this capability as well.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know		Essentially all hospital resuscitation teams and all ALS-based emergency medical services (EMS) systems already provide advanced airway interventions. It is uncertain whether the removal of advanced airway capabilities would be acceptable to key stakeholders. Accepted practice based on long-held beliefs (unsupported by data) mean these interventions are considered highly beneficial to perform paediatric advanced life support. Some might believe their local system and skills to differ from the population represented in the included studies. Also, during the COVID pandemic, many pre-hospital services and hospitals prioritised early intubation to reduce risk of infection with COVID.

Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know		Varies, and is related to acceptability. Advanced airway interventions are currently offered in hospitals and in prehospital services with ALS capability. This varies by country and region.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		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

	JUDGEMENT						
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

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

Recommendation

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].

Justification

There is currently no supporting evidence that an advanced airway (supraglottic airway or tracheal intubation) during CPR improves survival or survival with a good neurological outcome after pediatric cardiac arrest in any setting when compared with bag-mask ventilation.

Advanced airway (AAW) interventions, particularly TI, have been long-established components of the advanced life support bundle of care in children. As a result of inherent limitations in their design and data sources, the available studies, though individually well conducted, can provide only very low certainty evidence about whether attempting advanced airway placement prior to ROSC improves resuscitation outcomes.

Most of the available data has been obtained from registries and an unknown proportion of events labelled as BMV resuscitation may have had failed TI and/or SGA attempts (which would bias against BMV). Conversely, most of the included studies are susceptible to resuscitation-time bias ie. the longer the child is in cardiac arrest, the more likely they will receive interventions but the less likely they will survive (which should bias against TI/SGA).

The best available data show no benefit from advanced airway interventions, and some suggested association with harm, for the critical outcome of survival with good neurologic outcome. Effective BMV, TI, and SGA are all difficult skills that require good initial training, retraining, and quality control to be done consistently, safely, and effectively. Pediatric advanced airway programs require a moderate investment in equipment and a significant investment in training, skills maintenance, and quality control programs to be successful.

Subgroup considerations

The benefit or harm associated with advanced airway interventions in paediatric resuscitation may differ across settings. Importantly, the available data do not inform the questions of whether better outcomes might be achieved by advanced airway-based strategies in long distance transportation, in prolonged resuscitation situations, with highly experienced airway operators, when advanced airway placement is only attempted when BMV is difficult, etc. The analyzed data are only relevant to advanced airway interventions during CPR and do not pertain to airway management in other critical situations.

Implementation considerations

Those needed to be able to perform advanced airway management outside CPR practice might differ from those who would do this as part of advanced CPR.

It is uncertain whether the removal of advanced airway capabilities would be acceptable to key stakeholders. Accepted practice based on long-held beliefs (unsupported by data) mean these interventions are considered highly beneficial to perform pediatric advanced life support. Some might believe their local system and skills to differ from the population represented in the included studies.

Monitoring and evaluation

See below

Research priorities

Prehospital, ED-based, and in-hospital studies, ideally comparing TI, SGA and BMV with planned subgroup analyses based on patient age and etiology of arrest (trauma vs non-trauma) are ethical, necessary, and critically important to help guide clinicians in making these complex decisions.

Further examination of the benefit of advanced airway interventions in particular settings (including patients with poor pulmonary compliance, long distance transportation) would be helpful.

The efficacy and speed of placement of advanced airway using newer technologies, such as video assisted laryngoscopy (compared to regular laryngoscopy), is not known during resuscitation and would benefit from further studies.

Future studies would benefit from including measures of quality of ventilation (& cardiac metrics), timing of airway intervention, duration of CPR and measures of the training and experience of the clinicians performing the interventions.

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