CoSTR Summary

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

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ABSTRACT

The International Liaison Committee on Resuscitation engages in a continuous review of new, peer-reviewed, published cardiopulmonary resuscitation and first aid science. Draft Consensus on Science With Treatment Recommendations are posted online throughout the year, and this annual summary provides more concise versions of the final Consensus on Science With Treatment Recommendations from all task forces for the year. Topics addressed by systematic reviews this year include resuscitation of cardiac arrest from drowning, extracorporeal cardiopulmonary resuscitation for adults and children, calcium during cardiac arrest, double sequential defibrillation, neuroprognostication after cardiac arrest for adults and children, maintaining normal temperature after preterm birth, heart rate monitoring methods for diagnostics in neonates, detection of exhaled carbon dioxide in neonates, family presence during resuscitation of adults, and a step-wise approach to resuscitation skills training. Members from 6 International Liaison Committee on Resuscitation task forces have assessed, discussed, and debated the quality of the evidence, based on Grading of Recommendations Assessment, Development, and Evaluation criteria, and their statements include consensus treatment recommendations. Insights into the deliberations of the task forces are provided in the Justification and Evidence-to-Decision Framework Highlights sections. In addition, the task forces list priority knowledge gaps for further research. Additional topics are addressed with scoping reviews and evidence updates.

1 **Key words:** Heart arrest; resuscitation; infant, newborn; child; first aid

1 ABBREVIATIONS

Abbreviation	Definition
ACNS	American Clinical Neurophysiology Society
AED	automated external defibrillator
AHA	American Heart Association
ALS	advanced life support
aOR	adjusted odds ratio
aRR	adjusted relative risk
BIS	bispectral index
BLS	basic life support
BMV	bag-mask ventilation
COPD	chronic obstructive pulmonary disease
COSCA	core outcome set for cardiac arrest
CoSTR	Consensus on Science With Treatment Recommendations
CPC	Cerebral Performance Category
CPR	cardiopulmonary resuscitation
CT	computed tomography
DSED	double sequential defibrillation
ECG	electrocardiography
ECMO	extracorporeal membrane oxygenation
ECPR	extracorporeal cardiopulmonary resuscitation
EEG	electroencephalogram

EIT	Education, Implementation, and Teams
EMS	emergency medical services
EXACT	Reduction of Oxygen After Cardiac Arrest Trial
FPR	false positive rate
GCS	Glasgow Coma Scale
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
ICU	intensive care unit
IHCA	in-hospital cardiac arrest
ILCOR	International Liaison Committee on Resuscitation
IPPV	intermittent positive-pressure ventilation
IVH	intraventricular hemorrhage
MRI	magnetic resonance imaging
NfL	neurofilament light
NICU	neonatal intensive care unit
NLS	neonatal life support
NNTB	number needed to treat to benefit
NNTH	number needed to treat to harm
NSE	neuron-specific enolase
OHCA	out-of-hospital cardiac arrest
OR	odds ratio
PAD	public access defibrillation

PICO	population, intervention, comparator, outcome
PICOST	population, intervention, comparator, outcome, study design, time frame
PICU	pediatric intensive care unit
PLS	pediatric life support
PPE	personal protective equipment
PROSPERO	Prospective Register of Systematic Reviews
RCT	randomized controlled trial
ROC	return of circulation
ROSC	return of spontaneous circulation
SD	Standard defibrillation
SSEP	somatosensory evoked potentials
THAPCA	Therapeutic Hypothermia After Pediatric Cardiac Arrest
VABS-II	Vineland Adaptive Behavior Scales Second Edition
VC	vector change
VF	ventricular fibrillation
WASI	Weschler Abbreviated Scale of Intelligence

INTRODUCTION

This is the seventh in a series of annual International Liaison Committee on Resuscitation (ILCOR) Consensus on Science With Treatment Recommendations (CoSTR) summary publications summarizing the ILCOR task forces' analyses of published resuscitation evidence since ILCOR began the more continuous process of evidence evaluation in 2015. Including work from the 6 task forces, this year's review encompasses 90 topics reviewed in some capacity, including 25 systematic reviews (SysRevs). Although only SysRevs can generate a full CoSTR and new treatment recommendations, many other topics were evaluated with more streamlined processes.

Draft CoSTRs for all topics evaluated with SysRevs were posted on a rolling basis between April 2022 and January 2023 on the ILCOR website.[1] Each draft CoSTR includes the data reviewed and draft treatment recommendations, with public comments accepted for 2 weeks after posting. In some cases, if requested, public comment was permitted for longer. Task forces considered public feedback and provided responses. The 25 draft CoSTR statements and scoping reviews (ScopRevs) were viewed approximately 20 900 times, and 76 comments were provided. All CoSTRs are now available online, adding to the existing CoSTR statements.

This summary statement contains the final wording of the treatment recommendations and good practice statements as approved by the ILCOR task forces, but it differs in several respects from the online CoSTRs: The language used to describe the evidence is not restricted to

standard Grading of Recommendations Assessment, Development, and Evaluation (GRADE) terminology, making it more accessible to a wider audience; in some cases only the high-priority outcomes are reported; the Justification and Evidence-to-Decision Framework Highlights sections are shortened in some cases but aim to provide a transparent rationale for treatment recommendations; and finally, the task forces have prioritized knowledge gaps requiring future research studies. Links to the published reviews and full online CoSTRs are provided in the corresponding sections.

The CoSTRs are based on analysis of the data using the GRADE approach.[2] SysRevs are conducted by expert systematic reviewers or by task force members, always with the involvement of ILCOR content experts. The GRADE approach that is part of this process rates the certainty of evidence that supports the intervention effects (predefined by the population, intervention, comparator, outcome [PICO] question) as high, moderate, low, or very low. Randomized controlled trials (RCTs) begin the analysis as high-certainty evidence, and observational studies begin the analysis as low-certainty evidence. Certainty of evidence can be downgraded for risk of bias, inconsistency, indirectness, imprecision, or publication bias; it can be upgraded for a large effect, a dose-response effect, or if any residual confounding would be thought to decrease the detected effect.

The format for outcome data reporting varies by the data available but ideally includes both relative risk and the absolute risk difference, both with 95% confidence interval (CI). The

absolute risk difference is the absolute difference between the risks and is calculated by subtracting the risk in the control group from the risk in the intervention group. This absolute effect enables a more clinically useful assessment of the magnitude of the effect of an intervention and enables calculation of the number needed to treat (NNT=1/RD). In cases where the data do not allow for absolute effect estimates, alternative measures of effect such as odds ratios (ORs) are reported.

Treatment recommendations are generated by the task forces after evaluating the evidence and after task force discussion. The strength of a recommendation is determined by the task force and is not necessarily tied to the certainty of evidence. Although ILCOR generally avoids providing guidance when evidence is insufficient to support a recommendation, in some cases, good practice statements have been provided for topics thought to be of particular interest to the resuscitation community. Good practice statements are not recommendations but represent expert opinion in light of very limited data.

ILCOR's goal is to review at least 20% of all PICO questions each year so that the CoSTRs reflect current and emerging science. Acknowledging that many PICO topics will not have sufficient new evidence to warrant a systematic review, ILCOR implemented 2 additional levels of evidence review in 2020. ScopRevs are undertaken when there is a lack of clarity on the amount and type of evidence on a broader topic. Search strategies are similar in rigor to those of SysRevs, but ScopRevs do not include bias assessments or meta-analysis. The third and least

rigorous form of evidence evaluation is the evidence update (EvUp), in which a minimum of a PubMed search is carried out to screen for significant new data and assess whether there has been sufficient new science to warrant a more extensive review and updated CoSTR. Both ScopRevs and EvUps can inform a decision about whether a SysRev should be undertaken but are not used to generate a new or updated CoSTR because they do not include bias assessment, GRADE evidence evaluation, or meta-analysis. ScopRevs may be used to generate good practice statements, which represent expert opinion of the task force in light of limited evidence. In this document, ScopRevs are summarized in the relevant Task Force section, with references to the more complete online review. EvUps are listed at the end of each task force section in table form, with information including the prior treatment recommendation(s) related to the PICO question, how many new studies were identified, key findings, and whether an updated SysRev is recommended. Complete EvUps are provided in Appendix X.

The following topics are addressed in this CoSTR summary:

Basic Life Support

- SysRevs
  - Immediate resuscitation in water or on boat in drowning
  - Automated external defibrillator (AED) use first versus cardiopulmonary resuscitation (CPR) first in drowning
  - Ventilation equipment in cardiac arrest following drowning
  - Chest compression–only CPR in drowning

- Public access defibrillation programs for drowning
- Prehospital oxygen administration in cardiac arrest following drowning
- CPR by rescuers wearing personal protective equipment (PPE)

- ScopRevs
  - Drone delivery of AEDs
- EvUps
  - Paddle size and placement for defibrillation
  - Barrier devices
  - Chest compression rate
  - Rhythm check timing
  - Timing of CPR cycles (2 minutes versus other)
  - Public access AED programs
  - Check for circulation during basic life support (BLS)
  - Rescuer fatigue in chest compression–only CPR
  - Harm from CPR to victims not in arrest
  - Harm to rescuers from CPR
  - Hand position during compressions
  - Dispatch-assisted compression-only versus conventional CPR
  - Emergency medical services chest compression–only versus conventional CPR
  - Compression-ventilation ratio
  - CPR prior to defibrillation
  - Chest compression depth
  - Chest wall recoil

- Foreign body airway obstruction
- Firm surface for CPR
- In-hospital chest compression–only CPR versus conventional CPR
- Analysis of rhythm during chest compressions
- Alternative compression techniques (cough, precordial thump, fist pacing)
- Tidal volumes and ventilation rates
- Lay rescuer chest compression–only versus conventional CPR
- Starting CPR (circulation-airway-breathing versus airway-circulation-breathing)
- Dispatcher recognition of cardiac arrest
- Resuscitation care for suspected opioid-associated emergencies
- CPR prior to call for help
- Video-based dispatch
- Head-up CPR

Advanced Life Support

- SysRevs
  - Extracorporeal CPR (ECPR) for cardiac arrest
  - Double sequential defibrillation for cardiac arrest with refractory shockable rhythm
  - Calcium during cardiac arrest
  - Prognostication of favorable neurologic outcome
    - Use of the Glasgow Coma Scale motor score for prediction of good neurological outcome after cardiac arrest
    - Imaging for prediction of good neurological outcome

        - Use of brain injury biomarkers for the prediction of good outcome after cardiac arrest
        - Electroencephalogram (EEG) for prediction of good neurological outcome
        - Short-latency somatosensory evoked potentials (SSEPs) for prediction of good neurological outcome
- EvUps
    - Cardiac arrest in pregnancy
    - Steroids after return of spontaneous circulation (ROSC) from cardiac arrest

Pediatric Life Support

- SysRevs
    - ECPR for cardiac arrest in pediatrics
    - Prediction of survival with good neurological outcome after return of circulation following pediatric cardiac arrest
        - Clinical examination for the prediction of survival with good neurological outcome
        - Blood biomarkers for the prediction of survival with good neurological outcome
        - Electrophysiology for the prediction of survival with good neurological outcome
        - Brain imaging for the prediction of survival with good neurological outcome
- EvUps
    - Pulse check accuracy

- Pad size, type, and placement for pediatric defibrillation
- Antiarrhythmics for cardiac arrest with shockable rhythms at any time during CPR or immediately after ROSC
- Adenosine use in supraventricular tachycardia during resuscitation
- Energy doses for pediatric defibrillation
- Single or stacked shocks for pediatric defibrillation
- Epinephrine frequency during CPR
- Bedside ultrasound to identify perfusing rhythm
- End-tidal CO_2 monitoring during CPR
- Invasive blood pressure monitoring during CPR
- Use of near infrared spectroscopy during cardiac arrest
- Resuscitation of the pediatric patient with a single ventricle, post Stage I repair
- Resuscitation of the pediatric patient with single-ventricle, status-post Stage III/Fontan/total cavopulmonary connection/anastomosis in cardiac arrest
- Resuscitation of the pediatric patient with hemi-Fontan/bidirectional Glenn circulation in cardiac arrest
- Resuscitation of children with cardiac arrest associated with sepsis
- FIO_2 titrated to oxygenation during cardiac arrest

Neonatal Life Support

- SysRevs
  - Maintaining normal temperature: preterm
  - Heart rate monitoring: diagnostic characteristics
  - Exhaled CO_2 detection to guide noninvasive ventilation

- ScopRevs
  - Heart rate to initiate chest compressions
  - Supplemental oxygen during chest compressions
  - Neonatal chest compression technique (other techniques versus 2-thumb technique)
  - Compression-to-ventilation ratio for neonatal CPR
  - Use of feedback CPR devices for neonatal cardiac arrest

Education, Implementation, and Teams

- SysRevs
  - Family presence in adult resuscitation
  - Stepwise approach to skills training in resuscitation
- ScopRevs
  - Disparities in layperson resuscitation education
- EvUps
  - Patient outcomes from team member(s) attending a CPR course
  - Cardiac arrest centers
  - Technology to summon providers
  - Futile resuscitation rules (termination of resuscitation out of hospital)
  - CPR feedback devices during training
  - CPR self-instruction versus instructor-guided training
  - In-situ training

First Aid

- ScopRevs

- Pulse oximetry use in the first aid setting
- Use of supplemental oxygen in first aid
- Recognition of anaphylaxis
- Potential harms from bronchodilator administration

Readers are encouraged to monitor the ILCOR website[1] to provide feedback on planned SysRevs and to provide comments when additional draft reviews are posted.

BASIC LIFE SUPPORT

Out-of-Hospital Cardiac Arrest Following Drowning

Seven drowning questions were part of 1 large systematic review conducted by an expert review group on drowning and members of the ILCOR BLS Task Force. This systematic review was registered in International Prospective Register of Systematic Reviews (PROSPERO) (CRD42021259983).[3] A summary of the treatment recommendations for all PICO questions covered in this SysRev is given in Table 1. The same population, outcome, study design, and time frame were used for all 6 questions related to drowning.

Population, Outcome, Study Design, and Time Frame

- Population: Adults and children in cardiac arrest following drowning
- Outcomes:
  - Critical: Survival to discharge or 30 days with favorable neurological outcome and survival to discharge or 30 days
  - Important: ROSC
- Study designs: RCTs and nonrandomized studies (nonrandomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols), manikin studies, narrative reviews, and animal studies were excluded.
- Time frame: All years and all languages were included as long as there was an English abstract. Literature search updated to October 16, 2021.

Immediate Resuscitation in Water or on Boat in Drowning (SysRev)

Rationale for Review

This topic was prioritized by the BLS Task Force after the ScopRev[4] that was completed for the 2020 CoSTR.[5,6] This systematic review was registered in PROSPERO (CRD42021259983). The full online CoSTR can be found on the ILCOR website.[7]

Intervention and Comparator

- Intervention: Immediate resuscitation in water or on boat
- Comparator: Delaying resuscitation until on land

Consensus on Science

One retrospective observational study (n=46) from coastal regions in Brazil was found that addressed in-water resuscitation,[8] and no studies were found that addressed on-boat resuscitation. In-water ventilation-only resuscitation performed by trained lifeguards compared with resuscitation delayed to land was associated with improved survival with favorable neurological outcome (52.6% versus 7.4%; relative risk, 7.1 [95% CI,1.8–28.8]) and survival to hospital discharge (52.6% versus 16.7%; relative risk, 5.7 [95% CI, 2.3–14.3]).[8]

Prior Treatment Recommendations (2005[9,10])

In-water expired-air resuscitation may be considered by trained rescuers, preferably with a flotation device, but chest compressions should not be attempted.

Drowning victims should be removed from the water and resuscitated by the fastest means available.

2023 Treatment Recommendations

- We suggest in-water resuscitation (ventilations only) may be delivered if rescuers, trained in this technique, determine that it is feasible and safe with the equipment available and the distance to shore warrants its use (weak recommendation, very low–certainty evidence).
- We suggest on-boat CPR may be delivered if rescuers, trained in this technique determine that it is feasible and safe to attempt resuscitation (good practice statement).
- If the rescuers feel that the application of immediate CPR is or becomes too difficult or unsafe, then the rescuers may delay resuscitation until on dry land (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[7] Key discussion points include the following:

- Hypoxemia is the leading cause of cardiac arrest in drowning.[11] Experimental and clinical data support the importance of early reversal of hypoxia as a critical intervention for improving outcomes.[8,11] The logical extension of these data is to train likely rescuers to initiate resuscitation as soon as practicable (ie, either in the water or just after removal from the water, in a boat).[4] Chest compressions are ineffective in water and should never be attempted.[12]
- In-water ventilation-only resuscitation is feasible with proper training, sufficient rescuers, and/or equipment to assist with flotation.[8,13-16] Similar survival rates to those achieved by Szpilman and Soares[8] were reported in a case series from Australia in trained lifeguards performing in-water resuscitation in deep water.[16] As identified in the ILCOR Scoping Review on drowning,[4] to avoid risks to the patient and themselves, rescuers need to consider

their own safety, including the weather and water conditions, distance to land, and the availability of supportive and floating equipment and additional rescuers. Training should also include important learnings from manikin studies, such as avoiding the unintentional submersion of the patient[13,14,17] and the potential for fatigue and failed rescue.[13,17]

- The good practice statement on resuscitation in boats was informed by observational and simulation studies showing that it is feasible for trained rescuers to initiate resuscitation on moving boats.[18-23]
- For both in-water and in-boat resuscitation, the drowning expert group and the BLS Task Force emphasize the importance of continuous assessment of the safety and efficacy while performing these interventions. If either or both are compromised, rescuers should delay resuscitation until on land.

Task Force Knowledge Gaps

- High-quality evidence evaluating the impact of in-water ventilation and on-boat resuscitation on patient outcomes, CPR quality, and rescuer safety
- To enable future reviews and meta-analysis, data collection should be standardized and guided by the Utstein Drowning Statement,[24,25] CPR metrics recommended by the American Heart Association (AHA),[26] and core outcome set for cardiac arrest (COSCA) outcomes.[27,28]

Automated External Defibrillator Use First Versus CPR First in Cardiac Arrest in Drowning (SysRev)

Rationale for Review

AED use in drowning was covered in the ILCOR ScopRev.[4] The BLS Task Force prioritized 2 questions relating to AED use. This first question explored whether CPR or AED use should be prioritized in cardiac arrest following drowning. This systematic review was

registered in PROSPERO (CRD42021259983). The full text of this CoSTR can be found on the ILCOR website.[29]

Intervention and Comparator

- Intervention: AED administered before CPR
- Comparator: CPR administered before AED

Consensus on Science

No studies were identified that addressed the population, intervention, comparator, outcome, study design, and time frame (PICOST) question.

Prior Treatment Recommendations

None specific to drowning

2023 Treatment Recommendations

We recommend that CPR should be started first and continued until an AED has been obtained and is ready for use for adults and children in cardiac arrest caused by drowning (good practice statement).

When available, we recommend an AED is used in cardiac arrest caused by drowning in adults and children (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website.[29] Key discussion points include the following:

- In 2020, the ILCOR systematic review (for cardiac arrest of all causes) found low-certainty evidence with no clear benefit for CPR before defibrillation in meta-analysis.[5,6] The 2020 recommendation of beginning with CPR first during unmonitored cardiac arrests while the

defibrillator is prepared was based on a lack of new evidence since the 2015 review and the value of remaining consistent with the previous treatment recommendation.[5,6]

- We found no evidence that directly examined this question in the specific context of drowning. The rationale for CPR first is based on the hypoxic mechanism of cardiac arrest in drowning[30] and the low incidence of shockable rhythm in drowned out-of-hospital cardiac arrests (OHCAs) found in our prior scoping review.[4] Nevertheless, cardiac arrest following drowning may be a primary cardiac event in some adults and children.[31]
- For these reasons, and since the 2021 ILCOR scoping review on drowning did not find evidence of harm[4] and AEDs are associated with improved outcomes generally,[32] we recommend that an AED be used in cardiac arrests following drowning once CPR has started. Training and guidelines should highlight the importance of drying the chest and ensuring that the patient is not in water during attempted defibrillation. We recognize that AED use following drowning may not be feasible to implement in low-resource settings due to associated costs for equipment, training, and maintenance.

Task Force Knowledge Gaps

- High-quality evidence of the effectiveness of AED use on outcomes, CPR quality, and safety in drowned patients is required.
- To enable future reviews and meta-analysis, data collection should be standardized and guided by the Utstein Drowning Statement,[24,25] AHA-recommended CPR metrics,[26] and COSCA outcomes.[27,28]

Ventilation Equipment in Cardiac Arrest Following Drowning (SysRev)

Rationale for Review

This topic was prioritized by the BLS Task Force after the ScopRev[4] that was completed for the 2020 CoSTR.[5,6] This systematic review was registered in PROSPERO (CRD42021259983). The full text of this CoSTR can be found on the ILCOR website.[33]

Intervention and Comparator

- Intervention: Ventilation with equipment before hospital arrival
- Comparator: Ventilation without equipment before hospital arrival

Consensus on Science

No studies were identified that addressed the PICOST question.

Prior Treatment Recommendations

None specific to drowning

2023 Treatment Recommendations

We recommend using mouth-to-mouth, mouth-to-nose, or pocket-mask ventilation for BLS providers and laypersons for adults and children in cardiac arrest caused by drowning (good practice statement).

We suggest that bag-mask ventilation (BMV) can be used by lifeguards or other BLS providers with a duty to respond, on the condition that it is part of a competency-based training program with regular retraining and maintenance of equipment (good practice statement).

We recommend that health care professionals follow the advanced life support (ALS) treatment recommendations for airway management for adults and children in cardiac arrest caused by drowning.[34,35]

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website.[33] Key discussion points include the following:

- In making these treatment recommendations, we considered the following indirect evidence from retrospective studies comparing airway and ventilation equipment in drowning. One study reported that the use of a supraglottic airway was associated with lower odds of survival to hospital admission compared with tracheal intubation (adjusted odds ratio [aOR], 0.56 [95% CI, 0.42–0.76]) and lower odds of survival to discharge compared with BMV (aOR, 0.40 [95% CI, 0.19–0.86]).[36] A case study argued that an supraglottic airway might be unsuitable for drowned patients because of low lung compliance and high airway resistance.[37] Two studies in children showed worse outcomes with emergency medical services (EMS) tracheal intubation of children when compared with BMV (OR, 0.04 [95% CI, 0.01–0.20[38]]; OR, 0.25 [95% CI, 0.08–0.83])[39]; however, tracheal intubation is also an indicator of severity of injury in drowned OHCAs.[4]
- We found no evidence to suggest a change from current BLS, ALS, and pediatric life support (PLS) treatment recommendations for BLS providers, laypersons, and health care professionals.[34,35,40-43] In making the conditional treatment recommendation for the use of BMV by non–health care professionals with a duty to respond, such as lifeguards, the review group and BLS Task Force considered the following: that drowning resuscitation is likely to be initially performed by these groups; that there is widespread use of BMV by lifeguards in some regions and the need for a BMV treatment recommendation to ensure safe practice in the use of this equipment; that work conditions (professional/volunteer), availability of equipment, and training widely vary both between and within countries; that BMV can be

difficult to perform[44] and requires competency-based training, retraining, and monitoring; and that BMV equipment needs to be regularly checked and maintained.

Task Force Knowledge Gaps

- High-quality evidence evaluating airway and ventilation strategies on patient outcomes and CPR quality is needed.
- To enable future reviews and meta-analysis, data collection should be standardized and guided by the Utstein Drowning Statement,[24,25] AHA-recommended CPR metrics,[26] and COSCA outcomes.[27,28]

Chest Compression–Only CPR in Cardiac Arrest in Drowning (SysRev)

Rationale for Review

This topic was prioritized by the BLS Task Force following the review of CPR in drowning in the ScopRev[4] that was completed for the 2020 CoSTR.[5,6] This systematic review was registered in PROSPERO (CRD42021259983). The full text of this CoSTR can be found on the ILCOR website.[45]

Intervention and Comparator

- Intervention: Chest compression–only CPR
- Comparator: Conventional CPR (compressions and ventilations)

Consensus on Science

Two retrospective observational studies were identified that addressed the PICOST question in bystander CPR and provided very low–certainty evidence for all outcomes.[46,47] There was no difference between groups in either study for survival with favorable neurological outcome or ROSC.[46,47] One study[46] found no difference in 30-day survival, whereas the other[47] found that conventional CPR was associated with increased survival to discharge overall (aOR,

1.54 [95% CI, 1.01–2.36]; *P*=0.046) and, in a post hoc subgroup analysis, documented increased odds of favorable neurological outcome in children aged 5 to 15 years (aOR, 2.68 [95% CI, 1.10–6.77]; *P*=0.03).

Prior Treatment Recommendations

None specific to drowning

2023 Treatment Recommendations

For lay responders, the treatment recommendations for CPR in drowned OHCA patients who have been removed from the water remain consistent with CPR for all patients in cardiac arrest (good practice statement).

Adults:

We recommend that bystanders perform chest compressions for all patients in cardiac arrest.[5,6]

We suggest that bystanders who are trained, able, and willing to give rescue breaths and chest compressions do so for adults in cardiac arrest.[5,6]

Children:

We suggest that bystanders provide CPR with ventilation for infants and children younger than 18 years with OHCA.[40,41]

We recommend that if bystanders cannot provide rescue breaths as part of CPR for infants and children younger than 18 years with OHCA, they should at least provide chest compressions.[40,41]

For health care professionals and those with a duty to respond to drowning (eg, lifeguards), we recommend providing ventilation in addition to chest compressions if they have been trained and are able and willing to do so (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website.[45] Key discussion points include the following:

- Cardiac arrest in drowning is primarily the result of a lack of oxygen in the blood.[30] Therefore, providing ventilation in CPR in drowning is important.
- The existing evidence, from 2 registry studies comparing conventional CPR with compression-only CPR,[46,47] is at high-risk of bias and is considered very low–certainty evidence. Although we acknowledge that bystanders are more willing to perform compression-only CPR, particularly on strangers,[48] and compression-only CPR is well known in some regions,[49] CPR with ventilations and compression in drowning is the preferred method of CPR when bystanders are capable and trained. Compression-only CPR should be considered only if ventilations are not possible.

Task Force Knowledge Gaps

- High-quality evidence evaluating the effect of different CPR strategies on patient outcomes is needed. Such studies should stratify by the patient's age (adults and children) and adjust for important confounders.[24,25]
- To enable future reviews and meta-analysis, data collection should be standardized and guided by the Utstein Drowning Statement,[24,25] AHA-recommended CPR metrics,[26] and COSCA outcomes.[27,28]

Public Access Defibrillation Programs for Drowning (SysRev)

Rationale for Review

AED use in drowning was covered in the ILCOR Scoping Review.[4] The BLS Task Force prioritized 2 questions relating to AED use. This second question explored public access

defibrillation (PAD) programs for drowning. This systematic review was registered in PROSPERO (CRD42021259983). The full text of this CoSTR can be found on the ILCOR website.[50]

Intervention and Comparator

- Intervention: PAD program
- Comparator: Absence of PAD program

Consensus on Science

No studies were identified that addressed the PICOST question.

Prior Treatment Recommendations

None specific to drowning

2023 Treatment Recommendations

This treatment recommendation is unchanged from the standing recommendation for all OHCAs.

We recommend implementing PAD programs for all patients with OHCA (strong recommendation, low-certainty evidence).[5,6]

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website.[50] Key discussion points include the following:

- The BLS Task Force and review group considered that drowning often occurs in high-use public spaces where AED placement may benefit both drowning and nondrowning OHCAs. No adverse events were noted related to AEDs use in drowning in the ILCOR Scoping Review.[4] AEDs should be properly signposted—and, ideally, registered with EMS or in AED registries—and available and accessible for use in nearby OHCAs.[51,52] We recognize that

PAD programs may not be feasible to implement in low-resource settings due to associated costs for equipment, training, and maintenance.

Task Force Knowledge Gaps

- High-quality evidence evaluating the effectiveness of AED programs in aquatic environments on patient outcomes, CPR metrics, and safety, including their cost effectiveness, is needed.
- It is unclear to what extent traditional PAD program coverage includes aquatic settings and the cost-benefit in these settings.
- To enable future reviews and meta-analysis, data collection should be standardized and guided by the Utstein Drowning Statement,[24,25] AHA-recommended CPR metrics,[26] and COSCA outcomes.[27,28]

Prehospital Oxygen Administration in Cardiac Arrest Following Drowning (SysRev)

Rationale for Review

This topic was prioritized by the BLS Task Force after the ScopRev[4] that was completed for the 2020 CoSTR.[5,6] This systematic review was registered in PROSPERO (CRD42021259983). The full text of this CoSTR can be found on the ILCOR website.[53]

Intervention and Comparator

- Intervention: Oxygen administration before hospital arrival
- Comparator: No oxygen administration before hospital arrival

Consensus on Science

No studies were identified that addressed the PICOST question.

Prior Treatment Recommendations

None specific to drowning

2023 Treatment Recommendations

When available, we recommend trained providers use the highest possible inspired oxygen concentration during resuscitation for adults and children in cardiac arrest following drowning (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website.[53] Key discussion points include the following:

- This treatment recommendation is based on the understanding that most cardiac arrests in drowning are caused by low oxygen in the blood (ie, hypoxemia)[30] and supplemental oxygen administered by trained providers is likely to be beneficial. We also note that indirect observational research found in the ILCOR Scoping Review on drowning suggests that hypoxemia in submerged patients is associated with worse patient outcomes.[4]
- This good practice statement focuses on oxygen during resuscitation from drowning. The results of the recent Reduction of Oxygen After Cardiac Arrest Trial (EXACT) RCT do not support the prehospital titration of oxygen in successfully resuscitated adults with presumed OHCA.[54] We recommend following ILCOR's ALS and PLS treatment recommendations for oxygen titration following ROSC. However, we also recognize that peripheral vasoconstriction may make pulse oximetry unreliable following drowning. Although 2 simulation studies in healthy subjects suggest that pulse oximetry is feasible and reliable after immersion for up to 30 minutes,[55,56] we found no data on the reliability of pulse oximetry in drowned patients. Furthermore, a recent meta-analysis reports that pulse oximetry may overestimate oxygen saturation in people with dark skin pigmentation.[57]

- Oxygen therapy is expensive in terms of the equipment, maintenance, and training required for effective delivery. Oxygen is already available in many aquatic settings, such as pools and beaches, for use in drowning resuscitations. The use of supplemental oxygen has regulatory restrictions in some countries, and access to it may be limited in low- and middle-income countries. Those responsible for deciding whether to make oxygen therapy available will need to weigh the costs, regulatory requirements, setting, skills and training needs of those with a duty to respond, and time taken for an ALS provider to arrive with oxygen against the potential but uncertain benefits. Safe storage of oxygen should be regulated and be part of the training.

Task Force Knowledge Gaps

- High-certainty evidence evaluating the effect of early oxygen therapy on patient outcomes, safety, and cost benefit is needed.
- To enable future reviews and meta-analysis, data collection should be standardized and guided by the Utstein Drowning Statement,[24,25] AHA-recommended CPR metrics,[26] and COSCA outcomes.[27,28]

Table 1. A Summary of the BLS Task Force Treatment Recommendations for Drowning Resuscitation

Intervention	Lay rescuers	BLS providers with a duty to respond	Emergency medical services
On-boat resuscitation		On-boat CPR may be delivered if rescuers trained in this technique determine that it is feasible and safe to attempt resuscitation. If the rescuers feel that the application of immediate CPR is or becomes too difficult or unsafe, then the rescuers may delay resuscitation until on dry land.	

In-water resuscitation		In-water resuscitation (ventilations only) may be delivered if rescuers, trained in this technique, determine that it is feasible and safe with the equipment available and the distance to shore warrants its use. If the rescuers feel that the application of immediate resuscitation is too difficult or unsafe, then the rescuers may delay resuscitation until on dry land.	
AED	CPR should be started first and continued until an AED has been obtained and is ready for use. When available, an AED should be used.		
CPR	CPR commences with compressions first (adults)* CPR commences with ventilation first (children)*	CPR commences with ventilation first*	
	CPR with ventilations and chest compressions. Chest compression-only CPR may be considered when ventilations are not possible.		
Ventilation equipment	Mouth-to-mouth or pocket-mask ventilation	Bag-mask ventilation can be used by rescuers who are trained in a competency-based program with regular retraining and	Follow the ALS/PLS treatment recommendations for airway management.

		equipment maintenance.	
Oxygen		When available, use the highest possible inspired oxygen concentration.	
Public access defibrillation	PAD programs should be considered in aquatic environments.		

AED indicates automated external defibrillator; ALS, advanced life support; BLS, basic life support; CPR, cardiopulmonary resuscitation; PAD, public access defibrillation; PLS, pediatric life support.
*This treatment recommendation was published in the 2022 CoSTR summary.[58,59]

CPR by Rescuers Wearing Personal Protective Equipment (SysRev)

Rationale for Review

This topic was prioritized by the BLS Task Force because the current COVID-19 pandemic has resulted in increased use of PPE, which may increase fatigue and impact on CPR quality and patient outcomes. This systematic review was registered in PROSPERO (CRD42022347746).[60] The full text of this CoSTR can be found on the ILCOR website.[61]

PICOST

- Population: Adults and children in any setting (in-hospital or out-of-hospital) with cardiac arrest (including simulated cardiac arrest)
- Intervention: CPR by rescuers wearing PPE
- Comparators: CPR by rescuers not wearing PPE
- Outcomes:
  - Critical: Survival to discharge, ROSC
  - Important: CPR quality, time to the procedure of interest, and rescuer's fatigue and neuropsychiatric performance such as concentration and dexterity

- Study designs: RCTs and nonrandomized studies (nonrandomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: All years and all languages were included as long as there was an English abstract. Literature search updated to May 23, 2022.

Consensus on Science

The search strategy found 1 clinical study[62] and 10 simulation studies (6 RCTs[63-68] and 4 non-RCTs[69-72]) comparing PPE with no PPE. In studies comparing different types of PPE, there was too much variation in the type of PPE worn, and these studies were not analyzed.

A before-and-after observational study comparing conventional PPE (surgical mask, gloves, and gown) with enhanced PPE (complete bodysuit, boots, N95 respirator, and powered air-purifying respirator) in an emergency department setting reported no difference in 30-day survival (aOR, 0.38 [95% C, 0.07–2.10]; *P*=0.27) or ROSC (aOR, 0.79 [95% CI, 0.38–1.67]; *P*=0.54) in the enhanced PPE period.[62]

A meta-analysis of simulation RCTs and observational studies showed no difference for key measures of CPR quality in rescuers wearing PPE compared with no PPE (Table 2). Two observational studies reported increased self-reported fatigue in the group wearing PPE (absolute risk reduction, Visual Analogue Scale score 2.7 out of 10 [95% CI, 1.4–4.0]).[69,70]

Table 2. CPR Quality Outcomes for Randomized and Observational Simulation Studies Comparing PPE With No PPE

Outcome	Studies	Certainty of evidence	Mean difference (95% CI)
Compression depth	5 RCTs[63-67]	Very low	1.8 mm (− 4.3 mm to 0.8 mm)
	4 observational[69-72]	Very low	4.4 mm (− 8.9 mm to 0.1 mm)

Compression rate	5 RCTs[63-67]	Very low	1.0/min (− 5.8/min to 3.7/min)
	4 observational[69-72]	Very low	2.4/min (− 5.9/min to 1.2/min)
Appropriate compression depth	4 RCTs[65-68]	Very low	6.5% (− 25.3% to 12.2%)
Appropriate compression rate	3 RCTs[66-68]	Very low	3.7% (− 18.3% to 10.9%)
Hands-off time	2 RCTs[67,68]	Very low	5.1 sec (− 1.7 sec to 11.8 sec)
Appropriate chest recoil	2 RCTs[64,73]	Very low	4.3% (0.8%–7.8%)
Rescuer fatigue	2 observational[69,70]	Very low	VAS score 2.7 out of 10 (1.4–4.0)

RCT indicates randomized controlled trial; VAS, Visual Analogue Scale.

Prior Treatment Recommendations

None

2023 Treatment Recommendations

We recommend monitoring for fatigue in all rescuers performing CPR (good practice statement).

We suggest increased vigilance for fatigue in rescuers wearing PPE (weak recommendation, very low–certainty evidence).

Justification and Evidence- to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[61] Key discussion points include the following:

- In making this treatment recommendation, we put a high value on protecting health care professionals from potential infection transmission and on consistency with current recommendations on using PPE during resuscitation.
- The delivery of chest compressions is physically tiring. In the 2 studies reporting greater fatigue in the groups wearing PPE, CPR was performed in pairs, and the person performing chest compressions was changed every 2 minutes.[69,70] Although both studies reported worse CPR quality with PPE, the overall results of our meta-analysis show no effect on CPR quality. The studies included in this review were predominately simulation, manikin-based studies and varied significantly in the procedures used, including the type of PPE, the design of simulated scenarios, the duration of CPR performed, and the measures of CPR quality used. Therefore, results should be interpreted carefully and may not be generalizable to the clinical setting.
- There was a lack of clinical studies examining the impact of PPE on patient outcomes. The BLS Task Force considered a treatment recommendation that included an option to shorten CPR cycles while wearing PPE; however, we decided against this because there was no overall evidence that PPE influenced CPR quality, and a shorter CPR cycle may also increase hands-off-chest time.[74] An ILCOR systematic review in 2019, in adults and children, also suggested against pausing chest compressions at intervals other than every 2 minutes to assess the cardiac rhythm.[42]

Task Force Knowledge Gaps

Current knowledge gaps include

- The effect of PPE on patient outcomes
- The effect of PPE on CPR quality in actual resuscitation
- The relationship between PPE use, CPR duration, and rescuer fatigue
- The best type of PPE or appropriate modification strategies to mitigate rescuer fatigue

Drone Delivery of AEDs (ScopRev)

Rationale for Review

This topic was chosen for scoping review by the BLS Task Force because of increasing worldwide interest in drone-delivered AEDs for OHCA. No previous ILCOR review or scoping review existed to give an overview and status of this emerging field. The full text of this CoSTR can be found on the ILCOR website.[75,76]

PICOST

- Population: Adults and children in OHCA
- Intervention: Drone-delivered AEDs
- Comparator: Standard EMS response times (or time for EMS-delivered AED), AEDs delivered by bystanders or activated volunteer responders
- Outcome: Real-world/estimated feasibility, time gain of drone-delivered AEDs (compared with standard EMS delivery), predicted survival, predicted quality-adjusted life years gained, cost-effectiveness, and calculated proportion of defibrillation and survival compared with cases where AEDs are brought to the OHCA scene by standard means.
- Study design: Theoretical feasibility studies, prediction models (eg, spatial analysis, geographic information system models), observational studies, simulation studies, qualitative

studies of human-drone interaction, and real-world feasibility studies. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.

- Time frame: English languages studies published to December 1, 2022.

Summary of Evidence

The evidence was divided into the following 3 categories:

- Computer/prediction models: 17 studies used different strategies to localize optimal sites for placement of AED-drone bases and estimate time gain compared with EMS response time.[36,77-92] The data used varied according to geographic areas, quality and accessibility of historical OHCA data, drone type and input of diverse drone-flight details, existing EMS system, and volunteer responder programs.
- Test flights/simulation studies and qualitative analysis: 9 studies of various aims, geography, and testing areas.[93-101]
- Real-life drone AED-delivery for OHCA: One feasibility study examined 14 suspected OHCAs eligible for drone takeoff in which 12 drone flights were performed and successful AED delivery was achieved in 11 of 12 suspected OHCA incidents (92%).[102] A drone AED arrived before the ambulance in 64% of cases. The success rate was 90% among 61 additional test flights with AED delivery. The other study was a case report with the first-ever person reported to survive after OHCA and defibrillation with a drone-delivered AED.[103]

All included studies (from all 3 categories) found drone delivery of AEDs to be feasible. One qualitative study highlights the importance of assessing a community's cardiac arrest literacy levels, information needs, and readiness for innovation to ensure successful uptake in

smaller communities.[100] Five cost-effectiveness studies predicted the cost effectiveness of a drone AED system to supplement existing systems to secure early defibrillation.[77,78,85,88,90]

Task Force Insights

A limited evidence base was identified, with most studies focused on theoretical drone base placement and estimated AED drone delivery times compared with standard EMS times. In contrast, only 1 pilot and 1 case study reported on the drone delivery of AEDs to real-world OHCAs. Air Traffic Control and regulatory aspects concerning Specific Operations Risk Assessment are the major obstacles toward the widespread use of AED-delivering drones beyond line of sight.

Future studies should examine the delivery of AEDs to real-world OHCA patients and document the impact on patient outcomes. No RCTs were identified concerning AED delivery by drones.

Treatment Recommendations

The heterogeneity of the studies and the lack of data on patient outcomes do not currently support the need for a specific systematic review or a meta-analysis.

BLS Topics Reviewed by EvUps

Topics reviewed by EvUps are summarized in Table 3, with the PICO, existing treatment recommendation, number of studies identified, key findings, and whether a SysRev was deemed worthwhile provided. Complete EvUps can be found in Appendix X.

Table 3. BLS Topics Reviewed by Evidence Updates

Topic/PICO	Year last updated	Existing treatment recommendation	RCTs since last review, n	Observational studies since last review, n	Key findings	Sufficient data to warrant SysRev?
ALS-E-030A Paddle size and placement for defibrillation	2010 (ScopRev 2020)	It is reasonable to place pads on the exposed chest in an anterior-lateral position. An acceptable alternative position is anterior posterior. In large-breasted individuals, it is reasonable to place the left electrode pad lateral to or underneath the left breast, avoiding breast tissue. Consideration should be given to the rapid removal of excessive chest hair before the application of pads, but emphasis must be on minimizing delay in shock delivery. There is insufficient evidence to recommend a specific electrode size	1	1	RCT in refractory VF (AP position vs SA + double sequential external defibrillation): survival to hospital discharge (RR, 1.71 [95% CI, 1.01–2.88]) Retrospective observational study (n=484): no difference was observed in defibrillation efficacy between AP and SA pad placement.	No (Refractory VF; see ALS CoSTR double sequential external defibrillation)

		for optimal external defibrillation in adults. However, it is reasonable to use a pad size >8 cm.				
BLS 342 Barrier devices	2005	Providers should take appropriate safety precautions when feasible and when resources are available to do so, especially if a victim is known to have a serious infection (eg, HIV, tuberculosis, HBV, or SARS).	0	0	No new studies identified	No
BLS 343 Chest compression rate	2015 (ScopRev 2020)	We recommend a manual chest compression rate of 100–120/min (strong recommendation, very low–certainty evidence).	0	6	Six new observational studies on rate and depth—but not recoil—since last ScopRev Findings consistent with current guidelines	No
BLS 345 Rhythm check timing	2020	We suggest immediate resumption of chest compressions after shock delivery for adults in cardiac arrest in any setting (weak	0	0	No new studies identified	No

		recommendation, very low–certainty evidence).				
BLS 346 Timing of CPR cycles (2 min versus other)	2020	We suggest pausing chest compressions every 2 min to assess the cardiac rhythm (weak recommendation, low-certainty evidence).	0	0	No new studies identified	No
BLS 347 Public access AED programs	2020	We recommend the implementation of PAD programs for patients with OHCAs (strong recommendation, low-certainty evidence).	0	3	Introduction of a PAD program at Tokyo railroad stations presented significant benefits and cost-effectiveness in line with previous recommendations . The annual rate of SCDs in Japanese individuals aged 5–64 years decreased following a national PAD program. A Canadian study reported longer time to AED	No

					access was associated with lower survival to discharge.	
BLS 348 Check for circulation during BLS	2015	Outside of the ALS environment, where invasive monitoring is available, there are insufficient data about the value of a pulse check while performing CPR. We therefore do not make a treatment recommendation regarding the value of a pulse check.	0	0	No new studies. Some relevant papers showing the effectiveness of ultrasound to check for circulation were identified.	No
BLS 349 Rescuer fatigue in CCO CPR	2015	We recommend no modification to current CCO-CPR guidelines for cardiac arrest to mitigate rescuer fatigue (strong recommendation, very low–certainty evidence).	0	0	No new studies	No
BLS 353 Harm from CPR to	2020	We recommend that lay people initiate CPR for presumed cardiac arrest without concerns of harm to patients not in	0	0	No new studies identified	No

victims not in arrest		cardiac arrest (strong recommendation, very low–certainty evidence).				
BLS 354 Harm to rescuers from CPR	2015 (ScopRev 2020)	Evidence supporting rescuer safety during CPR is limited. The few isolated reports of adverse effects resulting from the widespread and frequent use of CPR suggest that performing CPR is relatively safe. Delivery of a defibrillator shock with an AED during BLS is also safe. The incidence and morbidity of defibrillator-related injuries in the rescuers are low.	0	3	One study found low risk of physical injury in citizen responders dispatched to OHCA. One study reported slightly greater pain with 2-handed (vs 1-handed) CPR in children. One study found low risk of harm from defibrillation in rescuers wearing polyethylene gloves.	No
BLS 357 Hand position during compressions	2020	We suggest performing chest compressions on the lower half of the sternum on adults in cardiac arrest (weak recommendation, very	0	0	No new studies addressing this question, but 2 simulation/training studies highlighted difficulties for lay	No

		low–certainty evidence).			rescuers in identifying correct hand position. No new studies in 2022	
BLS 360 EMS chest compression-only versus conventional CPR	2020	We recommend that EMS providers perform CPR with 30 compressions to 2 breaths (30:2 ratio) or continuous chest compressions with positive pressure ventilation delivered without pausing chest compressions until a tracheal tube or supraglottic device has been placed (strong recommendation, high-certainty evidence). We suggest that, when EMS systems have adopted minimally interrupted cardiac resuscitation, this strategy is a reasonable alternative to conventional CPR for witnessed shockable	0	1	One new study in 2021. Median inspiratory tidal volume generated by manual chest compressions without ventilation was 20 mL (IQR 13–28 mL), which was judged as inadequate to provide adequate alveolar ventilation.	No

		OHCA (weak recommendation, very low–certainty evidence).				
BLS 362 Compression-ventilation ratio	2017	We suggest a CV ratio of 30:2 compared with any other CV ratio in patients with cardiac arrest (weak recommendation, very low–quality evidence).	0	0	No new studies identified	No
BLS 363 CPR prior to defibrillation	2020	We suggest a short period of CPR until the defibrillator is ready for analysis and/or defibrillation in unmonitored cardiac arrest (weak recommendation, low-certainty evidence).	0	0	No new studies identified	No
BLS 366 Chest compression depth	2015 (ScopRev 2020)	We recommend a chest compression depth of approximately 5 cm (2 in) (strong recommendation, low-certainty evidence) while avoiding excessive chest compression depths (>6 cm [>2.4 in] in an	0	6	Six new observational studies since last ScopRev. Findings consistent with current guidelines	No

		average adult) during manual CPR (weak recommendation, low-certainty evidence).				
BLS 367 Chest wall recoil	2015 (ScopRev 2020)	We suggest that rescuers performing manual CPR avoid leaning on the chest between compressions to allow full chest wall recoil (weak recommendation, very low–quality evidence).	0	4	Four new observational studies on chest wall recoil since last ScopRev. Findings consistent with current guidelines	No
BLS 368 Foreign body airway obstruction	2020	We suggest that back slaps are used initially in adults and children with a foreign-body airway obstruction and an ineffective cough (weak recommendation, very low–certainty evidence). We suggest that abdominal thrusts are used in adults and children (older than 1 year) with a foreign-body airway obstruction and an ineffective cough when backslaps	0	1	A single new case series identified that describes 8 cases of the use of a vacuum cleaner to clear foreign body airway obstruction. No new studies in 2022	No

		are ineffective (weak recommendation, very low–certainty evidence). We suggest that rescuers consider the manual extraction of visible items in the mouth (weak recommendation, very low–certainty evidence). We suggest against the use of blind finger sweeps in patients with a foreign-body airway obstruction (weak recommendation, very low–certainty evidence). We suggest that appropriately skilled healthcare providers use Magill forceps to remove a foreign-body airway obstruction in patients with OHCA from foreign body airway obstruction (weak recommendation,				

		very low–certainty evidence). We suggest that chest thrusts be used in unconscious adults and children with a foreign-body airway obstruction (weak recommendation, very low–certainty evidence). We suggest that bystanders undertake interventions to support foreign-body airway obstruction removal as soon as possible after recognition (weak recommendation, very low–certainty evidence). We suggest against the routine use of suction-based airway clearance devices (weak recommendation, very low–certainty evidence).				
BLS 370	2020	We suggest performing chest compressions on a	3	0	Three manikin RCTs identified	No

Firm surface for CPR		firm surface when possible (weak recommendation, very low–certainty evidence). During in-hospital cardiac arrest, we suggest, where a bed has a CPR mode which increases mattress stiffness, it should be activated (weak recommendation, very low–certainty evidence). During in-hospital cardiac arrest, we suggest against moving a patient from a bed to floor, to improve chest compression depth (weak recommendation, very low–certainty evidence). During in-hospital cardiac arrest, we suggest in favor of either a backboard or no-backboard strategy, to improve chest			in 2021. No new studies in 2022	

		compression depth (conditional recommendation, very low–certainty evidence).				
BLS 372 In-hospital chest compression–only CPR versus conventional CPR	2017	Whenever tracheal intubation or a supraglottic airway is achieved during in-hospital CPR, we suggest that providers perform continuous compressions with positive-pressure ventilation delivered without pausing chest compressions (weak recommendation, very low–certainty evidence).	0	0	No new studies identified	No
BLS 373 Analysis of rhythm during chest compression	2020	We suggest against the routine use of artifact-filtering algorithms for analysis of electrocardiographic rhythm during CPR (weak recommendation, very low–certainty evidence).	0	3	Three new observational studies since last SysRev. Analysis during CPR leads to fewer pauses in chest compressions. High proportion of rhythms unable	No

		We suggest that the usefulness of artifact-filtering algorithms for analysis of electrocardiographic rhythm during CPR be assessed in clinical trials or research initiatives (weak recommendation, very low–certainty evidence).			to be assessed by algorithm (43%). No studies reported patient outcomes.	
BLS 374 Alternative compression techniques (cough, precordial thump, fist pacing)	2020	We recommend against the routine use of cough CPR for cardiac arrest (strong recommendation, very low–certainty evidence). We suggest that cough CPR may be considered only as a temporizing measure in exceptional circumstance of a witnessed, monitored IHCA (eg, in a cardiac catheterization laboratory) if a nonperfusing rhythm is recognized promptly	0	0	No new studies identified	No

		before loss of consciousness (weak recommendation, very low–certainty evidence). We recommend against fist pacing for cardiac arrest (strong recommendation, very low–certainty evidence). We suggest that fist pacing may be considered only as a temporizing measure in the exceptional circumstance of a witnessed, monitored, IHCA (eg, in a cardiac catheterization laboratory) due to bradyasystole if such a nonperfusing rhythm is recognized promptly before loss of consciousness (weak recommendation, very low–certainty evidence).				

		We recommend against the use of a precordial thump for cardiac arrest (strong recommendation, very low–certainty evidence).				
BLS 546 Tidal volumes and ventilation rates	2010	For mouth-to-mouth ventilation for adult victims using exhaled air or bag-mask ventilation with room air or oxygen, it is reasonable to give each breath within a 1-s inspiratory time and with an approximate volume of 600 mL to achieve chest rise. It is reasonable to use the same initial tidal volume and rate in patients regardless of the cause of the cardiac arrest.	0	0	No new studies identified	No
BLS 547 Lay rescuer chest compression	2020	We continue to recommend that bystanders perform chest compressions for all patients in cardiac	0	0	Only manikin/training studies since 2020. No new studies in 2022	No

only versus standard CPR		arrest (good practice statement). We suggest that bystanders who are trained, able, and willing to give rescue breaths and chest compressions do so for all adult patients in cardiac arrest (weak recommendation, very low–certainty evidence).				
BLS 661 Starting CPR (CAB versus ABC)	2020 CoSTR	We suggest commencing CPR with compressions rather than ventilation in adults with cardiac arrest (weak recommendation, very low–certainty evidence).	0	0	No new studies identified in 2021 or 2022 in adults	No
BLS 811 Resuscitation care for suspected opioid-associated emergencies	2020	We suggest that CPR be started without delay in any unconscious person not breathing normally and that naloxone be used by lay rescuers in suspected opioid related respiratory or	0	0	No new studies identified	No

		circulatory arrest (weak recommendation based on expert consensus).				
BLS 1527 CPR prior to call for help	2020	We recommend that a lone bystander with a mobile phone should dial EMS, activate the speaker or other hands-free option on the mobile phone, and immediately begin CPR with dispatcher assistance, if required (strong recommendation, very low–certainty evidence).	0	0	No new studies identified	No
BLS Video-Based Dispatch	2021	We suggest that the usefulness of video-based dispatch systems be assessed in clinical trials or research initiatives (weak recommendation, very low–certainty evidence).	2: manikin (pediatric and infant)	2	Two observational studies identified in 2021. Two new manikin RCTs in 2022: 1 reported better CPR quality with video compared with T-CPR in untrained participants but also longer times (eg, to	No

					recognition, first compression). The other reported no difference in the evaluation for foreign body airway obstruction.	
BLS Head-up CPR	2021	We suggest against the routine use of head-up CPR during CPR (weak recommendation, very low–certainty evidence). We suggest that the usefulness of head-up CPR during CPR be assessed in clinical trials or research initiatives (weak recommendation, very low–certainty evidence).	0	2	Two new studies identified in 2022. One observational study found no difference in survival outcomes overall; suggestion of improved outcomes with rapid initiation. One pilot observational study reported increased cerebral blood flow with head-up positioning during CPR.	No

ABC indicates airway-breathing-circulation; AED, automated external defibrillator; ALS, advanced life support; AP, anteroposterior; BLS, basic life support; CAB, circulation-airway-breathing; CCO-CPR, chest compression–only CPR; CoSTR, Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations; CPR, cardiopulmonary resuscitation; CV, compression-to-ventilation; EMS, emergency medical services; HBV, hepatitis B virus; HIV, human immunodeficiency virus; IHCA, in-hospital cardiac arrest; IQR, interquartile range; OHCA, out-of-hospital cardiac arrest; PAD, public access defibrillation; RCT, randomized controlled trial; SA, sternal apical; SARS, severe acute respiratory syndrome; SCD, sudden cardiac death; T-CPR, telecommunicator CPR; VF, ventricular fibrillation.

ADVANCED LIFE SUPPORT

ECPR for Cardiac Arrest (SysRev)

Rationale for Review

ECPR usage continues to increase in some centers, while still not being widely available. Since the last review of this topic,[104] the task force was aware of 2 new RCTs. This significant addition to the body of evidence prompted the task force to update the systematic review (SysRev) completed for the 2019 CoSTR. The SysRev was registered before initiation (PROSPERO Registration CRD42022341077).[105] The full online CoSTR can be found on the ILCOR website.[106]

PICOST

- Population: Adult (≥18 years) patients with cardiac arrest in any setting
- Intervention: ECPR including extracorporeal membrane oxygenation or cardiopulmonary bypass during cardiac arrest
- Comparators: Manual or mechanical CPR
- Outcomes: Any clinical outcome
- Study designs: This was an update of the ILCOR SysRev addressing ECPR for cardiac arrest in 2018.[104] New RCTs, non-RCTs, and observational studies (cohort studies and case-control studies) with a control group (patients not receiving ECPR) were included. Ecological studies, case series, case reports, reviews, abstracts, editorials, comments, letters to the editor, and unpublished studies were not included. Studies assessing cost-effectiveness were included for a descriptive overview. Studies exclusively assessing the use of extracorporeal life support for cardiac and/or respiratory failure after sustained ROSC were not included.

Studies assessing extracorporeal circulation for deep hypothermia (or other conditions) were only included if cardiac arrest was documented.

- Time frame: New studies published between January 1, 2018, and June 21, 2022. All languages were included if there was an English abstract.

Consensus on Science

Because 3 randomized trials[107-109] were identified, observational studies were not considered for the updated consensus on science because of the high risk of bias. A summary of the observational studies is provided in the SysRevs.[104,105]

Key outcomes from the 3 included randomized trials are summarized in Table 4. One trial was stopped early for benefit after 30 patients,[107] one was stopped early because of slow enrollments after 15 patients,[108] and one was terminated early because of futility in the primary outcome, although there was an overall signal toward benefit.[109]

Table 4. Key Outcomes by Treatment Group and ARD for Patients Treated With an ECPR Strategy, Compared With Standard Care

Author, year	n	Survival to discharge/30 days		ARD (95% CI)	Favorable functional outcome* at discharge/30 days		ARD (95 % CI)	Favorable functional outcome* at 6 months		ARD (95% CI)
		ECPR strategy	Standard care		ECPR strategy	Standard care		ECPR strategy	Standard care	
Yannopoulos, 2020[107]	30	6/14 (43%)	1/15 (7%)	36% (7.4%	3/14 (21%)	0	21% (0%–43%)	6/14 (43%)	0	43% (17%

				–65%)						–69%)
Hsu, 2021[108]	15	0	1/3 (33%)	–33% (–87%–20%)	0	0	0	NA	NA	NA
Belohlavek, 2022[109]	264	52/124 (42%)	43/132 (33%)	9.4% (–2.4%–21%)	38/124 (31%)	24/132 (18%)	13% (2%–23%)	39/124 (32%)	29/132 (22%)	10% (–1.3%–20%)

*Favorable functional outcome defined as mRS score 0 to 3 or CPC score of 1 or 2.
ARD indicates absolute risk difference; CPC, Cerebral Performance Category; ECPR, extracorporeal cardiopulmonary resuscitation; mRS, modified Rankin Scale; and NA, not applicable.

The overall certainty of evidence was rated as low because of inconsistency and imprecision, and was considered very low for in-hospital cardiac arrest (IHCA), as there were no trials for IHCA. Because of a high degree of heterogeneity between the randomized trials, no meta-analyses were performed.

Prior Treatment Recommendation (2019)

We suggest ECPR may be considered as a rescue therapy for selected patients with cardiac arrest when conventional CPR is failing in settings where this can be implemented (weak recommendation, very low–certainty evidence).

2023 Treatment Recommendations

We suggest ECPR may be considered as a rescue therapy for selected patients with OHCA when conventional CPR is failing to restore spontaneous circulation in settings where this can be implemented (weak recommendation, low-certainty evidence).

We suggest ECPR may be considered as a rescue therapy for selected patients with IHCA when conventional CPR is failing to restore spontaneous circulation in settings where this can be implemented (weak recommendation, very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[106]

- In making this weak recommendation, we note that this patient population (ie, cardiac arrest where conventional CPR is failing) has a very high mortality rate. Therefore, the potential for benefit and value of this intervention remains despite the overall low certainty in the evidence.
- The published randomized trials have included highly selected patients for ECPR. The trial by Yannopoulos et al enrolled patients with OHCA with an initial shockable rhythm refractory to at least 3 shocks, and randomized patients upon hospital arrival. The trials by Hsu et al and Belohlavek et al enrolled patients with OHCA with any initial rhythm, and randomized patients in the prehospital setting. In all 3 trials, the intervention was a treatment strategy that included ECPR. The percentage of patients in the intervention group who received ECPR was 80%, 42%, and 66% in the Yannopoulos, Hsu, and Belohlavek trials, respectively. The ECPR strategy in the trials by Yannopoulos et al and Belohlavek et al included immediate access to a catheterization laboratory. Guidelines for clinical practice

should ideally apply to similar populations as those enrolled in the trials to date, although randomized trials have not been performed to define the optimal population. For this reason, the findings of individual trials should be interpreted cautiously in the context of the trial setting and population.

- We acknowledge that ECPR is a complex intervention that requires considerable resources and training that are not universally available but also acknowledge the value of an intervention that may be successful in individuals where usual CPR techniques have failed.

Task Force Knowledge Gaps

- Few, and no large, randomized trials of ECPR compared with standard care
- The optimal patient population who may benefit from ECPR
- Whether subgroups of patients such as those with cardiac arrest related to pregnancy or pulmonary embolism benefit from ECPR
- The optimal time to initiate ECPR in cases of refractory cardiac arrest
- Whether ECPR should be initiated in the prehospital or in-hospital setting
- The optimal techniques for providing safe and timely ECPR
- The optimal post–cardiac arrest care strategy for patients resuscitated by using ECPR
- Population-specific differences in performing ECPR for IHCA and OHCA
- Cost-effectiveness of ECPR

Double Sequential Defibrillation for Cardiac Arrest With Refractory Shockable Rhythm (SysRev)

Rationale for Review

A 2020 SysRev conducted by the ALS Task Force found no evidence of improved outcomes with the use of double sequential defibrillation (DSED); however, there was a

recognized lack of high-quality data.[110] The recent publication of an RCT prompted an update of the 2020 SysRev (registered on PROSPERO October 6, 2022). The full online CoSTR can be found on the ILCOR website.[111]

PICOST

- Population: Adults in any setting (in-hospital or out-of-hospital) with cardiac arrest and a shockable ventricular fibrillation (VF)/pulseless ventricular tachycardia cardiac arrest rhythm
- Intervention: DSED
- Comparators: Standard defibrillation (SD) strategy
- Outcomes:
  - Critical: Survival to hospital discharge or good neurological survival at discharge or 30 days, or greater than 30 days
  - Important: ROSC, survival to hospital admission
  - Other: Termination of VF/pulseless ventricular tachycardia
- Study designs: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) were excluded. All relevant publications in any language were included as long as there was an English abstract.
- Time frame: Literature search for this update included studies published from February 28, 2020, to November 7, 2022.

Consensus on Science

We identified 1 cluster RCT, which included the pilot trial identified in the prior review.[112,113] No new observational studies were identified. The cluster RCT compared DSED and vector change (VC) (anteroposterior pad placement) defibrillation with SD (anterolateral pad

placement) defibrillation. Therefore, this CoSTR includes the data comparing VC with SD as well as that comparing DSED with SD. Data were not available for adjusted statistical comparison of DSED with VC, because the trial was not designed for that comparison and this post-hoc analysis could not be obtained. All calculations of adjusted relative risk (aRR) were adjusted for cluster (cluster randomized trial), age, sex, and receipt of lay rescuer CPR. Unadjusted relative risk and absolute risk difference are provided in the online Grading of GRADE tables, along with the primary adjusted results.[111]

DSED Compared With SD

A single trial[113] including 261 patients with OHCA provides low-certainty evidence (downgraded for risk of bias and imprecision) for improved functional outcome (defined as modified Rankin Scale [mRS] score of 0–2) at hospital discharge with DSED compared with SD (27.4% versus 11.2%, aRR 2.21 [95% CI, 1.26, 3.88]) and improved survival to hospital discharge (30.4% versus 13.3%, aRR 2.21 [95% CI, 1.33, 3.67]). There was also an improved rate of ROSC with DSED compared with SD (46.4% versus 26.5%, aRR 1.72 [95% CI, 1.22, 2.42]) and a higher rate of termination of VF (84% versus 67.6%, aRR 1.25 [95% CI, 1.09, 1.44]).

VC Defibrillation Compared With SD

A single trial[113] including 280 patients provides very low–certainty evidence (downgraded for serious risk of bias and very serious imprecision) of no significant improvement in favorable functional survival at discharge (defined as mRS score of 0–2) from VC compared with SD (16.2% versus 11.2%, aRR 1.48 [95% CI, 0.81, 2.71]) and no significant improvement in ROSC (35.4% versus 26.5%, aRR 1.39 [95% CI, 0.97, 1.99]). There was improved survival to hospital discharge with VC compared with SD (21.7% versus 13.3%, aRR 2.21 [95% CI, 1.01,

2.88]) and a higher rate of termination of VF with VC compared with SD (79.9% versus 67.6%, aRR 1.18 [95% CI, 1.03, 1.36]).

Prior Treatment Recommendation (2020)

We suggest against routine use of dual (or double) sequential defibrillation strategy in comparison to an SD strategy for cardiac arrest with a shockable rhythm (weak recommendation, very low–certainty evidence).

2023 Treatment Recommendations

We suggest that a DSED strategy (weak recommendation, low-certainty evidence) or a VC defibrillation strategy (weak recommendation, very low–certainty evidence) may be considered for adults with cardiac arrest who remain in VF or pulseless ventricular tachycardia after 3 or more consecutive shocks.

If a DSED strategy is used, we suggest an approach similar to that in the available trial, with a single operator activating the defibrillators in sequence (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[111]

- Current evidence does not permit distinguishing whether either strategy (DSED or VC defibrillation) is superior to the other.
- The task force discussed the importance of ensuring correct pad placement for SD before progressing to DSED or VC defibrillation and agreed with the descriptions of anterolateral pad placement provided in existing guidelines from the AHA and the European Resuscitation Council. These guidelines recommend that defibrillation pads be placed to anatomically encompass the heart (with one pad below the right clavicle, just to the right of the upper

sternal border, and the other with the center of the pad in the left midaxillary line) and that adequate contact be made at the pad-skin interface so as to optimize energy delivery.[114]

- Double shocks require the availability of 2 defibrillators, and this has resource implications. The task force noted that DSED is already used by some EMS systems for refractory shockable cardiac arrest and, therefore, may be easily implemented in some systems. In other systems, this practice could require significant new resource allocation for additional defibrillators or ambulances, and the task force acknowledged that such an increase in resource allocation may not be justified on the basis of a single relatively small study.
- The difference between truly refractory VF (failure to be terminated) and recurrent VF (recurring after successful defibrillation) may not be recognized clinically. Future "see through CPR" algorithms (enabling detection of underlying rhythm during CPR) may permit distinguishing patients with incessant refractory VF from recurrent VF after shock delivery, and, thus, better direct electrical versus pharmacologic or other therapies.
- The task force discussed the concern that a single smaller-than-planned study leaves significant uncertainty about treatment effect.
- The protocol used in the existing trial, with a single person providing 2 defibrillation shocks in quick succession (but not simultaneous), did not result in any reports of defibrillator damage and is, therefore, likely the best approach to use currently.
- The importance of not equating 2 sequential shocks with a single higher-energy shock was highlighted.
- Current evidence does not permit distinguishing whether the VC or the double shock employing the VC in addition to SD accounts for the observed benefit. The task force had

extensive discussions about whether the anteroposterior pad placement or the DSED provided most of the benefit seen.

- Sensitivity analyses included in the available trial did not see a difference in outcomes with DSED when patients were analyzed by treatment received rather than intent to treat (randomization group). Reasons why certain patients received a defibrillation strategy other than that to which they were randomized are not known.

Task Force Knowledge Gaps

- Whether the benefit from DSED seen in this single trial will be replicated in other settings
- Whether DSED is beneficial compared with changing pad placement (VC defibrillation)
- The optimal timing of shock delivery when a DSED strategy is used
- Whether DSED has an effect on health-related quality of life

Calcium During Cardiac Arrest (SysRev)

Rationale for Review

Calcium has not been recommended for routine use during cardiac arrest for many years,[115] but it continues to be given frequently. This topic was prioritized because of the publication of a recent RCT that adds significantly to the available evidence. A SysRev was conducted by members of the ALS Task Force (PROSPERO CRD4202234964). The SysRev included literature on adults and children. The evidence for adults was considered for this CoSTR. The full online CoSTR can be found on the ILCOR website.[116]

PICOST

- Population: Adults with cardiac arrest in any setting
- Intervention: Administration of calcium (intravenous or intraosseous) during cardiac arrest
- Comparators: No administration of calcium during cardiac arrest

- Outcomes: Any clinical outcome, including ROSC, short-term survival and neurological outcomes (eg, hospital discharge, 28 days, 30 days, and 1 month), and long-term survival and neurological outcomes (eg, 3 months, 6 months, 1 year)
- Study designs: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) with a control group were eligible for inclusion. Ecological studies, case series, case reports, reviews, abstracts, editorials, comments, letters to the editor, and unpublished studies were excluded.
- Time frame: All years and all languages were included as long as there was an English abstract. The literature search was conducted on July 8, 2022, and updated on September 31, 2022.

Consensus on Science

Three RCTs were identified, so because of the critical risk of bias inherent in the observational studies, only data from the 3 RCTs (one of which resulted in an additional paper reporting long-term outcomes) were considered.[117-120] The more recent and largest trial was stopped early because of concern for harm from the intervention. Key results from these trials are presented in Table 5. There were no statistically significant differences seen in any of the trials, with the exception of survival with favorable functional outcome at 90 days and at one year in the more recent trial, with results suggesting worse outcome with calcium in both cases.[119,120] All results are reported in full in the online CoSTR.[116] Calcium has not been studied in the IHCA setting. Therefore, the certainty of evidence for adult IHCA was additionally downgraded for indirectness.

Table 5. Selected Outcomes and Certainty of Evidence for Included Randomized Clinical Trials of Calcium During Cardiac Arrest

Study, year	n	ROSC		Survival at 30, 90, 180 days*		Survival at 1 year		Favorable neurological outcome at 1 year		Certainty of evidence
		Calcium	Control	Calcium	Control	Calcium	Control	Calcium	Control	
Stueven (PEA), 1985[117]	90	8/48 (16.7%)	2/42 (4.8%)	NR		NR		NR		Very low†
		RR 3.5 (95% CI, 0.79–15.58)								
Stueven (Asystole), 1985[118]	73	3/39 (7.7%)	1/34 (2.9%)	0 in both groups at discharge		NR		NR		Very low†
		RR 2.43 (95% CI, 0.26–22.31)								
Vallentin, 2021,[119] and	391	37/193 (19%)	53/198 (27%)	10/193 (5.2%)	18/198 (9.1%)	9/193 (4.7%)	18/198 (9.1%)	7/193 (3.6%)	17/198 (8.6%)	Moderate‡

Vallentin, 2022[120]		RR 0.72 (95% CI, 0.49–1.03)	RR 0.57 (95% CI, 0.27–1.18)	RR 0.51 (95% CI, 0.24–1.09)	RR 0.42 (95% CI, 0.18–0.97)	

*Survival at all 3 times points was the same in the Vallentin study.
†Downgraded for risk of bias and very serious imprecision.
‡Downgraded for imprecision.
NR indicates not reported; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; and RR, relative risk.

Prior Treatment Recommendation (2010)

Routine administration of calcium for treatment of IHCA and OHCA is not recommended.

2023 Treatment Recommendations

We recommend against routine administration of calcium for the treatment of OHCA in adults (strong recommendation, moderate-certainty evidence).

We suggest against routine administration of calcium for the treatment of IHCA in adults (weak recommendation, low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[116] Key points include the following:

- This CoSTR and its SysRev focus on the routine administration of calcium during cardiac arrest in adults.
- We did not identify any RCTs comparing calcium administration with no calcium administration during IHCA or for specific patient groups such as hyperkalemic cardiac arrest.

- The trial by Vallentin et al was stopped early on the basis of suggestions of harm in a preplanned interim analysis,[119] which could have increased the risk of effect size overestimation.
- The risk of harm with calcium administration may depend on the scenario in which the intervention is performed.
- The effect of calcium administration remains unknown for adults in cardiac arrest from special circumstances such as hyperkalemia, wide QRS interval on electrocardiogram, hypocalcemia, hypermagnesemia, calcium channel blocker overdose, or hemorrhage. Existing trials provide insufficient data on these subgroups to be able to evaluate this.
- Only small trials or observational studies have attempted to stratify based on initial rhythm or potassium values, and these have been limited by critical risk of bias because of confounding.

Task Force Knowledge Gaps

- No RCTs have evaluated calcium during IHCA
- The effect of calcium during cardiac arrest from special circumstances such as hyperkalemia, wide QRS interval on electrocardiogram, hypocalcemia, hypermagnesemia, calcium channel blocker overdose, or hemorrhage
- The mechanism of harm from calcium during cardiac arrest

Prognostication of Favorable Neurological Outcome (SysRev Adolopment)

Rationale for Review

This SysRev of prognostication after cardiac arrest (PROSPERO: CRD 420 1914 1169) was conducted by a SysRev team with involvement of content experts from the ILCOR ALS Task Force and consisted of 2 parts. The first part addressed prediction of poor neurological outcome and provided evidence for the 2020 CoSTR.[121,122] The second part addressed prediction

of favorable neurological outcome.[123] Because the SysRev on prognostication of favorable outcome was recent and met ILCOR criteria for being of sufficient quality, the task force deemed it appropriate for adolopment. An updated search including the dates October 31, 2021, through May 20, 2022, was conducted to identify any papers published since the search for the original SysRev. This evidence was divided into several sections: Glasgow Coma Scale (GCS) motor score, imaging, biomarkers, use of EEG, SSEP. These are summarized later. Sensitivity and specificity of each modality for prediction of favorable neurological outcome is reported for included studies. In this case, *sensitivity* refers to the percentage of patients with a favorable outcome who will have a positive (meaning favorable, as in a low or normal biomarker level or normal head computed tomography [CT] or EEG) test, and *specificity* refers to the percentage of patients with an unfavorable outcome who will have a negative (meaning unfavorable, as in a high biomarker level or abnormal head CT or EEG) test. None of the included predictors had the <1% rate of falsely optimistic prediction that most clinicians would consider appropriate based on a survey conducted in 2019.[124] However, the panel considered that achieving a 0% false-positive rate with narrow confidence intervals when predicting good outcome is less important than when predicting poor outcome because good outcome predictors are not used to withdraw life-sustaining treatment.

Except where noted, all PICOST questions for neuroprognostication used the same PICOSTs. These are, therefore, listed here once and not repeated. Similarly, certainty of evidence was very low–certainty for all neuroprognostication modalities included. Reasons for this are detailed in the individual online CoSTRs and not included here.

Population, Comparator, Outcomes, Study Design, and Time Frame for All Neuroprognostication PICOSTs

- Population: Adults (≥16 years) who are comatose after resuscitation from cardiac arrest (either in-hospital or out-of-hospital), regardless of target temperature
- Comparators: None
- Outcomes: Prediction of good neurological outcome defined as Cerebral Performance Categories (CPC) 1 or 2 or mRS score of 1 to 3 at hospital discharge or 1 month or later
- Study designs: Prognostic accuracy studies where the 2 x 2 contingency table (ie, the number of true/false negatives and positives for prediction of poor outcome) was reported, or where those variables could be calculated from reported data, were eligible for inclusion. Unpublished studies, reviews, case reports, case series, studies including fewer than 10 patients, letters, editorials, conference abstracts, and studies published in abstract form were excluded.
- Time frame: The original SysRev search was conducted on October 31, 2021, and included studies dating from 2001. The search was updated on May 20, 2022.

Use of the GCS Motor Score for Prediction of Good Neurological Outcome After Cardiac Arrest (SysRev Adolopment)

Intervention

GCS motor score evaluated within 4 days after cardiac arrest.

Consensus on Science

The full online CoSTR can be found on the ILCOR website.[125]

The original SysRev identified 2 observational studies on the prediction of good neurological outcome using the GCS motor score (scored from 1–6, with higher score being more favorable) on admission and within the first 4 days after cardiac arrest. No new studies

were identified in the updated search. In one study[126] including 342 OHCA patients, a GCS motor score >3 on day 4 after cardiac arrest predicted favorable outcome at 6 months with a specificity of 84% (95% CI, 79%–88%) and a sensitivity of 77% (95% CI, 67%–85%), and a GCS motor score 3 to 5 on day 4 predicted favorable outcome with 72% (95% CI, 66%–77%) specificity and 96% (95% CI, 93%–97%) sensitivity. In one study[127] including 302 OHCA patients, a GCS motor score of 4 to 5 evaluated on intensive care unit (ICU) admission after cardiac arrest predicted a favorable outcome at 3 months with specificity of 98% (95% CI, 93%–99%) and sensitivity of 12% (95% CI, 7%–17%).

Prior Treatment Recommendations

None (new recommendation)

2023 Treatment Recommendation

We suggest assessing the GCS motor score in the first 4 days after cardiac arrest to identify patients with a score higher than 3, which may indicate an increased likelihood of favorable outcome (weak recommendation, very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[125] Key points include the following:

- Sedation and pain medication may influence the assessment of the GCS motor score. Waiting time after stopping such medications to achieve a reliable test result varies.
- The assessment of the GCS motor score is an integral part of the identification of those unconscious patients who should undergo prognostication tests after cardiac arrest. Using the GCS motor score to identify those with a better motor response is not likely to have undesirable effects.

- Any possible withdrawal of life-sustaining therapies in post–cardiac arrest patients should be undertaken by using several prognostication modalities according to the 2020 CoSTR on the prediction of poor outcome.[121,122]

Task Force Knowledge Gaps

- Utility of GCS in post–cardiac arrest patients at various time points
- Utility of the GCS motor score after IHCA patients as well as those with a noncardiac cause of the arrest
- How GCS motor score compares with other means of assessing prognosis. This includes studies assessing costs and cost-effectiveness
- Whether there is significant interrater variability between different health care professionals assessing the GCS motor score in post–cardiac arrest patients

Imaging for Prediction of Good Neurological Outcome (SysRev Adolopment)

Intervention

Imaging studies assessed within 1 week after cardiac arrest.

Outcomes

CPC 1 to 3 or mRS score of 1 to 4 was accepted as an indirect outcome, in addition to the CPC 1 or 2 or mRS score of 0 to 3 used for this and other prognostication PICOSTs.

Consensus on Science

The full online CoSTR can be found on the ILCOR website.[128]

For the outcome of favorable neurological outcome, we identified 6 studies.[129-134] Because of considerable heterogeneity between the studies, no meta-analysis was performed. Favorable outcome was defined as a CPC 1 or 2 or mRS score of 0 to 3 in most studies. In one study,[133] good neurological outcome was measured as CPC 1 to 3 instead of 1 or 2.

Brain CT

A single study was identified by assessing the use of **brain CT** for prognostication of favorable neurological outcome. Key findings are summarized in Table 6, and details of the CT assessment techniques are provided in the online CoSTR and the SysRev.[123]

Table 6. GWR, QRA, and ASPECTS-b Using CT Brain: Sensitivity and Specificity for Favorable Neurological Outcome at 1 Month in a Single Study[129] of CT at 1 to 3 Hours After ROSC

CT variable	N	Timing after ROSC	Sensitivity (95% CI)	Specificity (95% CI)
GWR >1.25	67	124.5 min (±59.9 min)	25% (8.7%–49.1%)	77% (62.0%–87.7%)
QRA ≤5	67	124.5 min (±59.9 min)	25% (8.7%–49.1%)	77% (62.0%–87.7%)
ASPECTS-b ≥15	67	124.5 min (±59.9 min)	75% (50.9%–91.3%)	89% (76.9%–96.0%)

ASPECTS-b indicates Alberta Stroke Program Early CT Score; CT, computed tomography; GWR, gray-white matter; QRA, quantitative regional abnormality; and ROSC, return of spontaneous circulation.
Adapted from Sandroni et al. This is an Open Access article under the CC BY-NC 4.0 license.[123]

Brain Magnetic Resonance Imaging

Five observational studies were identified that examined the use of magnetic resonance imaging (MRI) for prognostication of good neurological outcome.[130-134] Time points of imaging ranged from 3.1 hours after ROSC to 8 days. Key study findings are summarized in Table 7.

Table 7. Sensitivity and Specificity of Findings on MRI—Including DWI, FLAIR, T2-Weighted GRE, and Average ADC—for Prediction of Favorable Neurological Outcome* at 6 Months

Study, year	n	MRI measure	Timing after ROSC	Sensitivity (95% CI)	Specificity (95% CI)
Park, 2020[132]	36	Absence of cortical necrosis	3.1 h (2.4–4)	100.0% (86.7%–100.0%)	60.0% (32.3%–83.7%)
Park, 2020[132]	36	Absence of cortical necrosis	77.6 h (75.9–80)	100.0% (86.7%–100.0%)	93.3% (68.1%–99.8%)
Oh, 2019[131]	134	No diffusion restriction in cortex or deep gray matter	After rewarming	72.2% (54.8%–85.8%)	94.9% (88.5%–98.3%)
Oh, 2019[131]	134	No or single diffusion restriction cortex or deep gray matter	After rewarming	94.4% (81.3%–99.3%)	91.8% (84.5%–96.4%)
Jang, 2019[130]	39	Absence of restricted diffusion	77.6 h (75.9–80)	91.7% (61.5%–99.8%)	92.6% (75.7%–99.1%)

Mlynash, 2010[†133]	33	No DWI or FLAIR lesions in cortex	≤8 days	77.8% (52.4%–93.6%)	80.0% (51.9%–95.7%)
Mlynash, 2010[†133]	33	No DWI or FLAIR lesions in deep gray nuclei	≤8 days	50.0% (26.0%–74.0%)	86.7% (59.5%–98.3%)
Mlynash, 2010[†133]	33	No DWI or FLAIR lesions in cerebellum and pons	≤8 days	100.0% (84.7%–100.0%)	20.0% (4.3%–48.1%)
Jang, 2019[130]	39	Summary GRE score of 0		75.0% (42.8%–94.5%)	100.0% (89.5%–100.0%)
Wouters, 2021[134]	58	Average ADC >931 x 10-6 mm^2/s	5 days (IQR 4–6)	100.0% (86.0%–100.0%)	38.0% (23.0%–58.0%)

*Defined as CPC 1 or 2 or mRS score of 0 to 3.
[†]Favorable neurological outcome defined as CPC score 1 to 3 for this study.
ADC indicates apparent diffusion coefficient; CPC, Cerebral Performance Category; DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery; GRE, gradient-recalled echo; IQR, interquartile range; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; and ROSC, return of spontaneous circulation.
Adapted from Sandroni et al. This is an Open Access article under the CC BY-NC 4.0 license.[123]

Prior Treatment Recommendations

None (new recommendation)

2023 Treatment Recommendations

We suggest using the absence of diffusion restriction on MRI between 72 hours and 7 days after ROSC, in combination with other tests, for predicting good neurological outcome of

adults who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence).

We suggest against using gray-white matter ratio, quantitative regional abnormality, Alberta Stroke Program Early CT Score on brain CT to predict good neurological outcome in patients who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence).

We suggest against using apparent diffusion coefficient on brain MRI to predict good neurological outcome in patients who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence).

We suggest against using gradient-recalled echo on brain MRI to predict good neurological outcome in patients who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[128] Key points include the following:

- Evidence from 5 studies consistently suggests that the absence of visible cytotoxic edema, assessed as the absence of cortical diffusion-weighted imaging changes on brain MRI, predicts good neurological outcome with high specificity at 72 hours or later after cardiac arrest.
- Apparent diffusion coefficient enables quantification of the diffusion changes on brain MRI. However, the evidence is limited to 1 study, and no apparent diffusion coefficient threshold for prediction of good neurological outcome has been established.

- Evidence showing that a high GWR, a low quantitative regional attenuation score, or a high Alberta Stroke Program Early CT score predicts good neurological outcome after cardiac arrest is limited to 1 study. There is considerable heterogeneity in measurement techniques (sites and calculation methods) for GWR in the medical literature.
- Evidence for GWR and gradient-recalled echo was limited to small, single-center studies.
- Lack of blinding was a limitation in all included studies.

Task Force Knowledge Gaps

- Whether there is a consistent GWR threshold for predicting good neurological outcome after cardiac arrest
- Standardization of the methods for GWR calculation, apparent diffusion coefficient calculation, and the criteria for defining an MRI as normal
- The optimal timing for prognostication using brain CT after cardiac arrest
- The value of serial brain CT after cardiac arrest to predict good neurological outcome

Use of Brain Injury Biomarkers for the Prediction of Good Outcome After Cardiac Arrest (SysRev Adolopment)

Intervention

A normal or a low level of one of the following brain injury biomarkers: neuron-specific enolase (NSE), S100 calcium-binding protein B (S100B), neurofilament light chain (NfL), tau, glial fibrillary acid protein, or ubiquitin carboxy-terminal hydrolase-1

Consensus on Science

The full online CoSTR can be found on the ILCOR website.[135] Six observational studies were identified on biomarkers for prediction of good neurological outcome, 4[136-139] in the initial

SysRev[123] and 2[140,141] in the updated search. Because of considerable heterogeneity between studies, no meta-analyses were performed.

Neuron-Specific Enolase

NSE was investigated in 4 observational studies, including a total of 2141 patients.[136-138,140] Sample acquisition ranged from 24 hours to 72 hours. Key results are presented in Table 8.

Table 8. Sensitivity and Specificity of NSE for Prediction of Favorable Neurological Outcome*

Study, year	n	Threshold value	Time of acquisition	Sensitivity (95% CI)	Specificity (95% CI)
Zellner, 2013[136]	103	<17 µg/L	24 h	26% (15%–40%)	89% (77%–96%)
	84		48 h	41% (25%–58%)	89% (77%–97%)
Moseby-Knappe, 2021[137]	650	≤17 µg/L	24 h	46% (41%–52%)	85% (81%–89%)
	614		48 h	58% (52%–63%)	84% (79%–88%)
	572		72 h	75% (70%–80%)	80% (75%–85%)
Streitberger, 2017†[138]	1053	≤17 µg/L	72 h	33% (29%–37%)	97% (95%–98%)
Wihersaari, 2022‡[140]	248	≤17 µg/L	48 h	90% (85%–95%)	54% (44%–64%)

*Defined as CPC score of 1 or 2 or mRS score of 0 to 3 at 6 months.
†Favorable neurological outcome defined as CPC 1 to 3 at ICU discharge in this study.
‡Outcome measured at 12 months in this study.
CPC indicates Cerebral Performance Category; ICU, intensive care unit; mRS, modified Rankin Scale; and NSE, neuron-specific enolase.
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S100B, Glial Fibrillary Acid Protein, Tau Protein, NfL, and Ubiquitin Carboxy-Terminal Hydrolase-1

Several studies were identified for other serum biomarkers to predict favorable neurological outcome. Thresholds varied across studies in many cases, as did sensitivity and specificity. An overview of findings, grouped by biomarker, is provided in Table 9. For full details, see the online CoSTR.[135]

Table 9. Overview of Studies on Blood S100B, GFAP, Tau Protein, NfL, and UCH-L1 to Predict Favorable Neurological Outcome at 6 Months

Study, year	n	Threshold value	Time of acquisition	Sensitivity (95% CI)	Specificity (95% CI)
S100B					
Zellner, 2013[136]	114	<0.61 µg/L	Admission	31% (20%–45%)	89% (78%–96%)
	110	<0.12 µg/L	24 h	37% (24%–51%)	89% (78%–96%)
Moseby-Knappe, 2021[137]	649	<0.105 µg/L	24 h	69% (64%–74%)	74% (69%–79%)
NfL					
Moseby-Knappe, 2021[137]	692	<55 pg/mL	24 h	26% (15%–40%)	89% (77%–96%)
	658		48 h	41% (25%–58%)	89% (77%–97%)

	608		72 h	51% (45%–56%)	97% (94%–98%)
Wihersaari 2021[139]	107	<30 pg/mL	24 h	79% (67%–88%)	100% (92%–100%)
	109		48 h	74% (62%–84%)	100% (92%–100%)
	103	<27 pg/mL	72 h	67% (56%–79%)	100% (91%–100%)
Wihersaari 2022[140]	227	≤55 pg/mL	24 h	74% (66%–82%)	86% (80%–92%)
	180		48 h	67% (58%–77)	87% (80%–95%)
GFAP					
Moseby-Knappe, 2021[137]	689	<22 pg/mL	24 h	41% (36%–46%)	97% (94%–98%)
	654		48 h	35% (30%–41%)	97% (95%–99%)
	599		72 h	44% (39%–50%)	95% (92%–97%)

Humaloja[141]	108	<210 pg/mL	48 h	100% (100%–100%)	43% (32%–54%)
	108	<439 pg/mL	48 h	94% (87%–100%)	75% (65%–85%)
Serum tau protein					
Moseby-Knappe, 2021[137]	694	≤1.55 pg/mL	24 h	28% (24%–33%)	94% (90%–96%)
	661		48 h	35% (30%–41%)	97% (95%–99%)
	611		72 h	44% (39%–50%)	95% (92%–97%)
Humaloja[141]	109	≤3.28 pg/mL	48 h	94% (87%–100%)	53% (42%–65%)
	105	≤2.1pg/mL	72 h	100% (100%–100%)	21% (12%–31%)
	105	≤3.37 pg/mL	72 h	94% (86%–100%)	52% (40%–64%)
UCH-L1					
	693	<327 pg/mL	24 h	64% (58%–69%)	85% (81%–88%)
	663		48 h	74% (69%–78%)	82% (77%–86%)

	610		72 h	88% (84%–91%)	70% (65%–76%)

GFAP indicates glial fibrillary acid protein; NfL, neurofilament light chain; S100B, S100 calcium-binding protein B; and UCH-L1, ubiquitin carboxyl-terminal hydrolase-L1.

Prior Treatment Recommendations

None (new recommendation)

2023 Treatment Recommendations

We suggest using normal NSE (<17 μg/L) within 72 hours after ROSC, in combination with other tests, for predicting favorable neurological outcome in adults who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence).

We suggest against using serum levels of glial fibrillary acidic protein, serum tau protein, or NfL in clinical practice for predicting favorable neurological outcome in adults who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[135] Key points include the following:

- The best evidence is for NSE, given the number of patients included in trials and the similar thresholds used to determine a normal value across studies.
- Evidence for the accuracy of the biomarkers S100B, NfL, glial fibrillary acid protein, tau, and ubiquitin carboxy-terminal hydrolase-1 is inconsistent. NfL may be more accurate, but there are few data on feasibility of measuring these novel biomarkers in regular clinical practice because all analyses have included thawed samples measured later in highly specialized laboratories. Threshold levels for predicting a good functional outcome have also varied considerably.

- Any possible withdrawal of life-sustaining therapies in cardiac arrest patients should be undertaken by using several prognostication modalities according to the 2020 CoSTR on the prediction of poor outcome.[121,122]

Task Force Knowledge Gaps

- The utility of biomarkers in patients with IHCA and those with a noncardiac cause of arrest
- The use of NSE in patients with variable degrees of hemolysis
- The accuracy of biomarkers when used together with other means of predicting a good outcome such as examination, imaging, EEG, SSEP, and other biomarkers
- The cost-effectiveness of the use of biomarkers for predicting outcome
- Whether the results of NSE measurements are consistent even if there is deviation from the recommended assessment time point
- The optimal thresholds for biomarkers for prediction of favorable outcome

EEG for Prediction of Good Neurological Outcome (SysRev Adolopment)

Intervention

Various EEG modalities assessed within 1 week after cardiac arrest

Outcomes

CPC 1 to 3 or mRS score of 1 to 4 was accepted as an indirect outcome, in addition to the CPC 1 or 2 or mRS score of 0 to 3 used for this and other prognostication PICOSTs.

Consensus on Science

The full online CoSTR can be found on the ILCOR website.[142]

The original SysRev[123] identified 24 studies. Of these, 15 investigated EEG, 5 investigated reduced montage and/or amplitude-integrated EEG, and 4 investigated EEG-derived indices, such as bispectral index (BIS). The updated review identified no additional studies

meeting inclusion criteria. Several studies did not report on use of medications that can impact EEG background continuity and voltage. All except 3 studies on EEG adopted the 2012 American Clinical Neurophysiology Society (ACNS) terminology. Sensitivity and specificity for all included EEG patterns, as well as timing of acquisition, are detailed for every included study in tables in the associated SysRev,[123] as well as being detailed in the online CoSTR. An overview of key results is provided here.

Continuous or Nearly Continuous EEG Patterns (ACNS-Defined)

Twelve studies investigated the ability of a favorable EEG pattern **during the first 5 days after ROSC** to predict good neurological outcome.[143-154] All studies used the ACNS terminology to describe the EEG patterns. A favorable EEG pattern was defined as a continuous or nearly continuous background without superimposed abundant or generalized periodic discharges or seizures. The criteria for both the background and the superimposed discharges varied slightly across studies (refer to the online CoSTR).[142]

Results of the 6 studies evaluating **continuous or nearly continuous, normal-voltage background with no abundant or generalized periodic discharges or seizures**[143,144,149-151,153] are presented in Table 10.

Table 10. Continuous or Nearly Continuous Normal-Voltage EEG With No Abundant/Generalized Periodic Discharges or Seizures for Prediction of Favorable Neurological Outcome

Study, year	N	Note	Timing	Outcome timing	Sensitivity (95% CI)	Specificity (95% CI), %
Admiraal, 2019[143]	66	a	12 h	6 months	63.2% (46.0%–78.2%)	82.1% (63.1%–93.9%)
Admiraal, 2019[143]	120		24 h	6 months	84.0% (73.7%–91.4%)	66.7% (54.0%–77.8%)

Duez, 2019[149]	44	b	24 h	6 months	38.8% (28.4%–50.0%)	100.0% (91.8%–100.0%)
Duez, 2019[149]	103		48 h	6 months	45.8% (25.6%–67.2%)	90.0% (68.3%–98.8%)
Westhall, 2016[153]	207		77 h (53–102)	6 months	29.6% (13.8%–50.2%)	100.0% (96.1%–100.0%)
Backman, 2018[144]	103	c	76 h (62–104)	6 months	77.3% (65.3%–86.7%)	80.1% (72.6%–86.4%)
Westhall, 2016[153]	120		77 h (53–102)	6 months	48.1% (28.7%–68.1%)	98.7% (92.9%–100.0%)
Sondag, 2017[151]	248	d	12 h	6 months	84.0% (73.7%–91.4%)	66.7% (54.0%–77.8%)
Duez, 2019[149]	120		24 h	6 months	51.2% (42.0%–60.3%)	88.0% (81.0%–93.1%)
Hofmeijer, 2015[150]	230		24 h	6 months	56.5% (45.3%–67.2%)	97.1% (85.1%–99.9%)
Duez, 2019[149]	44		48 h	6 months	77.8% (69.2%–84.9%)	80.5% (72.0%–87.4%)
Hofmeijer, 2015[150]	187		48 h	6 months	62.5% (40.6%–81.2%)	80.0% (56.3%–94.3%)
Hofmeijer, 2015[150]	97		72 h	6 months	95.7% (89.5%–98.8%)	52.7% (42.1%–63.1%)

Notes: a: Continuous or nearly continuous, normal voltage, without unequivocal electrographic seizures, or abundant (>50%) periodic discharges or abundant spike-wave (ACNS). b: As [a], *plus* no reversed anteroposterior gradient *plus* reactive. c: As a, *plus* no reversed anteroposterior gradient. d: Continuous, either diffusely slowed (dominant frequency <8 Hz) or normal (dominant frequency ≥8 Hz) with no evolving seizures or generalized periodic discharges.

ACNS indicates American Clinical Neurophysiology Society; EEG, electroencephalogram.
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Four of the 12 EEG studies[146-148,152] used less-restrictive voltage criteria, including not only a continuous or nearly continuous normal voltage EEG background but also a **low-voltage background** among the favorable EEG patterns. Results are presented in Table 11.

Table 11. Continuous or Nearly Continuous Normal or Low-Voltage EEG for Prediction of Favorable Neurological Outcome

Study, year	N	Note	Timing	Outcome timing	Sensitivity (95% CI)	Specificity (95% CI)
Carrai, 2021[147]	41	e	<6 h	6 months	70.6% (44.0%–89.7%)	95.8% (78.9%–99.9%)
Carrai, 2016[146]	38		6 h–12 h	6 months	90.9% (58.7%–99.8%)	96.3% (81.0%–99.9%)
Scarpino, 2021[148]	218		12 h	6 months	56.5% (45.3%–67.2%)	97.7% (93.5%–99.5%)
Carrai, 2016[146]	65		18 h–24 h	6 months	100.0% (85.4%–100.0%)	87.0% (73.7%–95.1%)
Rossetti, 2017[152]	357	f	≤48 h	6 months	76.1% (69.2%–82.1%)	87.6% (81.8%–92.0%)
Rossetti, 2017[152]	357		48 h–72 h	3 months	90.6% (85.3%–94.4%)	82.5% (76.1%–87.8%)
Carrai, 2016[146]	64	e		6 months	100.0% (77.9%–100.0%)	82.7% (69.7%–91.8%)

Notes: e: Continuous, normal, or low voltage, no epileptiform discharges. f: Continuous, normal, or low voltage, reactive, no epileptiform discharges.
EEG indicates electroencephalogram.
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Two of the 12 EEG studies used a less-restrictive *continuity* criteria, including not only a **continuous or nearly continuous normal-voltage EEG background** but also a **discontinuous normal-voltage EEG background.** Results of these studies are summarized in Table 12.[145,154]

Table 12. Continuous, Nearly Continuous, or Discontinuous Normal-Voltage EEG Background for Prediction of Favorable Neurological Outcome

Study, year	N	Note	Timing	Outcome timing	Sensitivity (95% CI)	Specificity (95% CI)
Sivaraju, 2015[154]	89	g	≤72 h	Hospital discharge	71.9% (53.3%–86.3%)	96.5% (87.9%–99.6%)
Sivaraju, 2015[154]	89	h		Hospital discharge	100.0% (88.7%–100.0%)	84.4% (73.1%–92.2%)
Beretta, 2019[145]	166	i	Day 0–5	6 months	77.1% (65.6%–86.3%)	77.1% (67.4%–85%)

Notes: g: Continuous, nearly continuous, or discontinuous, normal voltage, with no epileptiform patterns. h: As above but with any of periodic discharges, rhythmic delta activity, spike-and-wave, sharp-and-wave, or sporadic epileptiform discharges ("normal voltage plus"). i: Continuous and/or reactive, normal-voltage EEG background with no episodes of status epilepticus or generalized periodic discharges.
EEG indicates electroencephalogram.
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Other EEG Patterns or Grading Scales

A heterogeneous group of EEG patterns were described as favorable in 3 studies that did not use the ACNS terminology.[155-157] None of these studies excluded EEGs with superimposed discharges from favorable patterns. All 3 studies assessed EEGs within approximately 24 to 48 hours after cardiac arrest, and the specificities to predict good outcome ranged between 68% (95% CI, 55.3–79.4) and 91% (95% CI, 80–97) (sensitivities from 75% [95% CI, 42.8–94.5] to 96% [95% CI, 78.9–99.9]). Specificity was lower for later assessments.

EEG: Continuous Background Assessed via Reduced Montage and/or Amplitude-Integrated EEG

Five studies[130,158-161] investigated the predictive value of a **continuous normal-voltage background** using amplitude-integrated EEG[130,159] or original EEG with reduced electrode montages[158,160] at a time ranging from 6 to 72 hours after ROSC. Results are summarized in Table 13.

Table 13. Continuous or Discontinuous—Reduced Montage or Amplitude-Integrated EEG to Predict Favorable Neurological Outcome at 6 Months or Hospital Discharge

Study, year	N	Timing, h	Outcome timing	Sensitivity (95% CI)	Specificity (95% CI), %
Wennervirta, 2009[158]	30	<24 h	6 months	66.7% (43.0%–85.4%)	55.6% (21.2%–86.3%)
		24 h–48 h		95.2% (76.2%–99.9%)	66.7% (29.9%–92.5%)
Jang, 2019[130]	39	≤72 h	6 months	100.0% (77.9%–100.0%)	85.2% (66.3%–95.8%)
Oh, 2013[159]	55	≤72 h	Hospital discharge	57.1% (37.2%–75.5%)	96.3% (81.0%–99.9%)

Rundgren, 2010[160]	93	8 h (5–14)	6 months	52.7% (38.8%–66.3%)	92.1% (78.6%–98.3%)
	95	24 h–48 h		94.7% (85.4%–98.9%)	78.9% (62.7%–90.4%)
Eertmans, 2019[161]	60	6 h–12 h	6 months	54.8% (36.0%–72.7%)	79.3% (60.3%–92.0%)
	57	18 h–24 h		67.9% (47.6%–84.1%)	79.3% (60.3%–92.0%)
	56	36 h–48 h		85.7% (67.3%–96.0%)	78.6% (59.0%–91.7%)

EEG indicates electroencephalogram.
Adapted from Sandroni et al. This is an Open Access article under the CC BY-NC 4.0 license.[123]

EEG-Derived Indices

One study[162] of 54 patients reported that a **cerebral recovery index** above 0.57 at 18 hours or 0.69 at 24 hours predicted favorable neurological outcome at 6 months with 100% (95% CI, 89.5%–100%) specificity (sensitivities 65% [44.3–82.8] and 26% [11.1–46.3], respectively).

Three studies including 201 patients evaluated the predictive value of **BIS**.[163-165] In 2 studies,[163,164] a BIS value greater than 21 at 1 to 3 hours after ROSC or 24 at 3 to 6 hours after ROSC predicted good neurological outcome with 94% (95% CI, 79.8–99.3) and 86% (95% CI, 73.3–94.2) specificity, respectively (sensitivities 88% [95% CI, 61.7–98.4] and 94% [95% CI, 83.1–98.7]). In one study,[165] specificity increased from 41% (95% CI, 25.6–56.7) with a BIS of 30 to 92.9% [95% CI, 80.5–98.5] with a BIS of 60. Sensitivities decreased from 95% (95% CI, 75.1–99.9) to 20% (95% CI, 5.7–43.7) when the BIS of 60 was used.

Prior Treatment Recommendations

None (new recommendation)

2023 Treatment Recommendations

We suggest using a continuous or nearly continuous normal voltage EEG background without periodic discharges or seizures within 72 hours from ROSC in combination with other indices to predict good outcome in patients who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence).

There is insufficient evidence to recommend for or against using a low voltage or a discontinuous EEG background on days 0–5 from ROSC to predict good neurological outcome after cardiac arrest (weak recommendation, very low–certainty evidence).

We suggest against using heterogeneous, non-ACNS-defined favorable EEG patterns to predict good neurological outcome after cardiac arrest (weak recommendation, very low–certainty evidence).

We suggest against the use of other EEG metrics, including reduced montage or amplitude-integrated EEG, BIS, or EEG-derived indices, to predict good outcome in patients who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence).

We suggest that the ACNS terminology be used to classify the EEG patterns used for prognostication (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[142] Key points include the following:

- In making the recommendation in favor of a continuous or nearly continuous, normal-voltage EEG background without seizures or abundant or generalized periodic discharges as a predictor of good neurological outcome in patients who are comatose after cardiac arrest, the task force members considered the consistency of the evidence (12 studies, mostly with >80% specificity and >50% sensitivity) and the consistency of the definition made using an ACNS or ACNS-compatible terminology.
- The background definition was consistent in 6 of these studies. Although the criteria for periodic discharges varied slightly within this subgroup, this did not affect the prediction accuracy.
- Evidence from the remaining 6 studies confirmed the ability of a continuous or nearly continuous, normal-voltage EEG background without seizures or discharges to predict good neurological outcome. These studies also included a low-voltage or discontinuous EEG background among the “favorable” EEG patterns. These patterns are farther from normal than a continuous or nearly continuous background, and their accuracy could not be assessed separately. The ILCOR task force considered the evidence supporting these patterns insufficient for recommending their use.
- The remaining studies on EEG used definitions of favorable patterns that did not comply with the ACNS terminology and were highly heterogeneous.

- In recommending against using amplitude-integrated EEG or EEG-derived indices, such as BIS or cerebral recovery index, the panel considered that these techniques do not allow or allow only a limited morphologic assessment of the original EEG signal. Moreover, the evidence was limited to few studies (only 1 study for cerebral recovery index).

Task Force Knowledge Gaps

- The effects of sedation and systemic organ dysfunction on the predictive value of the EEG background
- The value of low-voltage background and discontinuous reactive/normal voltage background
- The value of EEG reactivity for predicting good outcome, using standardized stimulation and assessment
- Which aspect of periodic discharges (ie, distribution, morphology, prevalence, etc) has greatest importance in affecting the prognosis of a favorable EEG pattern
- The value of dominant EEG rhythms (eg, theta) in prognostication after cardiac arrest
- The predictive value of favorable EEG patterns defined according to the 2021 ACNS definitions, although the 2012 definitions for features used for predicting a good outcome are a little different from the 2021 definitions

SSEPs for Prediction of Good Neurological Outcome (SysRev Adolopment)

Intervention

SSEP N20 wave amplitude assessed within 1 week from cardiac arrest

Outcomes

CPC 1 to 3 or mRS score of 1 to 4 was accepted as an indirect outcome, in addition to the CPC 1 or 2 or mRS score of 0 to 3 used for this and other prognostication PICOSTs.

Consensus on Science

Complete results, including details on variation in definitions and criteria for SSEPs, can be found on the online CoSTR and are supported by the SysRev.[123,166] Five studies on SSEPs were identified.[131,148,167-169] The overall certainty of the evidence was rated as very low. Because of the inconsistency in N20 amplitude thresholds and timing of assessment, no meta-analyses were performed. Results of included studies are summarized in Table 14.

Table 14. Amplitude of the N20 Wave of the Short-Latency SSEPs to Predict Favorable Neurological Outcome at 6 Months or ICU Discharge

Author, year	Sample size, n	Threshold value	Timing	Timing outcome	Sensitivity (95% CI)	Specificity (95% CI)
Scarpino, 2021[148]	218	>3 μV	12 h	6 months	61.2% (50.0%–71.6%)	88.7% (82.1%–93.5%)
Scarpino, 2021[148]	218	>4 μV		6 months	48.2% (37.3%–59.3%)	91.0% (84.8%–95.3%)
Scarpino, 2021[148]	218	>5.3 μV		6 months	25.9% (17.0%–36.5%)	99.2% (95.9%–100.0%)
Scarpino, 2021[148]	218	>10 μV		6 months	5.9% (1.9%–13.2%)	100.0% (97.8%–100.0%)
Scarpino, 2021[148]	260	>4 μV	24 h	6 months	49.4% (38.7%–60.2%)	89.5% (83.9%–93.6%)

Scarpino, 2021[148]	260	>5 μV		6 months	37.1% (27.1%–48.0%)	93.0% (88.1%–96.3%)
Scarpino, 2021[148]	260	>8 μV		6 months	15.7% (8.9%–25.0%)	97.1% (93.3%–99.0%)
Oh, 2019[131]	192	>2.31 μV	48 h–72 h	6 months	52.9% (38.5%–67.1%)	96.5% (91.9%–98.8%)
Glimmerveen, 2020[169]	129	>3.6 μV		6 months	32.3% (16.7%–51.4%)	95.9% (89.9%–98.9%)
Oh, 2019[131]	192	>5.04 μV		6 months	9.8% (3.3%–21.4%)	100.0% (97.9%–100.0%)
Benghanem, 2022[168]	82	>3.2 μV	72 h	3 months	29.0% (23.0%–34.0%)	93.0% (90.0%–96.0%)
Benghanem, 2022[168]	82	>4 μV		3 months	14.0% (10.0%–18.0%)	95.0% (92.0%–97.0%)
Scarpino, 2021[148]	240	>4 μV		6 months	50.6% (39.0%–62.2%)	85.9% (79.6%–90.8%)
Scarpino, 2021[148]	240	>6.2 μV		6 months	24.7% (15.6%–35.8%)	92.6% (87.5%–96.1%)

Scarpino, 2021[148]	240	>9 μV		6 months	14.3% (7.4%–24.1%)	97.5% (93.8%–99.3%)
Endisch, 2015[167]	293	>4.197 μV	24 h–96 h	ICU discharge	27.5% (20.3%–35.6%)	92.1% (86.5%–95.8%)
Endisch, 2015[167]	293	>7.194 μV		ICU discharge	9.2% (5.0%–15.1%)	97.4% (93.4%–99.3%)

ICU indicates intensive care unit; SSEP, somatosensory evoked potential.
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Prior Treatment Recommendations

None (new recommendation)

2023 Treatment Recommendation

We suggest against using the amplitude of the N20 SSEP wave to predict good neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence to decision table is provided in Appendix X.[166] Key points include the following:

- Although very low–certainty evidence suggests that a high N20 amplitude predicts good neurological outcome after cardiac arrest with high specificity, the amplitude threshold for this prediction varied widely across studies.
- The methods to calculate the N20 amplitude were inconsistent.

- Observational evidence shows that sedative drugs, especially midazolam, decrease the N20 amplitude.
- The optimal timing for predicting good outcome by using SSEP amplitude has yet to be established.

Task Force Knowledge Gaps

- The methods to calculate the N20 SSEP amplitude need to be standardized.
- The optimal N20 SSEP amplitude for predicting good outcome needs to be established.
- The interrater variability in the assessment of the N20 SSEP amplitude must be investigated.
- The effects of sedation on the N20 SSEP amplitude must be investigated.
- There is still limited evidence on the correlation between time after ROSC and the N20 SSEP amplitude.

ALS Topics Reviewed by EvUps

Topics reviewed by EvUps are summarized in Table 15, with the PICOST, existing treatment recommendation, number of studies identified, key findings, and whether a SysRev was deemed worthwhile provided. Complete EvUps can be found in Appendix X.

Table 15. ALS Topics Reviewed With EvUps

Topic/PICOST	Year last updated	Existing treatment recommendation	RCTs since last review	Observational studies since last review	Key findings	Sufficient data to warrant SysRev?
Cardiac arrest in pregnancy	2020	We suggest delivery of the fetus by perimortem cesarean delivery for women in cardiac arrest in the second half of	None	2, plus one SysRev of extracorporeal life support in pregnancy (mostly case	Case series of 7 patients with cardiac arrest and	No

		pregnancy (weak recommendation, very low–quality evidence). There is insufficient evidence to define a specific time interval by which delivery should begin. High-quality usual resuscitation care and therapeutic interventions that target the most likely cause(s) of cardiac arrest remain important in this population. There is insufficient evidence to make a recommendation about the use of left-lateral tilt and/or uterine displacement during CPR in the pregnant patient.		reports and series), and one SysRev of maternal positioning during CPR	perimortem cesarean delivery. No women survived and 3 neonates survived.	

Steroids after ROSC from cardiac arrest	2010 (intra-arrest steroids reviewed in 2015, EvUps in 2019 and 2021)	There is insufficient evidence to support or refute the use of corticosteroids alone or in combination with other drugs during cardiac arrest.	1	None	RCT of adults with IHCA, randomized to methylprednisolone or placebo. No difference in any outcomes. Limited by very few patients surviving with good neuro outcome in either group, baseline imbalance between groups and cross	No

					contamination/steroids use in placebo group.	

ALS indicates advanced life support; CPR, cardiopulmonary resuscitation; EvUp, evidence update; IHCA, in-hospital cardiac arrest; PICOST, population, intervention, comparator, outcome, study design, time frame; RCT, randomized controlled trial; ROSC, return of spontaneous circulation; and SysRev, systematic review.

PEDIATRIC LIFE SUPPORT

Extracorporeal Cardiopulmonary Resuscitation for Cardiac Arrest in Pediatrics (SysRev)

Rationale for Review

The continuous evidence evaluation process to produce the CoSTR for this topic for children and for adults started with a systematic review (SysRev) in 2018.[170] Considering the new evidence available on this topic both in children and in adults, the decision was made to update the SysRev (PROSPERO CRD42022341077).[171] Evidence was sought and considered by the ALS Task Force and the PLS Task Force groups respectively. The CoSTR for adults is published separately by the ALS Task Force. The full online CoSTR can be found on the ILCOR website.[172]

PICOST

- Population: Adults (≥18 years of age) or children (<18 years of age) with cardiac arrest in any setting (out-of-hospital or in-hospital).
- Intervention: ECPR including extracorporeal membrane oxygenation or cardiopulmonary bypass during cardiac arrest
- Comparator: Manual or mechanical CPR
- Outcome: Any clinical outcome
- Study design: This was an update of the ILCOR SysRev addressing ECPR for cardiac arrest in 2018. New RCTs, nonrandomized controlled trials, and observational studies (cohort studies and case-control studies) with a control group (patients not receiving ECPR) were included. Ecological studies, case series, case reports, reviews, abstracts, editorials, comments, letters to the editor, and unpublished studies were not included. Studies assessing

cost-effectiveness were included for a descriptive overview. Studies exclusively assessing the use of extracorporeal life support for cardiac and/or respiratory failure after sustained ROSC were not included. Studies assessing extracorporeal circulation for deep hypothermia (or other conditions) were only included if cardiac arrest was documented.

- Time frame: Search included the dates January 1, 2018, to June 21, 2022. All languages were included if there was an English abstract or an English full-text article.

Consensus on Science

The updated SysRev[171] identified 4 observational studies in children. Adult studies included 3 randomized controlled trials, 24 observational studies, and 6 cost-effectiveness studies. All studies that included children evaluated IHCA events. There were no published or registered randomized clinical trials comparing ECPR with no ECPR in children. The calendar years of the events included in studies ranged from 2000 to 2017. The number of patients included ranged from 17 to 20 654, and the number of exposed patients receiving ECPR ranged from 6 to 1670.

Two studies were secondary analyses of the Therapeutic Hypothermia After Pediatric Cardiac Arrest (THAPCA) IHCA trial, in which patients aged >2 days to <18 years who were comatose after IHCA were randomized to 1 of 2 targeted temperature regimens.[173] In 1 secondary analysis,[174] odds of survival were lower in the patients supported with extracorporeal membrane oxygenation (ECMO) (N=180) at the time of initiation of targeted temperature therapy compared with the no ECMO group (N=149) (OR for survival at 12 months, 0.52 [95% CI, 0.29, 0.94] and OR for survival at 12 months with Vineland

Adaptive Behavior Scales Second Edition [VABS-II], ≥70, 0.34 [95% CI, 0.17, 0.67]).

Another secondary analysis of the THAPCA IHCA trial compared the cognitive and neurologic scores in 12-month survivors with prearrest VABS-II ≥ 70 between 3 groups: those treated with ECPR (N=57), those who did not receive ECMO (N=56), and those treated with ECMO later in their course (N=14).[175] VABS-II composite scores at 12 months were normal (≥70) for 39 (70.9%) ECPR survivors, 47 (83.9%) survivors treated with no ECMO, and 10 (71.4%) survivors who received later ECMO (OR for survival with VABS-II, ≥70 0.49 [95% CI, 0.22, 1.12] in ECPR survivors compared with the other 2 groups combined). The Pediatric Resuscitation after Cardiac Arrest form was used to score conventional age-appropriate neurologic examinations.[176] Neurological examination scores in the none/minimal impairment to mild impairment range were observed for 28 (59.5%) ECPR survivors, in 33 (73.3%) survivors treated without ECMO, and in 10 (83.3%) survivors treated with later ECMO. Cognitive assessments were completed using the VABS-II, the Mullen scale,[177] and the Weschler Abbreviated Scale of Intelligence (WASI) assessment.[178] Cognitive and neurological score distributions were similar between ECPR survivors compared with no-ECMO and later-ECMO groups.

A third study used an administrative inpatient national database in the United States to evaluate children with International Classification of Diseases, Tenth Revision codes for cardiac arrest and ECMO on the same day, thus assumed to have received ECPR.[179] These were

compared with those with codes for a cardiac arrest only. There was no difference in mortality between patients with ECPR (cardiac arrest and same-day ECMO) and those with CPR without ECMO (59.7% versus 60.2%, OR 0.98 [95%CI, 0.88–1.08; P<0.681). Secondary outcomes suggest that the group with ECPR (cardiac arrest and same-day ECMO) had longer lengths of stay and higher hospitalization costs compared with those with cardiac arrest and no ECMO.

A fourth study at a single center evaluated the quality of resuscitation measures with video recordings in 6 ECPR and 11 no-ECPR cardiac arrest events.[180] The OR for survival to hospital discharge was reported as 0.53 (95% CI, 0.04, 6.66) for the ECPR group compared with no ECPR. Similarly, the odds of having a Functional Status Scale[181] score of 1 at hospital discharge were calculated to be 0.53 (95% CI, 0.04, 6.66) for the ECPR groups compared with no ECPR. ECPR events were associated with lower adherence to resuscitation guidelines compared with CPR-only events.

Collectively, these 4 pediatric studies favored no ECPR, but the confidence intervals, when available, were broad, and risk of bias was assessed as critical for all studies.

Treatment Recommendations (Unchanged From 2021)

We suggest that 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.

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[172] Key discussion points included the following:

- In making this weak recommendation, the PLS Task Force noted that in select pediatric patient populations (ie, cardiac arrest with cardiac disease), the practice of using ECPR has become widespread across some institutions with systems that support postoperative cardiac surgical ecosystems.
- The task force acknowledges that ECPR is a complex system intervention that requires considerable resources and sustained training that may not be universally available.

Task Force Knowledge Gaps

- There are no comparative prospective studies or randomized trials of ECPR in children.
- Whether ECPR is beneficial in selected IHCA populations (eg, noncardiac) or in OHCA populations
- How the transition from conventional CPR to ECPR alters the quality of resuscitation measures
- 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
- How best to provide immediate and early post–cardiac arrest care with ECPR (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 incorporating the pediatric COSCA.[182] Moreover, an update in Utstein reporting definitions would serve to enhance the reporting of resuscitation measures applied during this technique.

Prediction of Survival With Good Neurological Outcome After Return of Circulation Following Pediatric Cardiac Arrest—Combined Prognostic SysRev

Rationale for Review

The PLS Task Force undertook a SysRev considering the use of individual prognostic tests using clinical signs, blood biomarkers, brain electrophysiology, and brain imaging to help the clinician in predicting a good neurological outcome (PROSPERO Registration CRD42021279221). For all topics, the search included studies from database inception to December 31, 2022.

This assessment is different from predicting a poor neurological outcome, which may involve consideration of withdrawal of life-sustaining therapies. Recommendations for or against tests to predict good neurological outcomes cannot automatically be transferred to recommendations for poor outcome prediction, and further research is required for this purpose.

The PLS Task Force defined good neurological outcome prediction as imprecise when the false positive rate (FPR) was above 30%. However, there is no universal consensus on what the acceptable limits for imprecision should be in prediction of good neurological outcome for infants and children after cardiac arrest.

All evaluated tests were used in combination with other tests by clinicians in these studies.

Except where noted, all PICOST questions for neuroprognostication used the same population, comparator, outcome, study design, and time frame. The timing of the intervention/diagnostic test was also the same for each. These parameters are therefore listed here once and not repeated in subsequent sections. Also for all topics, the available evidence had a high risk of bias based on heterogeneity across studies, few studies and patients included, lack

of blinding, variation in test assessment and performance, and variability in outcome measurement. Therefore, no meta-analysis was performed, and evidence is considered very low certainty. Overall assessment of test performance was based on visual assessment of forest plots. If only 1 study was available (with small patient sample size), then a suggestion or recommendation could not be made.

Population, Comparator, Outcome, Study Design, and Time Frame for All Neuroprognostication PICOSTs

Population: Children (<18 years of age) who achieve a return of circulation (ROC, which includes a return of spontaneous circulation or mechanical circulation) after resuscitation from IHCA and OHCA, from any cause.

Studies that included newly born infants or patients in hypoxic coma from causes without a cardiac arrest (eg, respiratory arrest, toxidromes, drowning, hanging) were excluded, except when a subpopulation of cardiac arrest patients could be evaluated separately.

Intervention: Index prognostic tests, recorded less than 12 hours, 12 to <24 hours, 24 to <48 hours, 48 to <72 hours, 72 hours to <7 days, and/or 7 to 10 days after cardiac arrest

Comparator: There was no control group for intervention/exposure. The accuracy of the prognostic index test was assessed by comparing the predicted outcome with the final outcome, which represents the comparator.

Outcome: Prediction of survival with good neurological outcome defined as a Pediatric CPC score of 1, 2, or 3 or VABS-II ≥ 70 at the pediatric intensive care unit (PICU) or hospital discharge, 1 month or later.

Study design: RCTs and nonrandomized studies (nonrandomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Case series were considered if greater than 5 cases were reported. Unpublished studies (eg, conference abstracts, trial protocols) and animal studies were excluded. We selected studies where the sensitivity and FPR of the prognostic (index) test were reported.

Time frame*:* All years and all languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. SysRev search to February 17, 2022, updated December 31, 2022.

Clinical Examination for the Prediction of Survival With Good Neurological Outcome

Intervention: Includes every part of a bedside neurological clinical examination, including pupillary response (assessed using manual light reflex or automated pupillometry), level of coma (eg, Glasgow Coma Scale score or Full Outline of Unresponsiveness [FOUR]) score), and brainstem reflexes.

Consensus on Science

See the ILCOR website for the full online CoSTR.[183]

Pupil Reactivity

The predictive ability of presence of pupil reactivity to classify good neurological outcome was evaluated in 8 studies[184-191] in 402 patients within 1 hour, 6 to 12 hours, 24 hours, and 72 hours after resuscitation. Most studies had a sensitivity greater than 82% at all assessment times and corresponding FPR ranged from 3.2% to 67%. Within 12 hours of ROC, the FPR was less than 33% in 3 out of 4 studies reporting this time period.[185,186,189] FPR increased to 38% to 68% at 24 to 72 hours, and corresponding sensitivity for predicting good neurological outcome

was 100% at 48 to 72 hours after ROC.[184,188] No studies evaluated automated pupillometer monitoring devices.

Coma Level

The relationship between coma assessment using the GCS motor score alone or total GCS and good neurological outcome at intensive care unit discharge, hospital discharge, and 6 months was evaluated in 3 studies[189,191,192] including 296 patients. In 1 study, GCS motor score of 4 or greater within 1 hour and at 4 to 6 hours after ROC had a sensitivity of 17% and 50% for predicting good neurological outcome at 6 months, with a corresponding FPR of 6% and 7% respectively.[189] Using total GCS measured at resuscitation or within 1 hour, a score of 5 or greater predicted good neurological outcome with a low sensitivity of 30% and an FPR of 14%.[192] A total GCS score of 8 or greater had a slightly higher sensitivity of 31%, with a low FPR of 6%.[191] However, only 1 study was available to assess each test using total GCS or GCS motor score cutoff or at each testing time point.

Motor Response

The presence of a motor response to any stimulus was evaluated in 1 study[184] at <1 hour, 48 hours, and 72 hours after ROC with up to 27 patients. Sensitivity and FPR improved with time: at <1 hour after ROC, the sensitivity was 38% and FPR was 30%, compared with 72 hours, when the sensitivity was 100% and the FPR was 23%.

Brainstem Reflex

The presence of brainstem reflexes to predict good neurological outcome at intensive care unit or hospital discharge was evaluated in 2 studies[186,190] including 118 patients. Evoked responses to pain, gag reflex, and cough reflex were assessed at 6 to12 hours and at 24 hours. Predictive sensitivity of presence of pain response at 6 to 12 hours was 100% with an FPR of

67%.[186] The presence of a gag and cough reflex at 24 hours both predicted a good neurological outcome with a sensitivity of 40% and FPR of 32% to 35%, respectively.[190]

Prior Treatment Recommendations (2015)

We suggest that practitioners use multiple variables when attempting to predict outcomes for infants and children after cardiac arrest (weak recommendation, very low–quality evidence).

No previous recommendation regarding use of clinical exam

2023 Treatment Recommendations

All evaluated tests were used in combination with other tests by clinicians in these studies. Although the predictive accuracy of tests was evaluated individually, we recommend that no single test should be used in isolation for prediction of good neurological outcome (good practice statement).

We suggest using pupillary light reflex within 12 hours after ROC for predicting good neurological outcome in children after cardiac arrest (weak recommendation, very low–certainty evidence).

We cannot make a recommendation for or against using total GCS, GCS motor score, or motor response after ROC for predicting good neurological outcome in children after cardiac arrest.

We cannot make a recommendation for or against the use of brainstem tests after ROC for predicting good neurological outcome in children after cardiac arrest.

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence to decision table is provided in Appendix X.[183] Key points include the following:

- For pupillary light reflex, limited evidence suggests that the specificity for prediction of good neurological outcome was highest within 12 hours of ROC after cardiac arrest. There was increased sensitivity (up to 100%) for predicting good outcomes at 48 to 72 hours; however, the point estimates had wide confidence intervals. Pupillary light reflex at 48 to 72 hours should be evaluated for use for predicting poor neurological outcome at these times.
- For all clinical examination modalities, inaccuracy of outcome prediction tests may be due to confounding from the effect of sedatives. No studies reported any assessment of the confounding influence of medication or specifically excluded the presence of residual sedation at the time of clinical examination.
- No studies included blinding of test results from treating clinicians and only 1 study had blinded outcome assessment (for pupil light reactivity). Lack of blinding is a major limitation of clinical examination tests, even if the withdrawal of life-sustaining therapy based on clinical examination has not been documented in any of the studies included in our review.
- The studies inconsistently reported the cointervention of temperature control on the clinical assessments.
- Despite the limitations of the assessment of pupil light reactivity and coma assessment, the balance between the costs and benefits favors benefit.

Task Force Knowledge Gaps

- Clinical examination for prognostication after cardiac arrest appears promising but more research is required in infants and children.
- The impact of residual medication or temperature on pupillary light reflex assessment, coma score, and motor response in infants and children

- The cost and benefits of the use of pupillometry compared with pupillary light reflex assessment
- Economic cost evaluation and cost-effectiveness studies are required.
- Further research is required on multimodal prognostication, timing, definitions of testing, accurate outcome timing, and outcome definition.
- A better understanding of survivorship after pediatric cardiac arrest—informed by wider research and consultation with patients, children, parents, guardians and caregivers, health care professionals, and members of the wider society—is needed to inform correct definitions and framework of good neurological outcome for prediction research.

Blood Biomarkers for the Prediction of Survival With Good Neurological Outcome

Intervention: Serum biomarkers either specific to neuronal damage (eg, neuron-specific enolase [NSE], S100B, glial fibrillary acidic protein, NfL) or blood markers of inflammation or systemic ischemic reperfusion (eg, procalcitonin, blood pH, or lactate)

Consensus on Science

See the ILCOR website for the full online CoSTR.[193]

Lactate

Lactate was evaluated in 5 studies.[173,194-197] Three studies documented <7% FPR for lactate <2 mmol/L at <1 hour and at 6 to 12 hours,[173,195,197] although sensitivity in these studies was low (16%–28%). Lactate <2 mmol/L at 24 to 48 hours was sensitive (69%–86%) for good neurological outcome; however, the FPR was high at 61% and 68%. Lactate <5 mmol/L at <1 hour had moderate sensitivity (66%) and FPR (62%) and at 24 hours had high sensitivity (89%) and low FPR (17%), making the latter a useful test for prediction. Lactate clearance over 48 hours to <2 mmol/L had high sensitivity (100%) and high FPR (77%).

pH

pH was evaluated in 4 studies.[173,194,195,197] pH thresholds were >7.0, >7.3, and <7.5 at resuscitation and within 1 hour, 6 to12 hours, and 24 hours of ROC. The blood pH measured after resuscitation or <1 hour from ROC had a wide range of sensitivities of 27% to 95% for predicting good neurological outcome. A pH >7.0 was reported in 3 studies and had a 68% to 98% sensitivity to predict survival and 71% to 97% sensitivity for good neurological outcome. FPR for good neurological outcome was above 80% for all except for pH threshold >7.0 at <1 hour after ROC (FPR 45%) and >7.3 at <1 hour after ROC (FPR 38%).

Neuronal Biomarkers

Only 1 study including 43 children reported NSE, S100B, and myelin basic protein values.[188] Threshold values were calculated and reported to classify either high sensitivity or low FPR for good neurodevelopmental outcome. At 24 hours, an S100B value of 0.128 ng/ml predicted a good neurodevelopmental outcome with a sensitivity of 100%, with a moderately high FPR of 62%. Sensitivity was high (100%) for predicting good outcome using an NSE threshold of 53.1 ng/ml at 24 hours and 76.7 ng/ml at 48 hours (with a corresponding FPR 81% and 77% respectively). Myelin basic protein level of 5.83 ng/ml at 24 hours and 5.43 ng/ml at 48 hours also had a high predictive sensitivity of 100% but high FPR of 96% and 88% respectively.

Lower threshold values of S100B (0.001 ng/ml at 24 h), NSE (0.48 ng/ml at 48 h), or myelin basic protein (0.05 ng/ml at 48 h) had a sensitivity of 6% to 29% with corresponding very low FPR of <6% for good neurological outcome.

Studies evaluating additional neuronal biomarkers (eg, glial fibrillary acidic protein, ubiquitin carboxyl-terminal hydrolase L1, NfL, and tau) in children after cardiac arrest with good

and poor outcomes were identified,[198-200] but we were unable to obtain sensitivity and specificity from these studies.

Prior Treatment Recommendations

No previous recommendations regarding the use of specific biomarkers

2023 Treatment Recommendations

All evaluated tests were used in combination with other tests by clinicians in these studies. Although the predictive accuracy of tests was evaluated individually, we recommend that no single test should be used in isolation for prediction of good neurological outcome (good practice statement).

We suggest using a normal plasma lactate value (<2 mmol/L) up to 12 hours following ROC for predicting good neurological outcome of children after cardiac arrest (weak recommendation, very low–certainty evidence).

We cannot make a recommendation for or against using time-to-lactate-clearance within 48 hours following ROC for predicting good neurological outcome.

We suggest against using pH following ROC for predicting good neurological outcome after cardiac arrest (weak recommendation, very low–certainty evidence).

We cannot make a recommendation for or against the use of blood neuro-biomarkers (eg, S100B NSE) after ROC for predicting good neurological outcome in children after cardiac arrest.

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[193] Key points include the following:

- Lactate and pH are potential markers of ischemia, poor perfusion, and anaerobic metabolism and are known to be associated with poor outcomes after cardiac arrest. Lactate metabolism is complex, and consideration of confounders and other predictors is critical.
- Included studies were observational studies and randomized controlled trials, but these were not primarily designed to test prognosis of blood biomarkers.
- Lactate is measured by blood gas analyzers and is easily accessible. Considering the low (but not negligible) cost of testing lactate and pH, a problem of inequity is unlikely but possible. Lactate and blood pH are widely available in settings with intensive care units, but many settings do not have intensive care units.
- Only 1 study[188] has identified threshold values for 2 blood neuronal biomarkers (S100B and NSE) that are associated with good neurological outcome with a high sensitivity. However, FPR is high, and these tests require specialized laboratory equipment and are not widely available.
- No studies reported any assessment of the confounding influence of medication.
- No studies included blinding of test results from treating clinicians, and only 1 study had blinded outcome assessment. Lack of blinding is a major limitation of biomarker tests, even if the withdrawal of life-sustaining therapy based on test results was not documented in any of the studies included in our review.

Task Force Knowledge Gaps

- The utility of other candidate biomarkers (eg, NfL, glial fibrillary acidic protein, tau, ubiquitin carboxyl-terminal hydrolase-L1) and whether subgroups may exist where FPR is much lower
- Cost-effectiveness of biomarker testing

- Further research is required on multimodal prognostication, timing, definitions of testing, accurate outcome timing, and outcome definition.
- A better understanding of survivorship after pediatric cardiac arrest—informed by wider research and consultation with patients, children, parents, guardians and caregivers, health care professionals, and members of the wider society—is needed to inform correct definitions and framework of good neurological outcome for prediction research.

Electrophysiology for the Prediction of Survival With Good Neurological Outcome

Intervention: Surface bioelectrical recordings from the central nervous system such as EEG and evoked potentials (EPs) (eg, brainstem auditory-evoked potentials, and short-latency somatosensory evoked potentials [SSEPs]). We included studies of the interpretation of raw signals or summary measures derived from processed EEG signals such as amplitude-integrated EEG (aEEG), quantitative EEG (qEEG), or BIS.

Consensus on Science

The full online CoSTR can be found on the ILCOR website.[201]

Absence of Clinical or Electrographic Seizure

Twelve studies reported the relationship between absence or presence of seizures in children after cardiac arrest and good neurological outcomes at PICU/hospital discharge, 6 months, and 12 months.[173,186,187,189,196,197,202-207] These studies included 1165 children, and 4 of the 12 studies reported using the ACNS criteria.[187,202,205,207]

Absence of seizures up to 24 hours after ROC had a sensitivity of 50% to100% with an FPR of 63% to 98% for predicting good neurological outcome at various time points.[189,202,205,206] Absence of seizure after 24 hours had a sensitivity of 50% to100% with an FPR of 42% to 100% for predicting good neurological outcome.[173,186,187,189,196,197,200,205,207]

Absence of Status Epilepticus

Absence of status epilepticus was reported in 3 studies.[202,206,207] Two of these studies used ACNS criteria to define status epilepticus. Good neurological outcome at PICU/hospital discharge was predicted with a high sensitivity of >90%, although FPR remained high at 81% to 91%.

Absence of Myoclonic Epilepsy

On the basis of 2 studies, absence of myoclonic seizures predicted good neurological outcomes with a sensitivity of 100% but a very high FPR of 79% to 83% at PICU/hospital discharge.[186,205]

SSEP

SSEPs, evaluating presence or absence of N20 waves, were reported in only 1 study, with few patients (n=12) reporting good neurological outcome (Pediatric CPC score 1 to 3) at 3 times (24, 48, and 72 h).[208] Clinicians were blinded to test results and the SSEP assessor was blinded to outcome. The sensitivity for prediction of good neurological outcome was 100% at 24 and 48 hours and 83% at 72 hours, with a very low FPR of 0% at all time points but wide 95% confidence intervals (0%–71%).

Presence of Continuous or Normal EEG Background

The presence of a normal EEG background (defined as normal, continuous and reactive, continuous and unreactive, and nearly continuous by ACNS definitions) was reported in 10 studies with 18 different testing timings and included 563 patients (although there was a risk of overlapping patient populations).[186-188,190,202,203,205-207,209] Studies using normal or continuous EEG reported a low to moderate sensitivity of less than 50% at 10 of 18 testing times for predicting good neurological outcome. However, FPR was also low (<50% in all cases and

<30% in 11/18). In the largest study,[206] the sensitivity of continuous EEG at 6 to12 hours was 7.3% with an FPR of 0%. FPR was higher in studies assessing prognostic accuracy at and beyond 48 hours after ROC.

Absence of Attenuated, Isoelectric, or Flat EEG Background

The absence of an attenuated, isoelectric, or flat EEG was reported in 10 studies including up to 526 patients (although there was a risk of overlapping patient populations).[186-188,190,202,203,205-207,209] The sensitivity to predict a good neurological outcome was very high in 8 studies (91%–100%)[186,187,190,200,202,205,206,209]; however, there was a wide range of FPR of 0% to 83%, with the majority of studies reporting >40% FPR.

Absence of Burst Suppression, Burst Attenuation, or Generalized Periodic Epileptiform Discharges on EEG

Absence of burst suppression, burst attenuation, or generalized periodic epileptiform discharges were reported in 6 unblinded studies including 395 patients.[186,190,202,205-207] Sensitivity increased from 81% to 100% within 6 to12 hours, to a highly sensitive test (100% with high precision [95% CI, 100–100]) at 24, 48, and 72 hours. However, the FPR was high at all time periods (67%–100%) for predicting a good neurodevelopmental outcome.

Presence of a Reactive EEG

The presence of reactivity within an EEG was reported in 3 studies, with a moderate sensitivity for good neurological outcome of 53% to 80% between 6 hours and 72 hours.[190,205-207] FPR ranged from 7% to 27% up to 24 hours after ROC in 2 studies.[190,205] However, it increased to 50% at 48 hours after ROC in 1 study.

Presence of Sleep II Architecture or Sleep Spindles on EEG

The presence of sleep II architecture or sleep spindles was reported in 2 studies including 123 patients at 6 to12 hours and 24 hours following ROC after cardiac arrest. The presence of these features had a predicted sensitivity of 57% to 80% and low FPR (8.3%–16%).[187,190]

Presence of EEG Variability and EEG Voltage Variability

EEG variability, defined using ACNS criteria, had a moderate sensitivity for predicting good outcome (60%–80%) in 2 studies of 132 patients, with a corresponding FPR of 18% to 50%.[190,205] However, EEG voltage variability had a higher sensitivity (75% to 100%) in 1 study at all measured time points (6–12, 24, and 48 h after ROC) and a higher corresponding FPR of 36% to 67%.[205]

Quantitative EEG Scoring

Only 1 study reported a composite score assessing EEG background from a 24-hour monitoring period, obtained from quantitative EEG using the amplitude integrated EEG trace in 30 patients.[210] A score of >15 had a predicted sensitivity of 94% and FPR 67% for a good neurological outcome.

Prior Treatment Recommendations (2015)

We suggest that the use of EEG within the first 7 days after pediatric cardiac arrest may assist in prognostication (weak recommendation, very low–quality evidence).

2023 Treatment Recommendations

All evaluated tests were used in combination with other tests by clinicians in these studies. Although the predictive accuracy of tests was evaluated individually, we recommend that no single test should be used in isolation for prediction of good neurological outcome (good practice statement).

We suggest using EEG within 6 to 72 hours after ROC for predicting good neurological outcome in children after cardiac arrest (weak recommendation, low-certainty evidence).

We suggest using the following EEG features after ROC for predicting good neurological outcome: presence of sleep spindle and sleep II architecture at 12 to 24 hours, or continuous or normal background EEG between 1 and 72 hours, or EEG reactivity between 6 to 24 hours (weak recommendation, very low–certainty evidence).

We suggest against using the following EEG features after ROC to predict good neurological outcome: absence of clinical or electrographic seizures; absence of status epilepticus; absence of myoclonic epilepsy; absence of burst suppression, burst attenuation, or generalized periodic epileptiform discharges; or absence of attenuated, isoelectric, or flat EEG (weak recommendation, very low–certainty evidence).

We cannot make a recommendation for or against the use of the presence or absence of N20 response SSEPs after ROC for predicting good neurological outcome.

We cannot make a recommendation for or against the use of EEG variability or EEG voltage or quantitative EEG score for predicting good neurological outcomes (weak recommendation, very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[201] Key points include the following:

- ACNS definitions for seizures and EEG indices were followed in only some studies. EEG and SSEP prognostic criteria require clear and reproducible definitions and require validation in the PICU environment.

- The complex interpretation of normality in background EEG patterns in preterm and term infants and the impact of brain maturation on EEG patterns in infancy and childhood require expert neurophysiology input. Studies reported limited information on the handling of this area, and further refinement of definitions and application of recommendation are required.
- There was limited or no accounting for when tests were undertaken in relation to concurrent pharmacological exposure, sedation, and ongoing treatment (eg, targeted temperature management) in patients after cardiac arrest.
- SSEPs have a high level of precision in adult studies of neuroprognostication in comatose patients after cardiac arrest. The PLS Task Force recognizes the lack of available data in children and strongly encourages further multicenter evaluation.

Task Force Knowledge Gaps

- Electrophysiology tests for prognostication after cardiac arrest appear promising, but more research is required in infants and children.
- The type of monitoring (intermittent or continuous EEG, use of reduced channel monitoring, quantitative EEG systems), duration of monitoring, and timing of prognostic assessment
- Validation of ACNS or other international definitions of EEG indices within the PICU environment for infants and children after cardiac arrest
- Further work is needed on multimodal prognostication, timing, definitions of testing, accurate outcome timing, and definition.
- A better understanding of survivorship after pediatric cardiac arrest—informed by wider research and consultation with patients, children, parents, guardians and caregivers, health care professionals, and members of the wider society—is needed to inform correct definitions and framework of good neurological outcome for prediction research.

Brain Imaging for the Prediction of Survival With Good Neurological Outcome

Intervention:Neuroimaging modalities included head CT, brain MRI, cranial ultrasound, or transcranial doppler ultrasound.

Consensus on Science

See the ILCOR website for the full online CoSTR.[211]

Computed Tomography Imaging

Head CT to predict good neurological outcome (Pediatric CPC 1–3) was evaluated in 3 studies including 173 patients.[188,207,212] The majority of CT imaging was acquired at 24 hours or 48 hours after the cardiac arrest. Neurological outcome was assessed on discharge from the intensive care unit or hospital in 2 studies and at 6 months in 1 study. Reported factors from CT included presence and absence of intracranial hemorrhage, cerebral edema or ischemia measured by the reversal sign, gray-white matter differentiation, and sulcal or basal cistern effacement. Two studies described methods of estimating gray-white matter differentiation[212,213] and 2 reported radiologists' qualitative reports.[188,212]

The presence of gray-white matter differentiation on CT at 24 hours had a sensitivity of 64% to 100% and FPR 35% to 70%. Absence of CT lesions, edema, or intracranial hemorrhage predicted good neurological outcome with a sensitivity ranging from 72% to 100%; however, a wide range of FPR (14%–90%) was reported. Absence of effacement of sulci or basal cisterns predicted good neurological outcome with a high sensitivity (93%–100%) with an FPR 32% to 73%. Clinicians were not blinded to the CT results in any study.

MRI

MRI imaging to predict good neurological outcomes was reported in 4 studies including 215 patients.[203,214-216] Median time from ROC to MRI ranged from 3 to 6 days across all studies,

although inclusion of patients' MRIs up to 14 days was reported in 3 studies.[203,214,216] Two studies reported presence or absence of abnormalities in multiple regions of the brain in 3 sequences (diffusion-weighted imaging, T1, and T2).[214,215] Another study presented a composite of presence or absence of 1 (or more) region of abnormality.[203] One study evaluated thresholds of apparent diffusion coefficient and overall qualitative MRI reporting of evidence of hypoxic ischemic injury.[216] Three studies ensured that the neuroradiologist's MRI assessment was blinded to patient clinical status. However, the MRI findings were known by the treating clinicians, and neurological outcome assessment was not blinded.[203,214,215]

Absence of any region of abnormality on restricted diffusion, at a median of 4 days after ROC, predicted good neurological outcome with a sensitivity of 88% and corresponding very low FPR 2% in 1 study.[203] Apparent diffusion coefficient threshold $>600\times10^{-6}$ mm2/s in >93% and $>650\times10^{-6}$mm2/s in >89% of brain volume, at a median of 4 days after ROC, predicted good neurological outcome with a sensitivity of 100% and low FPR (20%).[216] In the same study, a normal MRI by qualitative reporting of absence of hypoxic ischemic injury predicted a good neurological outcome at 6 months with a sensitivity of 81% and FPR of 10%.[216]

For individual regions of the brain, at 4 to 6 days after ROC, diffusion-weighted imaging MRI sequence had a sensitivity for predicting good neurological outcome ranging from 67% to 100%, although associated FPR rates were moderate to high. Absence of lesions in the Lentiform regions on T2 weighted imaging had a sensitivity of 67% and the lowest FPR (7.7%) for any single region of the brain.

Transcranial Doppler Ultrasound

The prediction of good neurological outcome using presence of flow velocities of intracranial vessels measured on transcranial doppler was evaluated in 1 study including 17

patients who were all treated with hypothermic targeted temperature management.[217] Flow patterns without any reversal (or absence of diastolic) flow, mean flow velocity, and pulsatility index were assessed before, during, and after hypothermia therapy. Continuous flow velocities without reversal of diastolic flow pattern had a sensitivity of 100% and FPR of 44%. Within 1 hour of the event in the pre-hypothermia phase, mean flow velocity had a sensitivity for good neurological outcome of 38% and FPR of 0%, and having a normal pulsatility index had a sensitivity of 38% and FPR of 22%. In the hypothermia phase, mean flow velocity had a sensitivity of 25% and FPR of 11%; pulsatility index had a higher sensitivity of 100% and FPR 22%. By 72 hours, normal pulsatility index predicted a good outcome, with 88% sensitivity and 11% FPR. Clinicians were not blinded to the transcranial doppler results in this study.

Cranial Ultrasound

We identified no studies examining the role of cranial ultrasound and good neurological outcome after cardiac arrest in children.

Prior Treatment Recommendations

No previous recommendations regarding the use of brain imaging

2023 Treatment Recommendations

All evaluated tests were used in combination with other tests by clinicians in these studies. Although the predictive accuracy of tests was evaluated individually, we recommend that no single test should be used in isolation for prediction of good neurological outcome (good practice statement).

We suggest against using normal CT imaging at 24 to 48 hours from ROC for predicting good neurological outcome (weak recommendation, very low–certainty evidence).

We suggest using normal MRI between 72 hours and 2 weeks after ROC for predicting good neurological outcome (weak recommendation, low-certainty evidence).

We cannot make a recommendation for or against the use of transcranial Doppler ultrasound for predicting good neurological outcome.

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence to decision table is provided in Appendix X.[211] Key points include the following:

- The low false positive rate (high specificity) for normal MRI on global assessment for predicting good neurological outcome reduces the chance of false optimism if a normal MRI predicts a good neurological outcome.
- The sensitivity of a normal MRI or CT to predict a good neurological outcome is moderate to high, but up to 30% may be falsely categorized and a falsely pessimistic prediction made. Therefore, with the very low–certainty evidence, we cannot make a recommendation for or against the use of normal or abnormal MRI or CT for predicting poor neurological outcomes.
- The precision of MRI and CT is affected by the timing of the investigation and is at risk of pseudonormalization.
- The definition of presence or absence of injury on diffusion-weighted imaging or cutoff values for apparent diffusion coefficient on MRI or gray-white matter ratio on CT was inconsistent in the included studies.
- MRI and CT are both expensive tests and require specialist equipment, training, interpretation, and, most often, patient transport to obtain the information. This may be prohibitive in physiologically unstable patients or some health care settings.

Task Force Knowledge Gaps

- Neuroimaging for prognostication after cardiac arrest appears promising but more research is required in infants and children.
- A standardization of definitions and assessment of optimal thresholds for GWR calculation on CT, and diffusion-weighted imaging and apparent diffusion coefficient thresholds on MRI is needed.
- The optimal timing for prognostication using CT and MRI after cardiac arrest; studies assessing serial imaging after cardiac arrest are desirable.
- The role of assessing regional areas of the brain for predicting outcome or the use of magnetic resonance spectroscopy
- Cost-effectiveness of CT and MRI for prognostication
- Further work is needed on multimodal prognostication, timing, definitions of testing, and accurate outcome timing and definition.
- A better understanding of survivorship after pediatric cardiac arrest—informed by wider research and consultation with patients, children, parents, guardians and caregivers, health care professionals, and members of the wider society—is needed to inform correct definitions and framework of good neurological outcome for prediction research

Pediatric Life Support Topics Reviewed by EvUps

Topics reviewed by EvUps are summarized in Table 16, with the PICO, existing treatment recommendation, number of studies identified, key findings, and whether a SysRev was deemed worthwhile provided. Complete EvUps can be found in Appendix X.

Table 16. PLS Topics Reviewed by EvUps

Topic/PICOST	Year last updated	Existing treatment recommendation	RCTs since last review, n	Observational studies since last review, n	Key findings	Sufficient data to warrant SysRev?
Pulse check accuracy	2020	The ILCOR treatment recommendations from 2020 remain unchanged: Palpation of a pulse (or its absence) is not reliable as the sole determinant of cardiac arrest and need for chest compressions. If the victim is unresponsive, not breathing normally, and	0	0	In the 2020 EvUp on the accuracy of pulse check in detecting ROC after cardiac arrest in children, 2 studies were identified describing the use of manual pulse check in pediatric cardiac arrest. Our EvUp in 2022 identified several adult studies comparing the utility of manual pulse palpation at different sites and manual pulse palpation versus other innovative techniques such as arterial doppler ultrasound, POCUS, photoplethysmography, and ECG-based pulse detection. However, no new pediatric studies were identified. Despite several recent adult studies comparing manual pulse palpation with other methods of detecting ROC after arrest, there remains very little pediatric specific evidence in this area.	No

		there are no signs of life, lay rescuers should begin CPR. In infants and children with no signs of life, health care providers should begin CPR unless they can definitely palpate a pulse within 10 sec.				
Pad size, type, and placement for pediatric defibrillation	2020	The ILCOR treatment recommendations remain unchanged: There is insufficient evidence to alter the current recommendations to use the largest	0	0	In the 2020 EvUp on the use of various pad sizes, types, and placement for pediatric defibrillation, 1 new pediatric study was identified since 2010 examining the use of different defibrillator pad positions in children with shockable rhythms in cardiac arrest. Our EvUp in 2022 did not find any new pediatric studies on the topics of defibrillator pad size, type, or placement in pediatric cardiac arrest.	No

		size paddles that fit an infant's or child's chest without touching each other or to recommend one paddle or pad position or type over another. Either self-adhesive defibrillation pads or paddles may be used in infants and children in cardiac arrest.			There are few pediatric-specific studies on the topics of defibrillator pad size, type, or placement in pediatric cardiac arrest.	
Antiarrhythmics for children in cardiac arrest with shockabl	2018	We suggest that amiodarone or lidocaine may be used for the treatment of pediatric shock–	0	1	The only new evidence since the last SysRev in 2018 is an observational study 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. A systematic review was also reported in a	No

e rhythms at any time during CPR or immediately after ROSC		resistant VF/pVT (weak recommendation, very low–quality evidence).			brief research letter with limited description of methods.	
Adenosine use in SVT	2020	This treatment recommendation is unchanged from 2010.	0	0	There have not been any new studies on the use of adenosine in SVT since our last review. For infants and children with SVT with a palpable pulse, adenosine should be considered the preferred medication. Verapamil may be considered an alternative therapy in older children, but it should not be routinely used in infants. Procainamide or amiodarone given by a slow IV infusion with careful hemodynamic monitoring may be considered for refractory SVT. Moderate-quality evidence shows no differences in effects of adenosine and calcium channel antagonists for treatment of SVT on reverting to sinus rhythm, and low-quality evidence suggests no appreciable differences in the incidence of hypotension. A study comparing patient	No

					experiences and prospectively studied adverse events would provide evidence on which treatment is preferable for management of SVT.	
Energy doses for pediatric defibrillation	2015	The ILCOR treatment recommendations from 2020 (Maconochie 2020 S140) remain unchanged: We suggest the routine use of an initial dose of 2–4 J/kg of monophasic or biphasic defibrillation waveforms for infants or children in VF or pVT cardiac arrest. There is insufficient evidence from which to	0	1	The 2020 ScopRev identified a single 2019 systematic review that identified no pediatric studies linking the initial or cumulative energy delivered with survival to hospital discharge and no link between long-term survival or survival with good neurological outcome. Meta-analysis could not be performed because the component population groups were extremely heterogeneous. Our EvUp in 2022 identified 1 new pediatric study on this subject. This in-hospital registry study had been noted in the 2020 ScopRev but had not been published until after the initial search so was not included in the analysis. Differences remain in the first shock dose recommended by ILCOR member councils, with the ERC and ANZCOR recommending 4J/kg for the first and all subsequent shocks and the AHA recommending an initial dose of 2–4 J/kg (for ease of teaching, a dose of 2 J/kg is used in algorithms and training materials). For refractory VF, the AHA guidelines recommend increasing the defibrillation	No

		base a recommendation for second and subsequent defibrillation dosages.			dose to 4 J/kg, suggesting that subsequent energy doses should be at least 4 J/kg and noting that higher levels may be considered, not to exceed 10 J/kg. The recently performed SysRev failed to show a significant benefit of one dosing regimen over another but was hampered by small sample sizes and study heterogeneity. The more recent large pediatric in-hospital registry study provided support for a 2 J/kg dose for initial defibrillation but did not provide guidance for subsequent doses.	
Single or stacked shocks for pediatric defibrillation (PLS 389)	2020	The ILCOR treatment recommendations from 2020 (Maconochie 2020 S140) should remain unchanged: a single-shock strategy followed by immediate CPR	0	0	In the 2020 EvUp, there were no new pediatric studies since 2010 on the comparative clinical outcomes from the use of single defibrillation versus more than 1 shock for the initial or subsequent defibrillation attempt(s) in children with shockable rhythms in cardiac arrest, in any setting. They identified a single observational study on transthoracic impedance during defibrillation in children 8 years of age or older (n=5) that suggested that stacked shocks may not improve defibrillation success. Our EvUp in 2022 did not find any new pediatric studies on this subject. As in the	No

		(beginning with chest compressions) is recommended for children with out-of-hospital or in-hospital VF or pVT.			previous EvUp, we identified several adult studies, but these were excluded in view of the differences in physiology and pathophysiology of shockable rhythms in pediatric cardiac arrests and may not be extrapolatable to the pediatric population. Despite several recent adult studies comparing single versus stacked shocked in very selected settings, there remains very little pediatric-specific evidence in this area.	
Epinephrine frequency during CPR	2020	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).	0	5	Time to first dose of epinephrine—OHCA: The new evidence suggest that epinephrine may not be effective if given beyond 15 minutes after EMS arrival. The evidence is low quality from observational studies. Time to first dose of epinephrine—IHCA: One study examined hospital-level average timing of first dose of epinephrine and found extensive differences between institutions. After adjustment for patient and hospital variables, those higher-performing hospitals (ie, shorter time to first dose of epinephrine) had higher ROSC and 24-h survival but no difference in critical outcomes.	No

		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.			For poorly perfused bradycardia requiring CPR but with a pulse, epinephrine administration was associated with worse critical outcomes and increased progression to pulselessness. This is a different population than cardiac arrest but was included in this EvUp because the patients received CPR for >2 min. The treatment for bradycardia is reviewed in a different PICOST and should not be considered in the context of this PICOST. Epinephrine dosing interval: One study examined the dosing interval of epinephrine during IHCA and found an interval of ≤2 min compared with >2 min had improved critical outcomes.	

Bedside ultrasound to identify perfusing rhythm	2020 (ScopRev)	There is insufficient evidence to recommend for or against the routine use of echocardiography during a pediatric arrest.	0	1	This topic was covered in guidelines from the AHA and the ERC. We identified 1 small case series. 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.	No
End-tidal CO_2 monitoring during CPR	2020 (ScopRev)	The confidence in effect estimates is so low that the panel decided a recommendation was too speculative.	1	5	This topic was covered in guidelines from the AHA and the ERC. We identified 1 randomized clinical trial, 4 observational studies, and 1 systematic review of pediatric extracorporeal resuscitation that reported end-tidal CO2 monitoring during CPR and/or outcomes. The available data indicates that monitoring of ETCO2 contributes to improving the quality of CPR and to the adherence to current guidelines. However, it has not been demonstrated the impact of ETCO2 monitoring and feedback on patients' outcomes that is the main focus of our PICOST.	No

Invasive blood pressure monitoring during CPR	2020 (ScopRev)	The confidence in effect estimates is so low that the panel decided a recommendation was too speculative	1	2	This topic was covered in guidelines from the AHA and the ERC. We identified 1 randomized control trial and 2 observational studies utilizing patients from the randomized control trial population. The potential value of personalized hemodynamic-directed CPR, where CPR efforts are adjusted in view of predefined (diastolic) BP goals and not limited by current standard guidelines, has yet to be defined. Indeed, current evidence suggests that at present there is a low rate of utilization of diastolic blood pressure during resuscitation.	No
Use of near NIRS during cardiac arrest	2020 (ScopRev)	There has not been, to date, a recommendation on the use of NIRS in cardiopulmonary arrest to guide resuscitation efforts or predict outcome.	0	2	Our EvUp in 2022 identified 1 observational study that reported NIRS monitoring during CPR and/or outcomes and 1 abstract. The observational study evaluated 21 patients with 23 events and found an association between higher rSO_2 measurements during the entire monitored event and last 5 min of the event with ROSC. The abstract of 32 patients including children with congenital heart disease from 3 centers did not show an association with outcomes or on multivariable analysis.	No

					There remains very little pediatric-specific evidence examining the use of NIRS during cardiac arrest. Our EvUp only identified 1 small observational study and 1 abstract. Therefore, a SysRev of pediatric cardiac arrest patients is not justified at this time. There continues to be insufficient data to support or advise against a treatment recommendation related to NIRS usage during CPR to provide physiologic feedback to guide resuscitation efforts or predict outcome.	
Resuscitation of the pediatric patient with a single ventricle, post-Stage I repair	2020 (EvUp)	The PLS task force recommendations from 2020 for the pediatric population therefore remain unchanged. Standard resuscitation (prearrest and arrest) procedures should be followed for	0	4	No new RCTs were identified. Four additional publications fulfilled inclusion criteria; however, none would change the current treatment recommendations of standard resuscitation procedures for infants and children with single-ventricle anatomy after Stage I repair. There is some evidence for the use of ECMO in post-cardiotomy SV patients and ECPR use in SV patients, but that topic should be included in the SysRev on ECPR by the ALS with PLS input.	No

		infants and children with single-ventricle anatomy after Stage I repair. Neonates with a single ventricle before Stage I repair who demonstrate shock caused by elevated pulmonary to systemic flow ratio might benefit from inducing mild hypercarbia (Paco2 50–60 mm Hg); this can be achieved during mechanical ventilation by reducing				

		minute ventilation, adding CO2 to inspired air, or administering opioids with or without chemical paralysis.				
Resuscitation of the pediatric patient with single-ventricle, status-post-Stage III/ Fontan/total cavopulmonary connection/anastomosis in	2010	This treatment recommendation is unchanged from 2010 with the exception of limiting the recommendation to children with hemi-Fontan or BDG physiology who are in a prearrest state; hypercarbia	0	1	This EvUp was performed to identify any evidence about this topic published after the PLS Task Force's most recent review in 2010. The EvUp identified 1 registry-based study that reported outcomes of infants and children with Fontan or BDG who had circulatory support initiated during a peri-arrest phase. The PLS Task Force agreed that there is insufficient evidence to recommend a new SysRev, and the 2010 treatment recommendation remains in effect, with the addition of a brief explanatory phrase within brackets. Optimizing outcomes for patients with single-ventricle physiology status-post total cavopulmonary connection (Fontan palliation) requires a nuanced understanding of anatomic and	No

cardiac arrest		achieved by hypoventilation may be beneficial to increase oxygenation and cardiac output. Negative-pressure ventilation, if available, may be beneficial for children with either hemi-Fontan or BDG or Fontan physiology by increasing cardiac output. Negative-pressure ventilation, if available, may be beneficial for children with			physiologic considerations as well as cardiopulmonary and cardio-cerebral interactions. The previous EvUp was performed by the PLS Task Force in July 2018 following revision of the original search strategy to include single ventricle patients who may undergo surgical palliation with PAB and/or nonsurgical repair in the cardiac catheterization lab to include PDA stent (hybrid palliation). This EvUp has identified no new RCTs or sufficient new data to proceed to full SysRev.	
Resuscitation of the pediatric patient with hemi-Fontan/BDG circulation in cardiac arrest	2010		0	1	This EvUp was performed to identify any evidence about this topic published after the PLS Task Force's most recent review in 2010. The EvUp identified 1 registry-based study by Jolley et al that reported outcomes of infants and children with Fontan or BDG who had circulatory support initiated during a periarrest phase.	No

		either hemi-Fontan or BDG or Fontan physiology by increasing cardiac output. During cardiopulmonary arrest, it is reasonable to consider ECPR for patients with Fontan physiology. There is insufficient evidence to support or refute the use of ECPR in patients with hemi-Fontan or BDG physiology.				
Resuscitation of children	New	There is no treatment recommendat	0	0	The management of children with septic shock–associated cardiac arrest has not	No

with cardiac arrest associated with sepsis		ion at this time.			been previously reviewed by the PLS Task Force. PICOST: Population: Infants and children in cardiac arrest with sepsis Intervention: Specific alteration in treatment algorithm Comparator: Standard care (according to current treatment algorithm) Outcome: All Study design: RCTs and nonrandomized studies (nonrandomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Time frame: All years and all languages were included as long as there was an English abstract. This EvUp was requested to determine the available evidence about this topic. The EvUp identified several studies involving prevention of cardiac arrest, but there was insufficient evidence of unique management approaches to the children with septic shock–associated cardiac arrest.	

FiO_2 titrated to oxygenation during pediatric cardiac arrest	2020	This treatment recommendation is unchanged from 2010. There is insufficient information to recommend a specific inspired oxygen concentration for ventilation during attempted resuscitation after cardiac arrest in infants and children.	0	0	This PICOST remains a challenge because finding any data during non-neonatal cardiac arrest is problematic. Although there is great interest in titration of oxygen after cardiac arrest and, more specifically, in the prevention of post-ROSC hyperoxia, titration of oxygen for intra-arrest management remains unreported in the human literature.	No

AHA indicates American Heart Association; ALS, advanced life support; ANZCOR, Australian and New Zealand Committee on Resuscitation; BDG, bidirectional Glenn; BP, blood pressure; CO_2, carbon dioxide; CPR, cardiopulmonary resuscitation; ECG, electrocardiogram; ECMO extracorporeal membrane oxygenation, ECPR extracorporeal cardiopulmonary resuscitation; EMS, emergency medical services; ERC, European Resuscitation Council; $ETCO_2$, end-tidal carbon dioxide; EvUp, evidence update; GWTG, Get With The Guidelines®; IHCA, in-hospital cardiac arrest; ILCOR, International Liaison Committee on Resuscitation; IV, intravenous; NIRS, near-infrared spectroscopy; OHCA, out-of-hospital cardiac arrest; PICOST, population, intervention, comparator, outcome, study design, time frame; PAB, pulmonary artery banding; $PaCO_2$, partial pressure of oxygen, arterial; PDA, patent ductus arteriosus; PLS, pediatric life support; POCUS, point-of-care ultrasound; pVT, pulseless ventricular tachycardia; RCT,

randomized controlled trial; ROC, return of circulation; ROSC, return of spontaneous circulation; rSO_2, regional cerebral oxygen saturation; SysRev, systematic review; SV, single ventricle; SVT, supraventricular tachycardia; VF, ventricular fibrillation.

NEONATAL LIFE SUPPORT

Maintaining Normal Temperature: Preterm (SysRev)

Rationale for Review

A previous SysRev conducted for ILCOR concluded that there was a dose-responsive association between hypothermia on admission to a neonatal unit or postnatal ward and increased risk of mortality and other adverse outcomes.[218] These findings are supported by more recent large observational studies.[219,220] A systematic review estimated that hypothermia was common among infants born both in hospitals and homes, even in tropical environments.[221] A SysRev was initiated from a priority list from the ILCOR Neonatal Life Support (NLS) Task Force; PROSPERO Registration CRD42021267301.[222] The full online CoSTR can be found on the ILCOR website.[223]

PICOST

- Population: Preterm infants (<34 weeks' gestation at birth)
- Intervention: Any of the following: increased room temperature ≥23.0°C, thermal mattress, plastic bag or wrap, hat, heating and humidification of gases used for resuscitation, radiant warmer (with or without servo control), early monitoring of temperature, warm bags of fluid, swaddling, skin-to-skin care with mother, or combinations of these interventions
- Comparators: Drying alone or with use of a plastic bag or wrap, or comparisons between interventions
- Outcomes:

- Critical: Survival to hospital discharge
- Important: Rate of normothermia, moderate hypothermia, cold stress, hyperthermia, body temperature, response to resuscitation (need for assisted ventilation, highest FIO_2), major morbidity including bronchopulmonary dysplasia, intraventricular hemorrhage (all grades), and severe (critical), necrotising enterocolitis, respiratory distress syndrome, late onset sepsis

For this review, the definitions in Table 17 were used.[224]

Table 17. Definitions

Normothermia	Body temperature 36.5ºC–37.5ºC	Measured by using a digital or mercury or contactless thermometer (axillary, rectal, or other defined site) upon admission to a postnatal ward or neonatal unit; or if admission temperature not reported, temperature measured between 30–60 min of age
Moderate hypothermia	Body temperature 32.0ºC–35.9ºC	
Cold stress	Body temperature 36.0ºC–36.4ºC	
Hyperthermia	Body temperature >37.5ºC	

- Study designs: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Unpublished studies were excluded.
- Time frame: No date restrictions were placed on the search. The literature search was updated to July 20, 2022. All years and all languages were included as long as there was an English abstract.

Consensus on Science

The SysRev identified 25 studies. Of these, 18 RCTs, including 4516 participants and 7 observational studies, provided data that could be extracted to evidence tables (for various comparisons between interventions) for the review.[219,225-247] Of the 13 comparisons from RCTs and 10 from observational studies for which evidence tables were developed, 5 comparisons provided sufficient data to inform the development of treatment recommendations. The studies were conducted in high-, middle-, and low-income countries, but few interventions were studied in all settings. None of the studies included out-of-hospital births. Temperature outcomes were reported in a wide variety of ways, constraining the meta-analysis. Except for the use of a plastic bag or wrap, there were insufficient data for the studied interventions to perform any of the prespecified subgroup analyses.

Comparison 1: Increased Room Temperature ≥23.0°C Versus Lower Room Temperature

Two RCTs[248,249] and 3 observational studies[219,250,251] addressed whether higher ambient temperature versus lower ambient temperature contributed to maintaining normal temperature in preterm infants. Because of heterogeneity, no meta-analysis was performed. A narrative summary of the comparison of room temperature ≥23.0°C versus lower room temperature is shown in Table 18 Additional outcomes are included in the full online CoSTR.[223]

Table 18. Increased Room Temperature ≥23.0°C Versus Lower Room Temperature for Birth of Newborn Infants Born at <34 Weeks' Gestation

Comparison	Participants (studies)	Certainty of the evidence (GRADE)	Results
Operating room temperature 20°C versus 23°C	22 (subgroup analysis, 1 RCT)[248]	Very low	Benefit or harm not excluded for any outcome
Higher (24°C–26°C) versus lower (20°C–23°C) DR temperature	91 (1 RCT)[249]	Very low	Increased body temperature on admission (MD, 0.5°C higher; 95% CI, 0.15°C to 0.85°C higher) Reduced moderate hypothermia (RR, 0.51; 95% CI, 0.32–0.80; RD 337 fewer infants per 1000 were hypothermic; 95% CI, from 467 fewer to 137 fewer infants)
Higher (25–28°C) versus lower(20°C) operating room temperature	108 (1 cohort study)[251]	Very low	Hypothermia less common when operating room temperatures were higher (RR, 0.69; 95% CI, 0.51–0.94)

DR temperature <25°C versus higher temperature	1764 (1 retrospective observational study)[219]	Very low	DR temperature <25°C was independently associated with risk of hypothermia (aOR, 1.44; 95% CI, 1.10–1.88)
High (34°C) versus lower (28°C) ambient temperature	202 (1 observational study)[250]	Very low	Higher admission temperatures (MD, 0.4°C higher, 95% CI, 0.24°C–0.5°C higher). Increased risk of hyperthermia (RR, 11.48; 95% CI, 1.54–85.54; RD, 115 more infants were hyperthermic per 1000; 95% CI, 6 more to 929 more infants)

aOR indicates adjusted odds ratio; DR, delivery room; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; MD, mean difference; RCT, randomized controlled trial; RD, risk difference; and RR, risk ratio.

Comparison 2: Thermal Mattress Versus No Thermal Mattress

The systematic review found 4 RCTs[228,233,235,241] and 5 observational studies[230,232,235,238,242] that examined the use of a thermal mattress. Data relating to the key critical and important outcomes for the comparison with no thermal mattress are summarized in Table

19. Additional outcomes (and those related to the comparison of a thermal mattress to a plastic bag or wrap[233,241]) are included in the full online CoSTR.[223]

Table 19. Thermal Mattress Compared With No Thermal Mattress for Newborn Infants Born at <34 Weeks' Gestation

Outcomes (importance)	Participants (studies)	Certainty of the evidence (GRADE)	RR (95% CI)	Anticipated absolute effect	
				Risk or mean with no thermal mattress	RD or MD with thermal mattress (95% CI)
Survival (critical)	174 (2 RCTs)[228,234]	Low	1.02 (0.98–1.06)	929 per 1000	19 more infants surviving per 1000 (19 fewer to 56 more)
Normothermia on admission (important)	72 (1 RCT)[234]	Moderate	0.53 (0.34–0.81)	771 per 1000	363 fewer normothermic infants per 1000 (509 fewer to 147 fewer), NNTH 3 infants
Mean body temperature (important)	174 (2 RCTs)[228,234]	Low	Not applicable	36.3°C	MD 0.46°C higher (0.22 higher to

					0.69°C higher)
Hyperthermia (important)	174 (2 RCTs)[228,234]	Low	2.77 (1.24–6.17)	71 per 1000	126 more hyperthermic infants per 1000 (17 more to 369 more), NNTH 8 infants
Hyperthermia (important)	703 (4 observational studies)[230,235,238,242]	Moderate	3.44 (1.91–6.20)		113 more hyperthermic infants per 1000 (42 more to 241 more), NNTH 9 infants

GRADE indicates Grading of Recommendations, Assessment, Development and Evaluation; MD, mean difference; NNTH, number needed to treat to harm; RCT, randomized controlled trial; RD, risk difference; and RR, risk ratio.

Comparison 3: Plastic Bag or Wrap Versus No Plastic Bag or Wrap

The systematic review found 15 RCTs including 1831 infants for this comparison.[225-227,229,231,239,240,243,245-247,252-255] Data relating to the key critical and important outcomes are summarized in Table 20. A subgroup analysis by gestational age suggested that a plastic bag or wrap was more effective in preventing moderate hypothermia in high-income countries and in infants born at <28 weeks' gestation compared with those born at 28 to 33+6 weeks; however, the clinical significance of these results is uncertain. Evidence for additional outcomes evaluated is included in the full online CoSTR.[223]

Table 20. Plastic Bag or Wrap Compared With No Plastic Bag or Wrap for Newborn Infants Born at <34 Weeks' Gestation

Outcomes (importance)	Participants (studies)	Certainty of the evidence (GRADE)	RR (95% CI)	Anticipated absolute effect	
				Risk or mean with standard care	RD or MD with plastic bag or wrap
Survival (critical)	1419 (11 RCTs)[225,227,229,231,239,240,243,245-247,253]	High	1.05 (1.00–1.10)	816 per 1000	41 more infants survived per 1000 (0 fewer to 82 more); NNTB 24 infants
Normothermia on admission (important)	449 (5 RCTs)[227,231,245,253,254]	Low	2.86 (1.66–4.91)	128 per 1000	238 more normothermic infants per 1000 (85 more to 501 more), NNTB 4 infants
Mean body temperature - axillary (important)	755 (10 RCTs)[225,226,229,240,243,245,252-255]	Low	Not applicable	35.6 °C	MD 0.65°C higher (0.42°C higher to

					0.87°C higher)
Hypothermia or cold stress (important)	489 (6 RCTs)[227,229,231,245,253,254]	Moderate	0.64 (0.50–0.82)	870 per 1000	313 fewer hypothermic or cold-stressed infants per 1000 (435 fewer to 157 fewer), NNTB 3 infants
Hyperthermia (important)	817 (9 RCTs)[226,229,239,243,245,247,252-254]	Moderate	RR 3.67 (1.77–7.61)	11 per 1000	33 more infants were hyperthermic per 1000 (9 more to 81 more), NNTH 30

GRADE indicates Grading of Recommendations, Assessment, Development and Evaluation; MD, mean difference; NNTB, number needed to treat to benefit; NNTH, number needed to treat to harm; RCT, randomized controlled trial; RD, risk difference; and RR, risk ratio.

Comparison 4: Cap Versus No Cap

The systematic review found a 3-arm RCT that compared use of a plastic cap (similar to a shower cap) with use of a plastic bag covering the body (no cap, only head dried) or with no plastic cap or bag.[245] Data relating to the key critical and important outcomes for the comparison between use of the plastic cap versus no plastic cap (or bag) are summarized in Table 21. Additional outcomes are included in the full online CoSTR.

Table 21. Plastic Cap Compared With No Cap for Newborn Infants Born at <34 Weeks' Gestation

Outcomes (importance)	Participants (studies)	Certainty of the evidence (GRADE)	RR (95% CI)	Anticipated absolute effect	
				Risk or mean with standard care	RD or MD with plastic cap
Survival (critical)	64 (1 RCT)[245]	Moderate	0.97 (0.84–1.12)	938 per 1000	28 fewer infants survived per 1000 (150 fewer to 113 more infants)
Normothermia (important)	64 (1 RCT)[245]	Moderate	6.00 (1.96–18.38)	94 per 1000	469 more normothermic infants per 1000 (90 more to 1629 more), NNTB 2 infants
Mean body temperature—axillary (important)	64 (1 RCT)[245]	Moderate	Not applicable	35.3°C	MD 0.8°C higher (0.41°C higher to 1.19°C higher)

Hypothermia or cold stress (important)	64 (1 RCT)[245]	Moderate	0.48 (0.32–0.73)	906 per 1000	471 fewer hypothermic or cold-stressed infants per 1000 (616 fewer to 245 fewer) NNTB 2 infants

GRADE indicates Grading of Recommendations, Assessment, Development and Evaluation; MD, mean difference; NNTB, number needed to treat to benefit; RCT, randomized controlled trial; RD, risk difference; and RR, risk ratio.

For the important adverse outcome of hyperthermia (>37.5°C), there were no events in either arm of the study.[245]

A retrospective observational study of 1764 infants compared the use of various interventions that included use of a plastic bag or wrap, a cloth (linen or woollen) cap, and a transport incubator. After adjustment for key variables, not using a cloth cap was an independent risk factor for hypothermia <36.0°C upon neonatal intensive care unit (NICU) admission (aOR 0.55; 95% CI, 0.39–0.78).[219]

Comparison 5: Heating and Humidification of Gases Used for Resuscitation Versus No Heating and Humidification

The systematic review found 2 RCTs including 476 infants and 1 observational study including 112 infants. Data relating to the key critical and important outcomes are summarized in Table 22. Additional outcomes and data for the observational study are included in the full online CoSTR.[223]

Table 22. Heating and Humidification of Gases for Resuscitation Compared With No Heating and Humidification of Gases for Newborn Infants Born at <34 Weeks' Gestation

Outcomes (importance)	Participants (studies)	Certainty of the evidence (GRADE)	RR (95% CI)	Anticipated absolute effect	
				Risk or mean with standard care	RD or MD with heated and humidified gases
Survival (critical)	476 (2 RCTs)[236,237]	Very low	1.00 (0.94–1.05)	918 per 1000	0 fewer/more infants survived per 1000 (55 fewer to 56 more)
Normothermia on admission (important)	476 (2 RCTs)[236,237]	Very low	1.23 (0.93–1.62)	471 per 1000	108 more normothermic infants were normothermic per 1000 (33 fewer to 292 more)
Mean axillary body temperature (important)	476 (2 RCTs)[236,237]	Moderate	Not applicable	36.6°C	MD 0.15°C higher (0.03°C higher to 0.26°C higher)

Moderate hypothermia	476 (2 RCTs)[236,237]	Low	0.58 (0.36–0.94)	172 per 1000	72 fewer hypothermic infants per 1000 (68 fewer to 7 fewer) NNTB 14 infants
IVH > grade 2	476 (2 RCTs)[236,237]	Moderate	0.39 (0.17–0.91)	82 per 1000	50 fewer infants had IVH per 1000 (68 fewer to 7 fewer), NNTB 42 infants

GRADE indicates Grading of Recommendations, Assessment, Development and Evaluation; IVH, intraventricular hemorrhage; MD, mean difference; NNTB, number needed to treat to benefit; RCT, randomized controlled trial; RD, risk difference; and RR, risk ratio.

Note: Gases refers to air and oxygen (reticulated or from cylinders).

Comparison 6: Radiant Warmer (With or Without Servo-Control)

No studies were found that compared the use of a radiant warmer with no radiant warmer. The only included study was an RCT that compared a servo-controlled radiant warmer with manual control. Data relating to the key critical and important outcomes are summarized in Table 23. Additional outcomes are included in the full online CoSTR.[223]

Table 23. Servo-Control of Radiant Warmer Compared With Manual Control for Infants Born at <34 Weeks' Gestation

Outcomes (importance)	Participants (studies)	Certainty of the evidence (GRADE)	RR (95% CI)	Anticipated absolute effect	
				Risk or mean with manual control	RD or MD with servo control
Survival (critical)	450 (1 RCT)[256]	Moderate	1.05 (0.99–1.11)	884 per 1000	44 more infants survived per 1000 (9 fewer to 97 more)
Normothermia on admission (important)	450 (1 RCT)[256]	Moderate	0.94 (0.75–1.17)	422 per 1000	25 fewer normothermic infants per 1000 (106 fewer to 72 more)
Mean body temperature (important)	450 (1 RCT)[256]	Moderate	Not applicable	36.5°C	MD 0.2°C lower (0.33°C lower to 0.07°C lower)
Hypothermia or cold stress	450 (1 RCT)[256]	Moderate	1.20 (1.01–1.42)	498 per 1000	100 more hypothermic or cold-stressed infants per

					1000 (5 more to 209 more), NNTH 2 infants

GRADE indicates Grading of Recommendations, Assessment, Development and Evaluation; MD, mean difference; NNTH, number needed to treat to harm; RCT, randomized controlled trial; RD, risk difference; and RR, risk ratio.

For the following comparisons, or for any combination of these interventions, the systematic review found no RCTs or evaluable observational studies:

- Comparison 7: Early monitoring of temperature versus first measurement on admission
- Comparison 8: Warm bags of fluid versus no warm bags of fluid
- Comparison 9: Swaddling versus no swaddling

For *Comparison 10: Skin-to-skin care versus no skin-to-skin care*, only 2 small RCTs were identified, and they reported only secondary outcomes.[257,258] Therefore, an evidence-to-decision table and treatment recommendations were not developed. However, good evidence for the benefits of skin-to-skin care for maintaining normal temperature immediately after birth in late preterm and term infants[259] and for maintaining subsequent normal temperature when used soon after birth for low- and very low–birth-weight infants in low- and middle-income countries was noted.[260]

Prior Treatment Recommendations (2015)

Among newly born preterm infants of less than 32 weeks of gestation under radiant warmers in the hospital delivery room, we suggest using a combination of interventions, which may include environmental temperature 23°C to 25°C, warm blankets, plastic wrapping without

drying, cap, and thermal mattress to reduce hypothermia (temperature <36.0°C) on admission to NICU (weak recommendation, very low–quality evidence).

We suggest that hyperthermia (>38.0°C) should be avoided because of the potential associated risks (weak recommendation, very low-quality evidence).

2023 Treatment Recommendations

In preterm infants (<34 weeks' gestation), as for late preterm and term infants (≥34 weeks' gestation), we suggest the use of room temperatures of ≥23°C compared with 20°C at birth in order to maintain normal temperature (weak recommendation, very low–certainty evidence).

In preterm infants (<34 weeks' gestation) immediately after birth, where hypothermia on admission is identified as a problem, it is reasonable to consider the addition of a thermal mattress, but there is a risk of hyperthermia (conditional recommendation, low-certainty evidence).

In preterm infants (<34 weeks' gestation) immediately after birth, we recommend the use of a plastic bag or wrap to maintain normal temperature (strong recommendation, moderate-certainty evidence).

Temperature should be carefully monitored and managed to prevent hyperthermia (good practice statement).

In preterm infants (<34 weeks' gestation) immediately after birth, we suggest the use of a head covering to maintain normal temperature (strong recommendation, moderate-certainty evidence).

In preterm infants (<34 weeks' gestation) immediately after birth, we suggest heated and humidified gases for respiratory support in the delivery room can be used where audit shows that admission hypothermia is a problem and resources allow (conditional recommendation, very low–certainty evidence).

In preterm infants (<34 weeks' gestation) immediately after birth, there is insufficient published evidence to suggest for or against the use of a radiant warmer in servo-controlled mode compared with manual mode for maintaining normal temperature.

In preterm infants (<34 weeks' gestation), there is insufficient published evidence to suggest for or against the use of skin-to-skin care immediately after birth. Skin-to-skin care may be helpful for maintaining normal temperature when few other effective measures are available (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website, and the evidence-to-decision table is provided in Appendix X.[223] Key discussion points included the following:

- For ambient temperature, some of the evidence was indirect from a study that included late preterm and term infants.[248] The safe upper limit of room temperature was not identified, and it may also be affected by ambient humidity.
- For plastic bags or wraps, which have been recommended by ILCOR since 2010,[261] the evidence of benefit for survival is now of high certainty and their use is considered standard of care in many neonatal services. They were considered feasible to use in low and high resource settings, including for out-of-hospital births.

- For head coverings, the only evidence from an RCT related to use of a plastic cap. Evidence from an observational study[219] as well as indirect evidence from studies of late preterm and term infants suggests that caps made of cloth are also likely effective.[259]
- For thermal mattresses, safety warnings exist for risk of hyperthermia and skin burns. Nevertheless, the task force concluded that thermal mattresses can be used with care, primarily when other methods to maintain normal temperature are unavailable or insufficient.
- Larger studies reporting short- and longer-term outcomes are needed to determine the role of heated and humidified gases for newborn resuscitation. Although their use for assisted ventilation is regarded as routine during subsequent neonatal intensive care, providing them for every birth at <34 weeks' gestation is likely to be unaffordable in many settings. A conditional recommendation was therefore developed.
- A common theme across comparisons was that each study examined the relevant intervention in the context of multiple cointerventions that may have impacted the reported effect size. Indeed, it is likely that a bundle of interventions operating through different mechanisms is needed for most preterm infants. However, the review did not identify sufficient evidence for any specific bundle. The design of such bundles should be based on the certainty of evidence for each intervention in addition to the availability of resources and local environmental considerations.
- The risk of harm from hyperthermia is likely to be higher when multiple interventions are used concurrently. Early measurement of temperature may detect when additional measures are needed for individual infants, and regular audit is needed to ensure that strategies achieve maintenance of normal temperature for most infants.

Task Force Knowledge Gaps

- Whether specific bundles of interventions are beneficial to maintain normal temperature, compared with other specific bundles
- How ambient temperature and humidity impact the effectiveness of any means to maintain normal temperature
- Cost-effectiveness of any of the interventions studied
- The optimal set temperatures for operating theatre and other delivery room settings
- The role of thermal mattresses for births in prehospital settings when other devices and methods for maintaining normal temperature are unavailable
- The risks and benefits of using head coverings composed of different materials
- Whether use of heated and humidified gases during resuscitation reduces lung injury or severe intraventricular hemorrhage in studies that meet the optimal information size for this outcome, and if so, what the mechanism is
- The role of servo-control in maintaining normal temperature in preterm infants requiring prolonged resuscitation
- Whether servo-controlled devices could be adapted for use during deferred cord clamping
- Whether position of the temperature sensor probe (eg, rectal versus various locations on the skin) affects outcomes
- Which other interventions to maintain normal temperature are effective (and can be safely adapted) for use during skin-to-skin care

Heart Rate Monitoring: Diagnostic Characteristics (SysRev)

Rationale for Review

Heart rate (HR) is considered one of the most important indicators of an infant's condition at birth. Limitations of assessing HR by palpation of pulses or by pulse oximeter were identified in a 2015 ILCOR systematic review, which found that electrocardiography (ECG) was faster and more accurate.[218] A 2020 evidence update found studies using newer devices and methods.[262] A 2022 ILCOR SysRev found that there was little evidence to suggest improvement in critical and important clinical outcomes with use of ECG compared with pulse oximetry.[59] Nevertheless, HR influences critical decisions about resuscitation at birth, so a systematic review was conducted to assess the diagnostic characteristics of various devices and methods for measuring HR in the first minutes after birth (PROSPERO Registration CRD 42021283364). See the ILCOR website for the full online CoSTR.[263]

PICOST

- Population: Newborn infants in the delivery room
- Intervention: Use of auscultation, palpation, pulse oximetry, Doppler device, digital stethoscope, photoplethysmography, video plethysmography, dry electrode technology, or any other newer modalities
- Comparators: ECG or between method comparisons
- Outcomes:
    - Important: Time to first HR assessment from the device placement, time to first HR assessment from birth, and accuracy of HR assessment

For the purposes of this systematic review, ECG HR was considered the gold standard. Accuracy of HR assessment by other methods was examined using the following:

1. Pooled Bland-Altman analysis[264-268] to estimate bias, a measure of accuracy, and the limits of agreement (LoA), a measure of precision. For the purposes of the review, agreement within ± 10 beats per minute (bpm) was considered acceptable.
2. Pooled sensitivity and specificity analysis to identify ECG HR <100 bpm and ECG HR <60 bpm

   Further detail about methods is included in the full online CoSTR.[263]

- Study designs: RCTs and nonrandomized studies (nonrandomized controlled trials, interrupted time series, controlled before-and-after studies, and cohort studies) were eligible for inclusion.
- Time frame: All years and all languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to August 5, 2022.

Consensus on Science

Comparison 1: Pulse Oximeter Versus ECG

The systematic review identified 3 RCTs[269-271] including 187 infants and 11 cohort studies[272-282] including 490 infants. Data relating to the key outcomes for the comparison of pulse oximeter versus ECG are summarized in Table 24. Additional outcomes are included in the full online CoSTR.[263]

Table 24. Pulse Oximetry Compared With ECG for Measuring HR at Birth—Diagnostic Characteristics

Outcomes	Participants (studies)	Certainty of the evidence (GRADE)	Pooled median difference or bias	MD (95% CI) or LoA (95% CI)
Time to first HR from device placement	136 (2 RCTs)[270,271]	Very low	12 s slower	38 s slower to 13 s faster
	323 (6 observational studies)[272,274,277,278,280,282]	Low	57 s slower	101 s slower to 13 s slower
Time to first HR from birth	87 (2 RCTs)[269,271]	Low	6 s slower	23 s slower to 10 s faster
	334 (6 observational studies) [272,273,275,281-283]	Low	52 s slower	94 s slower to 9 s slower
Accuracy of HR assessment	216 infants (1 RCT, 4 observational studies, 28 211 observations)[269,275,276,279,282]	Moderate	HR_{PO} – HR_{ECG}: –1.2 bpm	LoA: –17.9 to 15.5 bpm (95% CI, –32.8 to 30.4)

Accuracy of HR assessment (sensitivity and specificity of pulse oximetry for HR <100 bpm)	124 (3 studies)[269,277,279] 8342 observations	Very low	Sensitivity 0.83 (95% CI, 0.76 to 0.88) Specificity 0.97 (95% CI, 0.93 to 0.94)

ECG indicates electrocardiography; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; HR, heart rate; HR_{ECG}, heart rate measured using ECG; HR_{PO}, heart rate measured using pulse oximetry; LoA, limits of agreement; and RCT, randomized controlled trial.

Comparison 2: Auscultation Compared With ECG

The systematic review identified 5 observational studies including 171 infants.[273,283-286] Data relating to the key outcomes for the comparison of auscultation versus ECG are summarized in Table 25. Additional outcomes are included in the full online CoSTR.[263]

Table 25. Auscultation Compared With ECG for Measuring HR at Birth—Diagnostic Characteristics

Outcomes	Participants (studies)	Certainty of the evidence (GRADE)	Pooled median difference or bias	95% CI or LoA (95% CI)
Time for first HR from device placement	105 (3 observational studies)[273,285,286]	Moderate	4 s faster	10 s faster to 2 s slower
Time for first HR from birth	70 (3 observational studies)[273,285,286]	Low	24 s faster	45 s faster to 2 s faster

Accuracy of HR assessment	71 (3 observational studies)[283,285,286]	Low	HR_{aus} – HR_{ECG}: –9.9 bpm	LoA: –32 to 12 bpm (95% CI, –217, 198)

ECG indicates electrocardiography; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; HR, heart rate; HR_{aus}, heart rate measured using auscultation; HR_{ECG}, heart rate measured using ECG; and LoA, limits of agreement.

Comparison 3: Palpation Versus ECG

The systematic review identified 2 observational studies including 86 infants.[283,284] Data relating to the key outcomes for the comparison of palpation with ECG are summarized in Table 26 Additional outcomes are included in the full online CoSTR.[263]

Table 26. Palpation Compared With ECG for Measuring HR at Birth—Diagnostic Characteristics

Outcomes	Participants (studies)	Certainty of the evidence (GRADE)	Mean ± SD	MD ± SEM
Accuracy of HR assessment	21 (1 observational study)[283]	Very low	HR_{palp} 147 ± 19 bpm versus HR_{ECG} 168 ± 22 bpm	–21 ± 21 bpm

bpm indicates beats per minute; ECG, electrocardiography; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; HR, heart rate; HR_{ECG}, heart rate measured using ECG; HR_{palp}, heart rate measured using palpation; MD, mean difference; SD, standard deviation; and SEM, standard error of the mean.

Some studies were also found for each of the following comparisons, and the evidence is included in the full online CoSTR.[263] None of the evidence was considered sufficient to develop treatment recommendations:

- Comparison 4: Palpation compared with auscultation
- Comparison 5: Digital stethoscope compared with ECG
- Comparison 6: Doppler ultrasound compared with ECG
- Comparison 7: Dry electrodes incorporated into a belt compared with (conventional 3-lead) ECG

Prior Treatment Recommendations

2015: In babies requiring resuscitation, we suggest that ECG can be used to provide a rapid and accurate estimation of heart rate (weak recommendation, very low–quality evidence).

2022: Where resources permit, we suggest that the use of ECG for heart rate assessment of a newborn infant requiring resuscitation in the delivery room is reasonable (weak recommendation, low-certainty evidence).

Where ECG is not available, auscultation with pulse oximetry is a reasonable alternative for heart rate assessment, but the limitations of these modalities should be kept in mind (weak recommendation, low-certainty evidence).

There is insufficient evidence to make a treatment recommendation regarding use of digital stethoscope, audible or visible Doppler ultrasound, dry electrode technology, reflectance-mode green light photoplethysmography, or transcutaneous electromyography of the diaphragm for heart rate assessment of a newborn in the delivery room.

Auscultation with or without pulse oximetry should be used to confirm the heart rate when ECG is unavailable, not functioning, or when pulseless electrical activity is suspected (good practice statement).

2023 Treatment Recommendations

Where accurate heart rate estimation is needed for a newborn infant immediately after birth and resources permit, we suggest that the use of ECG is reasonable (conditional recommendation, low-certainty evidence).

Pulse oximetry and auscultation may be reasonable alternatives to ECG for heart rate assessment, but the limitations of these modalities should be kept in mind (conditional recommendation, low-certainty evidence).

There is insufficient evidence to make a treatment recommendation regarding use of any other device for heart rate assessment of a newborn infant immediately after birth.

Auscultation with or without pulse oximetry should be used to confirm the heart rate when ECG is unavailable, not functioning, or when pulseless electrical activity is suspected (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website,[263] and the evidence-to-decision table is provided in Appendix X. Key points of discussion include the following:

- The treatment recommendations reflect the results of both this review and the 2022 ILCOR systematic review of clinical outcomes of different methods of HR assessment.[59]

- The available data suggest that ECG provides a more rapid and accurate assessment of HR in the delivery room when compared with pulse oximetry, and more accurate assessment than palpation or auscultation, but the certainty of evidence ranges from moderate to very low.
- Most studies did not include the infants in whom rapid, accurate assessment of HR may be most important, eg, infants who were bradycardic, were requiring resuscitation, or were extremely premature. The companion systematic review which assessed clinical outcomes[59] found that it is unclear if rapidity, accuracy, and precision of HR estimation at birth results in clinically relevant differences in resuscitation interventions, resuscitation team performance, or clinical outcomes for newborn infants.
- Auscultation or pulse oximetry or both have been routinely used for HR assessment in newborns at birth. Where resources are limited, addition of another device may be impractical or unaffordable.

Task Force Knowledge Gaps

- More data on the characteristics of measurement of HR in the delivery room using devices such as digital stethoscope, Doppler ultrasound (audible or visible displays), reflectance-mode green light photoplethysmography, or transcutaneous electromyography of the diaphragm. Such studies should include evaluation of time to first HR assessment from birth and from device placement.
- Cost effectiveness of different modalities for HR assessment in the delivery room
- The impact of different HR assessment methods on resuscitation team performance, resuscitation interventions, and neonatal clinical outcomes
- Evidence as to whether different devices are better suited to different subgroups of infants (eg, by gestation or by anticipated need for advanced resuscitation)

Topic Title: Exhaled CO_2 Detection to Guide Noninvasive Ventilation (SysRev)

Rationale for Review

ILCOR has previously evaluated the use of CO_2 monitoring to confirm correct placement of tracheal tubes (colorimetric devices) and during invasive ventilation to improve CO_2 levels on admission to a neonatal unit, but these reviews did not include a GRADE evaluation.[261] CO_2 monitoring devices have also been systematically reviewed (as part of a review of several feedback devices) in newborn infants for detecting ROSC.[218] More recent studies have examined the use of CO_2 detection to guide noninvasive ventilation at birth, the focus of the current review. A SysRev was initiated from a priority list from the ILCOR NLS Task Force (PROSPERO Registration CRD42022344849).[287] See the ILCOR website for the full online CoSTR.[288]

PICOST

- Population: Newborn infants receiving intermittent positive-pressure ventilation (IPPV) by any noninvasive interface at birth
- Intervention: Use of exhaled CO2 monitor in addition to clinical assessment, pulse oximetry, and/or ECG
- Comparators: Clinical assessment, pulse oximetry, and/or ECG only
- Outcomes:
    - Critical: Survival
    - Important: Tracheal intubation in the delivery room, other resuscitation outcomes at birth, other major morbidities, and unexpected admission to special or intensive care unit in infants born at ≥34 weeks' gestation.

- Study designs: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, and cohort studies) were eligible for inclusion. Case series, case reports, animal studies, and unpublished studies (conference abstracts, trial protocols) were excluded.
- Time frame: All years and all languages were included as long as there was an English abstract. The literature search was updated to August 1, 2022.

Consensus on Science

The SysRev identified 23 studies that addressed the use of CO_2 monitoring during noninvasive IPPV. In only 8 of these (including 419 infants) were CO_2 detection devices or monitor displays visible to those performing the resuscitation.[289-296] The devices for positive-pressure ventilation varied (T-piece device, self-inflating bag, flow-inflating bag) but the interface in all studies was a face mask. None of the studies was designed to address the PICOST question, and differences in study design precluded any meta-analysis. The following summarizes the findings of a narrative review of these studies; further description is included in the full online CoSTR.[288]

Exhaled CO_2 Monitoring and Airway Obstruction

Two observational studies including 59 preterm infants described continuous use of a colorimetric CO_2 detection device during noninvasive IPPV and recorded that providers responded to its display with corrective actions.[289,291]

Exhaled CO_2 to Assess Lung Aeration

One RCT of sustained inflation including 162 infants[296] and 2 observational studies together including 95 infants[290,293] suggested that monitoring of exhaled CO_2 is feasible

(including while providing face mask IPPV during delayed umbilical cord clamping[290]) and a rise in exhaled CO_2 correlates with improvements in lung aeration.

Exhaled CO2 as a Predictor of Increase in HR in Initially Bradycardic Infants

One observational study including 41 bradycardic preterm infants concluded that a change in a colorimetric CO_2 detector device precedes a clinically significant increase in HR.[289] A second study including 7 infants found that an exhaled CO_2 level >15 mm Hg preceded a clinically significant increase in HR.[295]

Exhaled CO_2 and PCO_2 at NICU Admission

One RCT including 37 preterm infants born at <34 weeks' gestation compared a visible to a masked CO_2 monitor and found no difference in the proportion of infants with PCO_2 in the target range on NICU admission.[294] One RCT including 59 infants born at <32 weeks' gestation compared quantitative and qualitative CO_2 monitoring and found no differences in PCO_2 in the target range on NICU admission.[292]

Prior Treatment Recommendations

None

2023 Treatment Recommendations

There is insufficient evidence to suggest for or against the use of exhaled CO_2 to guide noninvasive IPPV with noninvasive interfaces, such as face masks, supraglottic airways, and nasal cannulae in infants immediately after birth.

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table for this topic can be found in Appendix X, and the full text of the evidence-to-decision highlights is on the ILCOR website.[288] Key discussion points included the following:

- There were no studies in infants receiving noninvasive IPPV in the delivery room that compared use of CO_2 monitoring (using quantitative or qualitative devices) with no device or a masked device that demonstrated improvement in any clinical outcome. The combined studies did suggest that both types of devices are feasible to use, that they may assist with detection of airway obstruction and other causes of inadequate lung aeration and ventilation, and that increases in exhaled CO_2 precede improvements in HR in bradycardic infants.
- Concerns about use of quantitative and qualitative exhaled CO_2 monitoring devices to improve noninvasive IPPV include the potential for misinterpretation; it may not be possible to differentiate inadequate tidal ventilation from very low pulmonary blood flow as a cause for low exhaled CO_2, and dead space ventilation (physiologic or equipment-related) could lead to overestimation of exhaled CO_2.
- The reliability of colorimetric CO_2 devices may be affected by contamination with gastric contents or medications.[289,297]

Task Force Knowledge Gaps

- The efficacy and effectiveness of different devices for CO_2 monitoring to guide noninvasive IPPV via face mask or supraglottic airway device in newborns immediately after birth for infants of various birthweights in a variety of clinical settings
- The optimal range for exhaled CO_2 in each minute after birth

- The effect of gastric reflux, other secretions, blood, meconium, or medications on the reliability of colorimetric CO_2 detectors
- The potential for CO_2 monitoring to distract or bias providers
- Cost effectiveness of CO_2 monitoring

Heart Rate to Initiate Chest Compressions (ScopRev)

Rationale for Review

The recommended HR threshold for initiating chest compressions during resuscitation at birth has been <60 bpm since 1999, while at the same time the optimal HR threshold for initiating chest compressions has been identified as a gap in knowledge.[298] A ScopRev was initiated from a priority list from the ILCOR NLS Task Force.[299] See the ILCOR website for the full online CoSTR.[300]

PICOST

- Population: Newborn infants immediately after birth who are being resuscitated with ventilation and who have a slow HR
- Intervention: Starting cardiac compressions at other HR thresholds
- Comparators: Starting cardiac compressions when the HR is <60 bpm.
- Outcomes:
    - Critical: survival, neurological outcomes
    - Important: Any other reported short- or long-term outcomes, including time to ROSC
- Study designs: RCTs, nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies), and case series were eligible for inclusion. Manikin,

computer model, and animal studies were eligible for inclusion. Conference abstracts and unpublished studies (eg, trial protocols) were excluded.

- Time frame: All years and all languages were included as long as there was an English abstract. The literature search was updated to November 22, 2021.

Summary of Evidence

No studies were found that examined different HR thresholds for initiating chest compressions in newborn infants immediately after birth. There is also very little evidence from animal studies.[301] Further description is included in the full online CoSTR.[300]

Task Force Insights

The HR threshold of <60 bpm was originally selected on the basis of expert opinion and a desire to simplify the resuscitation algorithm. The scoping review provided no data sufficient to alter the existing recommendation, but the optimal threshold and whether it differs for different subgroups of infants remain unknown.

Treatment Recommendations

ILCOR has not developed an evidence-based treatment recommendation on HR threshold to initiate chest compressions previously. However, ILCOR guidance since 1999 has been to initiate chest compressions if HR <60 bpm despite adequate assisted ventilation for 60 seconds.[298] There was insufficient evidence found in the scoping review to support a new systematic review or a different recommendation.

Supplemental Oxygen During Chest Compressions (ScopRev)

Rationale for Review

A 2015 ILCOR SysRev examined evidence for 100% O_2 as the ventilation gas during chest compressions compared with lower concentrations of O_2 and concluded that there were no

human data to inform this question.[218] Surveillance of resuscitation literature suggested that there may be more recent studies, including indirect evidence from animal models. A ScopRev was initiated from a priority list from the ILCOR NLS Task Force.[299] See the ILCOR website for the full online CoSTR.[302]

PICOST

- Population: Newborn infants immediately after birth who are receiving chest compressions
- Intervention: Any lower concentrations of O2
- Comparators: 100% O2 as the ventilation gas
- Outcomes:
    - Critical: Survival, neurological outcomes
    - Important: Any other reported short- or long-term outcomes, including time to ROSC
- Study designs: RCTs, nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies), and case series were eligible for inclusion. Manikin, computer model and animal studies were eligible for inclusion. Conference abstracts and unpublished studies (eg, trial protocols) were excluded.
- Time frame: All years and all languages were included as long as there was an English abstract. The literature search was updated to November 22, 2021.

Summary of Evidence

No human studies that compared any other oxygen concentration with 100% O_2 during chest compressions were identified. Six animal studies comparing 21% with 100% inspired O_2 concentrations during chest compressions after asphyxial cardiac arrest were identified. Overall,

they found no differences in time to ROSC, mortality, inflammation, or oxidative stress.[303-308] Further description is included in the full online CoSTR.[302]

Task Force Insights

The available evidence from animal studies suggests that resuscitation using 21% O_2 during chest compressions is feasible and results in similar short-term outcomes. However, the animal studies examined only asphyxia-induced asystole of brief duration in animals lacking other underlying pathological conditions, and there are no human infant data. The available evidence was insufficient to warrant a new systematic review or to suggest the need to alter the current treatment recommendation.

Treatment Recommendations

The 2015 good practice statement remains unchanged:

Despite animal evidence showing no advantage to the use of 100% oxygen, by the time resuscitation of a newborn infant has reached the stage of chest compressions, the steps of trying to achieve ROSC using effective ventilation with low-concentration oxygen should have been attempted. Thus, it would seem prudent to try increasing the supplementary oxygen concentration (good practice statement).[218]

Neonatal Chest Compression Technique (Other Techniques Versus 2-Thumb Technique) (ScopRev)

Rationale for Review

A 2015 ILCOR SysRev examined evidence for a 2-thumb technique compared with a 2-finger technique for neonatal chest compressions and recommended a 2-thumb technique based on very low–certainty evidence from nonrandomized studies and a single manikin study.[218] Surveillance of resuscitation literature identified more recent studies examining other techniques.

A ScopRev was initiated from a priority list from the ILCOR NLS Task Force and has been published.[299] See the ILCOR website for the full online CoSTR.[309]

PICOST

- Population: Newborn infants immediately after birth who are receiving chest compressions
- Intervention: Use of any other technique (2-finger or other) for chest compressions
- Comparator: 2-thumb technique for chest compressions
- Outcomes:
    - Critical: Survival, neurological outcomes
    - Important: Any other reported short- or long-term outcomes, including time to ROSC
- Study designs: RCTs, nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies), and case series were eligible for inclusion. Manikin, computer model, and animal studies were eligible for inclusion. Conference abstracts and unpublished studies (eg, trial protocols) were excluded.
- Time frame: All years and all languages were included as long as there was an English abstract. The literature search was updated to November 22, 2021.

Summary of Evidence

The current scoping review identified 29 randomized crossover manikin studies, 1 observational, and 1 randomized study comparing various finger/hand positions.[310-339]

The available data confirmed that the 2-thumb technique resulted in higher chest compression depth, lower fatigue, and higher proportion of correct hand placement when compared with the 2-finger-technique. No alternative finger and/or hand position techniques

resulted in overall better performance measures compared with the 2-thumb technique. Further description is included in the full online CoSTR.[309]

Task Force Insights

The information from the studies identified was considered insufficient to warrant a systematic review or to alter existing recommendations.

Treatment Recommendations

The 2015 treatment recommendation remains unchanged.

We suggest that chest compressions in newborn infants immediately after birth should be delivered by the 2-thumb, hands-encircling-the-chest method as the preferred option (weak recommendation, very low–quality evidence).

Compression-to-Ventilation Ratio for Neonatal CPR (ScopRev)

Rationale for Review

The 2015 CoSTR and a subsequent evidence update suggested continuing to use a 3:1 compression-to-ventilation ratio.[218,262] There was no evidence from human infants for this ratio and it was based on animal and manikin studies; however, the evidence update identified sufficient new animal and manikin studies as well as one small clinical trial to justify inclusion in the multifaceted scoping review of questions related to chest compressions. A ScopRev was initiated from a priority list from the ILCOR NLS Task Force.[299] See the ILCOR website for the full online CoSTR.[340]

PICOST

- Population: Newborn infants immediately after birth who are receiving chest compressions
- Intervention: Any other compression-to-ventilation ratio (5:1, 9:3, 15:2, asynchronous, etc)

- Comparators: 3:1 compression-to-ventilation ratio
- Outcomes:
    - Critical: Survival, neurological outcomes
    - Important: Any other reported short- or long-term outcomes, including time to ROSC hemodynamic parameters, tissue oxygenation, lung or brain inflammatory markers, compressor fatigue)
- Study designs: RCTs, nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies), and case series were eligible for inclusion. Manikin, computer model, and animal studies were eligible for inclusion. Conference abstracts and unpublished studies (eg, trial protocols) were excluded.
- Time frame: All years and all languages were included as long as there was an English abstract. The literature search was updated to November 22, 2021.

Summary of Evidence

The scoping review identified 23 studies examining different compression-to-ventilation ratios, continuous chest compressions with asynchronous ventilation, or chest compressions with sustained inflation.[303,304,306,341-360] These studies are summarized in Table 27 and further details are available in the full online CoSTR.[340]

Table 27. Chest Compression-to-Ventilation Ratio for Neonatal Resuscitation

Compression-to-ventilation ratio	2 RCTs, manikin studies[345,358]	3:1 versus 5:1 versus 15:2 ratios;3:1 was associated with more consistent CC depth and preferred by rescuers.[345] No differences in compressor fatigue between 3:1, 5:1, 10:2, 15:2 ratios, but 3:1 rated more difficult. [358]

	5 RCTs, piglet studies[303,304,306,351,356]	No differences in time to ROSC, survival, biomarkers of brain or organ injury between various ratios including 3:1, 9:3, 15:2, 2:1, 4:1
Continuous CC with asynchronous ventilation	5 RCTs, manikin studies[342-344,346,357]	Variable results but some studies found greater fatigue and lower CC depth with continuous CC with asynchronous ventilation versus 3:1 compression-to-ventilation ratio.
	6 RCTs, piglets (5) or lambs (1)[341,348,349,352,354,360]	For time to ROSC and for survival, 1 RCT found improvements with continuous CC with asynchronous ventilation versus 3:1 compression-to-ventilation ratio. One RCT found improved physiological measures with CC with asynchronous ventilation versus 3:1 compression-to-ventilation ratio.
Chest compression with sustained inflation	4 RCTs, piglets (3) or lambs (1)[347,350,359]	Faster time to ROSC but similar survival with CC combined with repeated 20 s sustained inflations versus 3:1 compression-to-ventilation ratio
	1 RCT, human infants[353]	Faster time to ROSC with CC combined with repeated 20 s sustained inflations versus 3:1 compression-to-ventilation ratio

CC indicates chest compressions; RCT, randomized controlled trial; and ROSC, return of spontaneous circulation.

Task Force Insights

The information from the studies identified was considered insufficient to alter the existing recommendation. The task force noted that a larger trial of chest compressions with sustained inflation is underway (ClinicalTrials.gov Identifier: NCT02858583).

Treatment Recommendations

The 2015 treatment recommendation remains unchanged.

We suggest continued use of a 3:1 compression-to-ventilation ratio for CPR in newborn infants immediately after birth (weak recommendation, very low–certainty evidence).

Use of Feedback CPR Devices for Neonatal Cardiac Arrest (ScopRev)

Rationale for Review

The use of feedback devices such as end-tidal carbon dioxide ($ETCO_2$) monitors, pulse oximeters, or automated compression feedback devices was considered in an ILCOR 2015 systematic review.[218] Surveillance of resuscitation literature suggested that there may be more recent studies, including indirect evidence from animal models. A ScopRev was initiated from a priority list from the ILCOR NLS Task Force.[299] See the ILCOR website for the full online CoSTR.[361]

PICOST

- Population: Newborn infants immediately after birth who are receiving chest compressions
- Intervention: Use of any feedback devices such as ETCO2 monitors, pulse oximeters, or automated compression feedback devices
- Comparators: Clinical assessments of compression efficacy
- Outcomes:
    - Critical: Survival and neurologic outcomes
    - Important: Hands-off time, time to ROSC, perfusion
- Study designs: RCTs, nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies), and case series were eligible for inclusion. Manikin,

computer model, and animal studies were eligible for inclusion. Conference abstracts and unpublished studies (eg, trial protocols) were excluded.

- Time frame: All years and all languages were included as long as there was an English abstract. The literature search was updated to November 22, 2021.

Summary of Evidence

The scoping review identified 18 studies that addressed chest compression feedback devices: 12 manikin studies,[362-372] 4 animal studies,[373-376] and 2 human infant studies.[377,378] Twelve of the studies used randomized allocation to study arms. Most of the manikin studies assessed musical, auditory, tactile, or other signals to improve the cadence of chest compressions, but one tested a decision support tool and other devices that detected chest compression depth and rate. All reported improvements in chest compression rate, consistency, depth, or other measures of quality in the simulation setting, but none reported translation of the device, or improvement in skills as a result of using the device, into improvements in performance or infant outcomes in clinical settings. The animal studies all tested the role of $ETCO_2$ in improving resuscitation outcomes or in predicting ROSC. No differences were found in ROSC or survival from using $ETCO_2$ to guide chest compressions.[373-376] One of the 2 retrospective human infant studies assessed a practice change to increase depth of chest compressions,[377] and one evaluated $ETCO_2$ as a predictor of ROSC.[378] Details are available in the full online CoSTRs.[361]

Task Force Insights

The body of available evidence does not justify an ILCOR systematic review at this time, because no studies assessed whether feedback devices result in improvements in resuscitation practice or outcomes in human infants. Further research is justified, including assessing whether

improvements measured in simulation settings result in improvement in clinical performance or outcomes and to assess the role of capnography and other types of clinical measurements in improving outcomes in infants who receive chest compressions.

Treatment Recommendations

The 2015 treatment recommendation remains unchanged.

In asystolic/bradycardic newborn infants, we suggest against the routine reliance on any single feedback device such as $ETCO_2$ monitors or pulse oximeters for detection of ROSC until more evidence becomes available (weak recommendation, very low–certainty evidence).

EDUCATION, IMPLEMENTATION, AND TEAMS

Family Presence in Adult Resuscitation (SysRev)

Rationale for Review

Low survival rates suggest that cardiac arrest is a pivotal event during which family members may wish to be present during resuscitative efforts.[379] Family presence has been advocated to improve coping and grieving outcomes for families, reduce litigation, and improve resuscitation team behaviors.[379-381] Conversely, concerns have been raised about the distress that family presence during resuscitation may cause families or health care professionals, and its impact on team performance.[379,382]

In 2021, an ILCOR SysRev of family presence during neonatal and pediatric resuscitation was conducted.[383] The current systematic review was undertaken on behalf of the Education, Implementation, and Teams (EIT), BLS, and ALS Task Forces to address this question in the adult population (PROSPERO registration CRD4202124238400).[384] The full online CoSTR can be found on the ILCOR website.[385]

PICOST

- Population: Adults requiring resuscitation for cardiac arrest in any setting
- Intervention: Family presence during resuscitation
- Comparators: Family not present during resuscitation
- Outcomes:
    - Patient outcomes (short- and long-term): ROSC, survival (to hospital admission, hospital discharge/30 days, 3 months, 6 months, 1 year), survival with good neurological outcomes (at same time points), depression or anxiety

  - Family (or significant other) outcomes (short- and long-term): Posttraumatic stress disorder, coping, perception of the resuscitation, depression or anxiety amongst family members, complicated grief syndrome
  - Health care professional outcomes: Perception of the resuscitation, performance, perceived futility in some circumstances, psychological stress including projection to provider's own family
- Study designs: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were included, and unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: All years and all languages were included as long as there was an English abstract. The literature search was updated to May 10, 2022.

Consensus on Science

The 31 studies[386-416] included were highly heterogenous, comprising a range of study designs with just over a half of all the studies having a qualitative study design and only 2 being RCTs (Table 28).[386,387] Evidence was very low certainty because of potential confounding and heterogeneity or a lack of information regarding patient, family, provider, and cardiac arrest setting characteristics. Evidence was also downgraded for inconsistency in the reporting of results, indirectness in terms of population, study design, and outcomes of interest and imprecision.

Overall, there was no evidence of harm for patients or families from family presence across the studies. However, there was variability in practices and outcomes of family presence during resuscitation and, therefore, no meta-analysis was possible.

Table 28 Family Presence During Adult Resuscitation, Study Characteristics

Study designs	Investigated environment
31 studies included[386-416]	24 studies examined in-hospital resuscitation[386,388,389,391-401,403,405,406,408,410-415]
2 randomized controlled trials[386,387]	11 studies in the emergency department[386,392-395,401,408,410-412,416]
16 observational studies[386-403]	5 in the intensive care unit[388,397,408,410,415]
12 qualitative studies[404-412,414-416]	5 in critical care areas[396,405,411,412,414]
1 mixed-methods study[413]	6 studies in all hospital areas[389,398,403,408,410,413]
	3 studies did not report the specific in-hospital context[391,399,400]
	8 studies reported more than 1 in-hospital location[396,403,408,410-413,416]
	5 studies reported out-of-hospital resuscitation[387,390,402,404,409]
	1 study reported on both in- and out-of-hospital resuscitation[416]
	1 study did not clearly report the context[407]

Supplemental table EIT-S1 summarizes the outcomes on (1) patients, (2) family, and (3) health care professionals, when family members are present during resuscitation of adult patients after cardiac arrest.

1. Patient outcomes were reported in 12 studies.[387-391,398,403,405,406,410,413,415] Four studies compared family presence with no family presence.[387-389,403] Only 1 study found higher rates of ROSC and survival to discharge when no family members were present during resuscitation.[388]

2. Family outcomes were reported in 15 studies[386,387,390-394,402,404-407,410,413,415] investigating depression, anxiety, posttraumatic stress disorder, and experience of witnessing the resuscitation of a family member. While 3 studies reported increased rates of depression[390] or posttraumatic stress disorder,[392,402] little evidence was found that witnessing a family member's resuscitation caused one of these mental health conditions.
3. Both positive and negative outcomes were reported when witnessing a family member's resuscitation. Many family members would witness resuscitation again,[393,394] as it enabled them to better manage their grief.[393] Reported negative outcomes included managing emotional responses,[406] interfering with resuscitation,[406] the dehumanizing nature of resuscitation,[404] and the long,[394] brutal, dehumanizing, and excessive nature of the resuscitation process.[404]
4. Health care professional outcomes were measured in 20 studies.[386,387,393-401,403,408-414,416] Varying experience with family witnessing resuscitation was evident, and few positive or negative outcomes were reported. Providers were generally supportive of family presence during resuscitation[394,413] and felt their function was not impaired by family presence.[393,394] However, across the studies, some apprehension toward family presence was noted in providers, and the need for family support personnel, training, and unit-based policies or protocols was identified.[395,398-400,409,411]

Prior Treatment Recommendations (year written)

New; no prior treatment recommendation

2023 Treatment Recommendations

- We suggest that family members be provided with the option to be present during in-hospital and out-of-hospital adult resuscitation from cardiac arrest (weak recommendation; very low–

certainty evidence) acknowledging that providers are often not able to control this in out-of-hospital settings.

- Policies or protocols about family presence during resuscitation should be developed to guide and support health care professional decision-making (good practice statement).
- When implementing family presence procedures, health care professionals should receive education about family presence during adult cardiac arrest resuscitation, including how to manage these stressful situations, family distress, and their own responses to these situations (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website.[385]

In making these recommendations, the EIT, BLS, and ALS Task Forces considered the following:

- Despite the variability in practices and outcomes of family presence during resuscitation, no evidence of harm for patients or families from family presence across the studies was found. Given the high desire for this choice and the potential for positive outcomes for family members, patients, and health care providers, it was our opinion that family members should be given a choice to be present during resuscitation.
- Some family members may have cultural, religious, or other sociological factors that influence their attitudes and behaviors regarding family presence during adult resuscitation. As none of the included studies investigated these factors, we have not made a formal recommendation about this; however, it will be important for resuscitation councils to adapt their recommendations accordingly.

- Attitudes and experiences of family presence during resuscitation may vary significantly by practice setting (out-of-hospital versus in-hospital).
- Specific characteristics of cardiac arrests or patients (ie, younger versus older adult, precipitating illness or condition) were not reported in the included studies. The overall findings on patient, family, and provider outcomes were considered in the absence of this information.
- There were only 2 RCTs, both with methodological limitations,[386,387] comprising between 100 and 630 participants. We acknowledge the difficulty of an RCT in this setting. It would be unethical to stop a family member from being present or absent in these circumstances.
- The task force considered the reported negative psychological and family management experiences of providers but thought implementation of provider education and unit-based policies and protocols would address many of these issues.
- Provider education and unit-based policies or protocols were not directly examined in any of the studies. However, 2 good practice statements were derived from included studies considering the absence of any evidence of harm.
- No evidence was found on factors that may contribute to detrimental mental health outcomes after family-witnessed resuscitation for family members or health care professionals. Education and/or structured follow-up regarding possible long-term effects of witnessed resuscitation on these cohorts is needed.

Task Force Knowledge Gaps

- The impact of specific factors on patient, family, or providers, such as patient characteristics, precipitating events or illness resulting in cardiac arrest, family members as CPR bystanders, or the resuscitation setting

- The cultural, religious, or other sociological or health equity factors influencing attitudes and behaviors regarding family presence during adult resuscitation
- The impact of unit-based policies and protocols or family support personnel on patient, family, and provider outcomes with family presence during resuscitation
- Cost-effectiveness of resourcing the resuscitation setting to accommodate family presence and the impact of these resources on health care professionals

Stepwise Approach to Skills Teaching in Resuscitation (SysRev)

Rationale for Review

The instructional approach for skills teaching is likely to impact later performance. The Peyton 4-step approach for skills teaching[417] has been implemented across standard course formats of the European Resuscitation Council,[418] the United Kingdom Resuscitation Council, the Australian Resuscitation Council, and various national resuscitation councils in Europe. Walker and Peyton defined the 4 steps as a sequence of (a) "demonstration" of the skill, at normal pace, without commenting; (b) "deconstruction" of the skill, by demonstrating in slow motion, with detailed explanations for the learner with a special focus on critical steps; (c) "comprehension" by the learner who explains each step while talking the teacher through the skill; and (d) "performance and practice" of the skill by the learner until performance is sufficient.[37] The superiority of the Peyton 4-step approach over other methods of skills teaching (eg, using fewer than 4 steps, substituting single steps by video,[419] no sequencing)[420] is unclear. A systematic review was therefore undertaken(PROSPERO registration CRD42023377398), and the full online CoSTR can be found on the ILCOR website.[421]

PICOST

- Population: Adults and children undertaking skills training related to resuscitation and first aid in any educational setting
- Intervention: Approaches to skills teaching that are not the Peyton 4-step approach. This includes approaches without distinct stages, or modified Peyton 4-step approaches with more or fewer than 4 steps, or with delivering 1 or more steps by alternative methods (eg, video).
- Comparators*:* The Peyton 4-step approach[417] for skills teaching, as most studies used Peyton's 4 steps as the standard and compared alternative approaches against it
- Outcomes: Improved educational outcomes: Skill performance after end of course; skill performance at end of course; participants' confidence to perform the skill on patients; participants' preference of teaching method
    - Patient outcomes: Skills performed appropriately on real patient after the course
    - Additional outcomes: Teachers' preference of teaching method; side effects of teaching
- Study designs:
    - Included studies: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies, published conference abstracts, and case series where n ≥5)
    - Excluded studies: Unpublished results (eg, trial protocols), commentary, editorial, reviews
- Time frame: Publications from all years and all languages as long as there was an English abstract. The literature search was updated to November 25, 2022.

Consensus on Science

This systematic review included 16 studies, of which 13 were RCTs[422-434] and 3 were non-RCTs.[435-437] All studies showed a high degree of heterogeneity with respect to skills and populations taught, skill complexity, student-to-instructor ratios, and alternatives that were tested against the classic 4-step approach. Therefore, no meta-analyses could be performed.

No study was found for the clinical outcome of skills performed appropriately on a real patient after the course.

We identified 5 studies for the critical educational outcome of skill performance after 3 or more months (Table 29).[424,427,431,432,436] Four studies showed no difference,[424,431,432,436] and 1 found superior results using a 4-step approach.[427] However, in this study, the 4-step approach was 1 element of a bundle of "best practice" strategies.

Table 29. Summary of Evidence for Skill Performance After 3 or More Months

Study	Study type	Skill taught/primary outcome	Population taught/n	Type of alternative	Overall results	Certainty of evidence
Bomholt (2019)[424]	RCT	BLS-AED/BLS-AED scenario test at 3 months	Laypersons/129	2-step skills teaching	Neutral	Low[a]
Herrmann-Werner (2013)[427]	RCT	Intravenous cannulation; insertion of nasogastric tube/performance scores at 6 months	First-year medical students/94	"Traditional teaching" (2 steps)	4-step approach[b] superior	High
Münster (2016)[431]	RCT	BLS/chest compression	First- and second-year	3 steps (step 3	Neutral	Low[d]

		quality[c] at 5–6 months	medical students/134	omitted) and 2 steps (Peyton steps 2 and 4)		
Nourkami-Tutdibi (2020)[432]	RCT	Neonatal life support/Megacode scenario score at 6 months	Fourth- and fifth-year medical students/94	Modified 4-step approach[e]	Neutral	Very low[f]
Sopka (2012)[436]	Non-RCT	BLS (chest compression only)/chest compression quality at 6 months	First-year medical students/220	Modified 4-step approach[g]	Neutral	Very low[h]

[a]Due to randomization and missing outcome data.
[b]"Best practice skills lab teaching," including "feedback," "manikin practice," and the 4-step approach.
[c]Chest compression rate, depth, and chest compression fraction.
[d]Due to randomization.
[e]Step 3 including additional functional verbalization by the student.
[f]Due to high dropout rate.
[g]Podcast for steps 1 and 2.
[h]Due to "confounding" and "deviations from the intended intervention."
AED indicates automated external defibrillator; BLS, basic life support; and RCT, randomized controlled trial.

For the important educational outcome of skill performance from end-of-course up to 3 months, (Table 30) we found 13 studies.[422,423,425,426,428-430,432-437] Eleven studies did not find differences for the primary outcomes,[422,423,426,428-430,432-436] but 2 studies found an advantage of 4 steps over 2 steps.[425,437]

Table 30. Summary of Evidence for Skill Performance at End of Course

Study	Study type	Skill taught/primary outcome	Population taught/n	Type of alternative	Overall results	Certainty of evidence
Archer (2015)[422]	RCT	Manual defibrillation/composite score for defibrillation skills at end of course and at 2 months	First-year medical students/294	Traditional 2-step and 5-step approaches	Neutral[a]	Very low[b]
Bjornshave (2018)[423]	RCT	Single-rescuer BLS plus AED/pass rate at end of course	Laypersons/142	"Traditional" 2-step approach	Neutral	High
Frangez (2017)[425]	RCT	BLS (without AED)/BLS scenario test[c] at end of course	First-year medical students/266	"Conventional" 2-step approach	4-step approach superior[d]	High
Greif (2010)[426]	RCT	Needle cricothyroidotomy/time needed to successful ventilation at end of course	Fourth-year medical students/128	3 alternatives: traditional 2 steps; step 2 omitted; step 3 omitted	Neutral (for all 4 approaches)	Low[e]
Jenko (2012)[428]	RCT	Chest compressions/BLS scenario test[c] at end of course	First-year medical students/126	2-step approach	Neutral	Concerns – Low[f]

Krautter (2011)[429]	RCT	Inserting a nasogastric tube/performing steps of the procedure at end of course	Second- and third-year medical students/34	2-step approach	Neutral[g]	High
Lapucci (2018)[430]	RCT	Chest compressions and ventilation	Nursing students/60	2-step approach	Neutral	Low[h]
Nourkami-Tutdibi (2020)[432]	RCT	Neonatal life support/Megacode scenario at 4 days after intervention	Advanced medical students/94	Modified 4 steps (step 3)[i]	Neutral	Low[j]
Orde (2010)[433]	RCT	Laryngeal mask insertion/proportion of participants achieving ventilation <30 seconds	Critical care nurses, ICU nursing students, final-year medical students/120	2-step approach	Neutral	Low[k]
Schauwin-hold (2022)[435]	Non-RCT	BLS/chest compression rate and depth at end of course	First-year medical, dentistry, and physiotherapy students/346	3 steps with TSP	Neutral (noninferiority of the TSP group)	Very low[l]
Schwerdt-feger (2014)[434]	RCT	Advanced trauma life support/median	Advanced medical students/256	Modified 4-step approach	Neutral[m]	Low[n]

		OSCE score at end of course		(steps 1 and 2 by video)		
Sopka (2012)[436]	Non-RCT	BLS (chest compression only)/chest compression quality at end of course	First-year medical students/220	Modified 4-step approach[o]	Neutral	Low[p]
Zamani (2020)[437]	Non-RCT	TI/"TI score" at "end of semester"	Advanced medical students/124	2 steps	4-step approach superior	Very low[l]

[a]For direct statistical comparison between 2 steps and 4 steps, the 2-step approach was superior.
[b]Due to high dropout rate.
[c]Scenario steps "call for help," "open airway," "hand position," and "chest compressions correct."
[d]The study analyzed students trained with the 2000 and 2005 European Resuscitation Council Guidelines. The authors found more pronounced effects of the 4-step approach for 2000 guidelines (compared to 2005, perceived as "simpler").
[e]Due to deviations from the intended intervention, measurement of the outcome (intervention included elements of mastery learning).
[f]Due to randomization.
[g]For primary outcome; for 3 secondary outcome advantages for the 4-step approach ("time to complete insertion," "professionalism," and "communication").
[h]Due to selection of reported results.
[i]Step 3 including additional functional verbalization by the student.
[j]Due to measurement of the outcome.
[k]Due to randomization.
[l]Due to confounding, selection, and measurement of outcomes.
[m]For a global score, the modified 4-step approach was superior to the original 4-step approach.
[n]Due to missing outcome data and measurement of outcomes.
[o]Podcast for steps 1 and 2.
[p]Due to confounding, deviations from intended intervention.
AED indicates automated external defibrillator; BLS, basic life support; ICU, intensive care unit; OSCE, objective structured clinical examination; RCT, randomized controlled trial; TI, tracheal intubation; and TSP, tele-instructor–supported peer feedback.

We found 5 studies for the important educational outcome of participants' confidence to perform the skill on patients (Table 31).[422,424,428,435,436] None of these studies showed differences between the groups.

Table 31. Summary of Evidence for Participants' Confidence to Perform the Skill on Patients

Study	Study type	Skill taught/outcome	Population taught/n	Type of alternative	Overall results	Certainty of evidence
Archer (2015)[422]	RCT	Manual defibrillation/confidence to perform manual defibrillation on a manikin and on a patient	First-year medical students/294	Traditional 2-step and 5-step approaches	Neutral	Very low[a]
Bomholt (2019)[424]	RCT	BLS-AED/self-confidence to perform BLS/AED on patient	Laypersons/129	2-step skills teaching	Neutral	Low[b]
Jenko (2012)[428]	RCT	Chest compressions/self-evaluated BLS competence	First-year medical students/126	2-step approach	Neutral[c]	Low[d]
Schauwin-hold (2022)[435]	Non-RCT	BLS/confidence in CPR performance, handling emergency situation, and real-life situation	First-year medical, dentistry, and physiotherapy students/346	3 steps with TSP	Neutral (noninferiority of the TSP group)	Very low[e]
Sopka (2012)[436]	Non-RCT	BLS (chest compression only)/self-confidence for	First-year medical students/220	Modified 4-step approach[f]	Neutral	Low[g]

		knowledge of the algorithm and chest compression performance				

[a]Due to high dropout rate.
[b]Due to randomization and missing outcome data.
[c]Both groups overrated their performance about 50% in relation to objective performance.
[d]Due to randomization.
[e]Due to confounding, selection, and measurement of outcomes.
[f]Podcast for steps 1 and 2.
[g]Due to confounding, deviations from intended intervention.
AED indicates automated external defibrillator; BLS, basic life support; RCT, randomized controlled trial; and TSP, tele-instructor–supported peer feedback.

Three studies addressed the important educational outcome of participants' preference of teaching method (Table 32).[422,423,437] One study reported advantages for 4 steps compared with 2 steps[437]; in another study, no difference was found.[423] Another study provided comments made by students.[422]

Table 32. Important Educational Outcome: Participants' Preference of Teaching Method

Study	Study type	Skill taught	Population taught/n	Type of alternative	Overall results	Certainty of evidence
Archer (2015)[422]	RCT	Manual defibrillation	First-year medical students/294	Traditional 2-step and 5-step approaches	Students in the 4-step group wanted more practice. Students found "Demonstration with explanation" and "Practice session with	Very low[a]

					educator feedback" the most useful parts (in 29% and 25%, respectively)	
Bjornshave (2018)[423]	RCT	Single rescuer BLS plus AED	Laypersons/142	"Traditional" 2-step approach	No difference of students' satisfaction	Very low
Zamani (2020)[437]	Non-RCT	TI/"TI score" at "end-of-semester"	Advanced medical students/124	2 steps	Higher satisfaction score in 4-step group (19% difference, P<0.001)	Very low[b]

[a]Due to high dropout rate.
[b]Due to confounding, selection, and measurement of outcomes.
AED indicates automated external defibrillator; BLS, basic life support; RCT, randomized controlled trial; and TI, tracheal intubation.

Prior Treatment Recommendations (year written)

This PICOST was new in 2022; therefore, no prior treatment recommendation was available.

2023 Treatment Recommendations

We suggest that stepwise training should be the method of choice for skills training in resuscitation (weak recommendation, very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision framework can be found on the ILCOR website.[421]

This topic aimed to provide evidence for the ongoing debate on the most appropriate training method for resuscitation skills, as several resuscitation councils strongly focus on the Peyton 4-step approach in their instructor courses, but this is not universally done.[418]

In making the recommendation, the EIT Task Force considered the following:

- Insufficient evidence was found for resuscitation skills training showing superiority of the 4-step approach as proposed[417] compared with other approaches.
- The optimal stepwise training approach (including the number and type of steps) may be dependent on the type of skills taught and should be adapted to the nature of the skill taught.
- The solid foundation of stepwise training approaches in educational theory was acknowledged. We do not support the use of nonstepwise training approaches.
- Two studies showed advantages of 4 steps compared with 2 steps. However, such 2-step approaches appear to have little educational structure (show it; do it) and should be regarded as nonstepwise approaches.
- Skills training using a 4-step approach, or modifications of it, should be limited to skills of low to moderate complexity. Really complex skills should break up into more than 1 training session.[438]
- Most of the studies were conducted with health care students of various professions. We cannot translate these results to other learner populations (eg, children).
- None of the studies controlled for the teaching quality of individual instructors.
- There is a risk that instructors may move away from all types of stepwise skills teaching. Instructor training needs to emphasize the importance of such stepwise skills training approaches.

Task Force Knowledge Gaps

- The impact of the quality of the individual teacher performance
- A need for an Utstein-like uniform reporting of educational outcomes in resuscitation science to allow comparative summaries of such studies
- The learning needs of different participant groups and how stepwise training should be adapted to their needs (eg, children or elderly)
- The effect of different approaches to skills teaching on participants' performance on real patients

Disparities in Layperson Resuscitation Education (ScopRev)

Rationale for Review

Layperson training in CPR is crucial, as well as increasing public awareness of cardiac arrest measures to enhance layperson involvement in lifesaving attempts.[439] Unfortunately, not every individual has equal access to resuscitation education programs, and many underserved populations lack access to CPR education. The reasons for these inequities have yet to be fully described.[440]

Identifying disparities in access to resuscitation education will help to target training and potentially increase public layperson involvement in OHCA. In this scoping review, we aimed to identify and describe factors that either promote or hinder laypersons from attending resuscitation education courses. The full online CoSTR can be found on the ILCOR website.[441]

Population, Exposure, Comparator, Outcome, Study Designs, and Time Frame

- Population: Laypersons (non–health care professionals)
- Exposure: Presence of any factors that would possibly enhance or hinder the opportunity for laypersons to undertake resuscitation education

- Comparators: Absence of the specific factor
- Outcomes: Likelihood of undertaking resuscitation education, including adult and pediatric BLS courses, and the neonatal resuscitation program
- Study designs: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols), letters, editorials, comments, case reports are excluded. All relevant publications in any language were included as long as there was an English abstract.
- Time frame: All years and all languages were included as long as there was an English abstract. The literature search was updated to August 31, 2022.

Summary of Evidence

This review included 22 studies[442-463]: 19 cross-sectional studies[442,443,445-452,454-456,458-463] and 3 retrospective cohort studies.[444,453,457] A complete overview of study characteristics and key findings is presented in supplemental table EIT-S2. All studies were related to resuscitation training for adults, published between 1987 and 2022. A thematic assessment of enablers or barriers to attending CPR education resulted in 3 main themes: (1) personal, (2) socioeconomic and higher education, and (3) geographic factors. Identified enablers and barriers within these thematic areas, and a summary of the studies finding higher, lower, or unchanged resuscitation training attendance associated with each variable, are summarized in Table 33.

Table 33. Factors Associated With Resuscitation Education Among Laypersons

	Higher attendance	Lower attendance	No difference in attendance
1. Personal factors			

Age		Older age[443-447,449,450,452,454-459,461,462]	No age difference[460,463]
Sex	In men[447,448,457] In women[445,455,462]		No difference or inconclusive among sex[443,446,449-452,456,460,461,463]
Race		Lower training rates Hispanic/Latino[444,449,461] or Black[444]	No difference between White and non-White[443]
Language		Poor proficiency in English[453,460]	
Family	Married or living as married[455]	Having small children at home[457]	
Experience	Witnessing a collapsed person[455,458] Awareness of AED in public places[458]		
Immigration	Longer stay in immigration country[460]		
2. Socioeconomic status and higher education factors			
Education	With higher level of education[442,443,445,448-451,454,460-463]		No significant association[444]
Income		With lower income[442,444,449,463]	No significant difference[461]
Socioeconomic status		With lower socioeconomic status[452,455,456]	

Occupation	Employees,[446,448,451,455] students,[446,448,455] skilled workers[458]		
Driver's license	Having driver's license[458]		
Legislation	Laws requiring school-based training[443]		
3. Geographic factors			
Born	Native-born in the country[446,450]	Southern European–born, Southeast Asian–born in Australia[453]	No significant difference[445]
Habitancy	Living in rural area[446,457]	Living in rural area[444]	No significant difference[445,463]

AED indicates automated external defibrillator.

Task Force Insights

Enablers and barriers for layperson resuscitation education were identified, which might inform targeted training initiatives for laypersons with a reduced likelihood of undertaking resuscitation education.

Older age groups are often out of reach of existing conventional CPR education strategies. Targeted approaches include increasing availability by providing convenient training locations, generating more publicity and awareness of resuscitation, and promoting group or couples' participation.[464] Targeted education should also be applied to laypersons with small children, and age-appropriate CPR training can be taught to school-aged children.[465-467]

Higher educational and income levels as well as socioeconomic status were associated with more resuscitation training. Specific targeted training for populations with lower educational standing and/or lower incomes may be beneficial. Mandatory CPR training (eg, before acquiring a driver's license) might increase layperson CPR willingness, but the downstream effects warrant further investigation.[457,458,468] Legal requirements for school-based resuscitation education increased resuscitation training amongst students and adults in such regions in 1 study.[443]

People of color were less likely to receive proper bystander resuscitation from laypersons or medical staff.[469-472] Deficiency of mutual trust in the community or inadequate language proficiency have been speculated as being barriers.[473-475] An interventional study aiming to teach refugees coming from 19 countries reported that English serving as a universal language was insufficient, and conducting BLS courses in the participants' native language was optimal.[476] Multifaceted system-wide interventions should be initiated to reduce structural biases or discrimination and increase resuscitation training for all populations living.

The influence of geographic factors and sex on resuscitation education is unclear and needs to be further investigated. The majority of the studies came from highly developed countries, and evidence from low-resource areas or remote areas is required to address this question.

Our search did not identify any studies assessing disparities in pediatric or neonatal resuscitation educational programs for laypersons or in CPR education programs for children. There were no studies looking at disparities in CPR training based on mental or physical disability, yet it is important for the disabled to have the opportunity to receive resuscitation training.[477]

Treatment Recommendations

Note: There was no prior treatment recommendation addressing disparities in layperson resuscitation education. This scoping review has not identified sufficient evidence to prompt a systematic review or a meta-analysis. However, on the basis of expert opinion from the ILCOR EIT Task Force, significant gaps in knowledge and open research questions were highlighted, specifically to include underserved populations.

Task Force Knowledge Gaps

- How to design or target resuscitation educational programs to best serve underrepresented or minority populations
- The influence of geographic factors (eg, urban or rural areas, low-resource settings, remote areas), sex of laypersons, or the impact of laws requiring CPR training on the attendance of resuscitation education courses
- Disparities in layperson resuscitation education in populations with special needs, such as disabled persons, pregnant women, schoolchildren, or kindergarten-aged children, and no studies were found in pediatric or neonatal resuscitation
- The influence of these barriers or enablers on the clinical outcome of OHCA

EIT Topics Reviewed by EvUps

Topics reviewed by EvUps are summarized in Table 34, with the PICO, existing treatment recommendation, number of studies identified, key findings, and whether a SysRev was deemed worthwhile provided. Complete EvUps can be found in Appendix X.

Table 34. EIT Topics Reviewed by Evidence Updates

Topic/PICO	Year last updated	Existing treatment recommendation	RCTs since last review, n	Observational studies since last review, n	Key findings	Sufficient data to warrant SysRev?
Patient outcomes from team member(s) attending a CPR course (EIT 6106)	2021	We recommend the provision of accredited adult ACLS/ALS training for healthcare providers who provide advanced life support care for adults (strong recommendation, very low–certainty evidence). We recommend the provision of accredited NRT courses for health care professionals who provide ALS care for newborns and babies (strong recommendation, very low–certainty evidence).	0	1	One new article was identified relevant to this PICO. The results of these studies support and strengthen the current ILCOR CoSTR recommendation. Given that this is an observational study and no new RCT is available, the identified study would not increase the existing very low certainty of	No. This EvUp does not meet the criteria to trigger a new SysRev.

		We recommend the provision of Helping Babies Breathe support training for healthcare providers who provide ALS care for newborns and babies (strong recommendation, very low–certainty evidence).			evidence and change the current recommendation.	
CACs (EIT 6301)	2021	We suggest that adult patients with nontraumatic OHCA be cared for in CACs rather than in non-CACs (weak recommendation, very low–certainty evidence). We cannot make a recommendation for or against regional triage by primary EMS transport of patients with	0 RCT 4 SysRevs	4	The SysRevs reported improved outcomes for OHCA patients who were transported to CAC. One observational study reported improved survival and neurological outcome for patients who	Yes. The new evidence will not change the 2020 treatment recommendation. EIT and ALS Task Forces should consider updating the SysRev after the publication of an RCT in 2023 (ARREST—ClinicalTrials.gov identifier: NCT03872960).

		OHCA to a CAC by primary EMS transport (bypass protocols) or secondary interfacility transfer to a CAC. The current evidence is inconclusive and confidence in the effect estimates is currently too low to support an EIT and ALS Task Force recommendation. For patients with in-hospital cardiac arrest, we found no evidence to support an EIT and ALS Task Force recommendation. For the subgroup of patients with shockable or nonshockable initial cardiac rhythm, the current			were transferred to CAC; another that patients transported to CAC in mixed urban/rural area may have improved survival compared to those in a metropolitan area. Two studies comparing high- versus low-volume hospitals reported conflicting results, with one reporting better outcomes from high-volume hospitals and one finding no	

		evidence is inconclusive, and the confidence in the effect estimates is currently too low to support an EIT and ALS Task Force recommendation.			difference in outcomes.	
Technology to summon providers (EIT 6302)	2020	We recommend that citizen/individuals who are in close proximity to a suspected OHCA event and willing to be engaged/notified by a smartphone app with an MPS or TM-alert system should be notified (strong recommendation, very low–certainty evidence).	3 SysRevs but none RCT	6	The 3 SysRevs favored first-responder systems; the RCT reported about alarming systems of laypersons by dispatchers. The summary of these studies supports the current ILCOR CoSTR recommendation. Given that no RCT data are available,	No. This EvUp does not meet the criteria to trigger a new SysRev. However, the focus on alarming laypersons as first responders might trigger a separate PICOST reviewing the evidence of such systems.

					the identified studies would not change the existing recommendation on the basis of very low certainty of evidence.	
Prehospital TOR rules (EIT 6303)	2021	We conditionally recommend the use of TOR rules to assist clinicians in deciding whether to discontinue resuscitation efforts out of hospital or to transport to hospital with ongoing CPR (conditional recommendation, very low–certainty evidence).	0	2	One study applied a medical TOR rule and a surgical TOR rule for pediatric patients (pTOR) and found 322/323 patients correctly as not eligible for the medical pTOR. The traumatic pTOR rule misclassified 4/54 patients with ROSC. This pTOR	Yes. As pediatric cardiac arrests may be considered a specific situation with many life years at risk, and only 1 historical cohort study looked at pTOR rules without showing convincing results, a new SysRev may find that TOR rules cannot be recommended for pediatric OHCAs. Accordingly,

					rule was unable to correctly classify all patients as not eligible for TOR.	updating the SysRev is recommended.
CPR feedback devices during training (EIT 6404)	2020	We suggest the use of feedback devices that provide directive feedback on compression rate, depth, release, and hand position during CPR training (weak recommendation, low-certainty evidence). If feedback devices are not available, we suggest the use of tonal guidance (examples include music or metronome) during training to improve compression rate only (weak	7	3	All studies examined the effect of corrective feedback on objectively measured CPR quality as a primary outcome measure. The 5 RCTs demonstrate significant benefits of the CPR feedback device used during resuscitation courses, although the study	Yes. The studies are consistent with the previous reviews and continue to support the use of CPR feedback devices during resuscitation training. Given the fairly large number of new studies, a formal SysRev with meta-analysis is recommended.

		recommendation, low-certainty evidence).			populations were mostly novice health care professionals and lay people. All studies focused on initial training rather than renewal course.	
CPR self-instruction versus instructor-guided training (EIT 6406)	2020	We recommend instructor-led training (with manikin practice with feedback device) or the use of self-directed training with video kits (instructional video and manikin practice with feedback device) for the acquisition of CPR theory and skills in lay-adults and high school–aged (>10 years)	1 narrative review	1 6-month follow up-study of an RCT	The narrative review suggests introducing self-directed learning, interactive digital, and abbreviated formats in communities and classroom teaching, as CPR performance seems equivalent to	No. The results of both of these studies support the current ILCOR CoSTR recommendation. Therefore, on the basis of the limited additional results, no new review was suggested.

		children (strong recommendation, moderate quality of evidence). We recommend instructor-led training (with AED scenario and practice) or the use of self-directed video kits (instructional video with AED scenario) for the acquisition of AED theory and skills in lay-adults and high school–aged (>10 years) children (strong recommendation, low quality of evidence). We suggest BLS video education (without manikin practice) be used when instructor-led training or self-directed training			traditional courses. The follow-up study reported still high willingness to perform CPR after 6 months.	

		with video kits (instructional video plus manikin with feedback device) are not accessible, or when quantity over quality of BLS training is needed in adults and children (weak recommendation, weak quality of evidence). There was insufficient evidence to make a recommendation on gaming as a CPR or AED training method. There was insufficient evidence to suggest a treatment effect on bystander CPR rates or patient outcomes.				

In situ simulation-based resuscitation training for health care professionals (EIT 6407)	2021	This EvUp does not enable a treatment recommendation to be made.	0	2	An in situ program for ECMO did not report significant changes in a before-and-after study. Another in situ interdisciplinary intraoperative code blue simulation training session on technical skills, nontechnical skills, and self-reported comfort reported significant improvements.	No. On the basis of the limited additional evidence of this search, with no RCTs identified, this EvUp does not meet the criteria to trigger a formal systematic or scoping review.

ACLS indicates advanced cardiovascular life support; AED, automated external defibrillator; ALS, Advanced Life Support; ARREST, A Randomized Trial of Expedited Transfer to a Cardiac Arrest Centre for Non-ST Elevation Out-of-Hospital Cardiac Arrest; BLS, basic life support; CAC, cardiac arrest center; CoSTR, International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; EIT, Education, Implementation, and Teams; EMS, emergency medical services; EvUp, evidence update; ILCOR, International Liaison Committee on Resuscitation; MPS, mobile positioning system;

NRT, Neonatal Resuscitation Training; OHCA, out-of-hospital cardiac arrest; PICO, population, intervention, comparator, outcome; PICOST, population, intervention, comparator, outcome, study design, time frame; pTOR, pediatric termination of resuscitation; ROSC, return of spontaneous circulation; RCT, randomized controlled trial; SysRev, systematic review; TM, text message; and TOR, termination of resuscitation.

FIRST AID

Pulse Oximetry Use in the First Aid Setting (ScopRev)

Rationale for Review

Pulse oximetry has been used for monitoring of hospitalized patients with obstructive sleep apnea, asthma, and chronic obstructive pulmonary disease (COPD) as well as, more recently, for home use during the COVID-19 pandemic. The First Aid Task Force considered it timely to undertake a ScopRev to identify evidence relating to the use of pulse oximetry as a component of first aid assessment of acute symptoms associated with illness or injury. The full online CoSTR can be found on the ILCOR website.[478]

PICOST

- Population: Adults and children in the out-of-hospital or home setting with an acute illness or injury
- Intervention: Use of pulse oximetry in addition to standard first aid assessment
- Comparators: Standard first aid assessment without the use of pulse oximetry
- Outcomes: Any clinical outcome
- Study designs: RCTs and nonrandomized studies (nonrandomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies), gray literature, social media and non-peer reviewed studies, unpublished studies, conference abstracts, and trial protocols were eligible for inclusion.
- Time frame: All years up to November 16, 2022

Summary of Evidence

Our search identified 4204 unique articles, of which 16 underwent full text review. All were ultimately excluded because they enrolled patients in home monitoring programs for a known, diagnosed infection or disease.

Although the search strategy for this ScopRev was not designed to capture studies evaluating the accuracy of pulse oximetry based on skin pigmentation, some such studies were identified. In 1 study, there was a greater discrepancy between oxygen saturation as measured by pulse oximetry and by blood gas (with pulse oximetry providing the higher number in general) in individuals identified as "Black, Asian or Mixed ethnicity" when compared with those identified as White (Black, +1.8% [95% CI, +0.2 to +3.4] *P*=0.04; Asian, +1.9% [95% CI, +0.6 to +3.2] *P*=0.005; mixed ethnicity, +3.2% [95% CI, −0.1 to +6.6] *P*=0.06).[479] In another study, Black patients had nearly 3 times the frequency of occult hypoxemia (hypoxemia not detected by pulse oximetry) as White patients.[480]

Task Force Insights

The evidence identified in this ScopRev is not directly relevant to the first aid use of a pulse oximeter as a means of assessment for acute symptoms from illness or injury. Though there were reports of the early detection of asymptomatic hypoxemia in the out-of-hospital setting with pulse oximeters, we also identified concerns regarding device limitations, accuracy, reliability, and disparities in oximetry accuracy based on skin pigmentation. Although this search strategy was not designed to capture studies comparing the accuracy of pulse oximetry based on factors like skin pigmentation, the First Aid Task Force is aware of multiple other studies evaluating this issue in addition to the ones identified. Findings generally support a small but statistically significant increase in occult hypoxemia in patients with darker skin.[481-485]

The First Aid Task Force expressed concerns about storage of oximeters in first aid kits, issues with readings due to movement and vibration, and outdoor use in settings with high humidity or extremes of temperature. Additional concern was expressed about the accuracy of oximeters sold as nonmedical-use devices and used by the public to assist with self-identification of hypoxemia without training in their use, limitations, and interpretation of findings.

Although there is not sufficient evidence to support a recommendation for (or against) the use of a pulse oximeter by first aid providers, we recognize that pulse oximeters are readily available for purchase, may be found in some first aid kits, and may be in use by some first aid providers. There is inadequate evidence to pursue a systematic review at this time.

Good Practice Statements

First aid providers who use pulse oximeters for the assessment of acute illness or injuries should be proficient in their use and understand their limitations, including equipment factors, environmental considerations, and patient-specific factors that may produce inaccurate and unreliable readings (good practice statement).

The use of a pulse oximeter for first aid assessment should not supersede or replace physical assessment (good practice statement).

Use of Supplemental Oxygen in First Aid (ScopRev)

Rationale for Review

Although supplemental oxygen has been advocated as a beneficial treatment in several conditions, recent work has found evidence of harm with excessive oxygen administration in some patient populations, such as those with suspected myocardial infarction.[486] Because supplemental oxygen may be administered in these conditions and others in the first aid setting,

an understanding of the potential risks and benefits of supplemental oxygen administration is critical to first aid providers. The full online CoSTR can be found on the ILCOR website.[487]

PICOST

- Population: Adults and children with signs or symptoms of shortness of breath, difficulty breathing, or hypoxia outside of a hospital
- Intervention: Administration of oxygen by a first aid provider
- Comparators: No administration of oxygen
- Outcomes: Functional outcome at discharge, 30 days, 60 days, 180 days, and 1 year; survival only, at discharge, 30 days, 60 days, 180 days, and/or 1 year; length of hospital stay, resolution of symptoms or signs, patient comfort, therapeutic endpoints (eg, oxygenation, ventilation)
- Study designs: RCTs and nonrandomized studies (nonrandomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies), case series and reports, gray literature, social media, non-peer reviewed studies, unpublished studies, conference abstracts, and trial protocols were eligible for inclusion. Only English-language articles were included.
- Time frame: January 1, 2000, to July 1, 2022

Summary of Evidence

Our search identified 2256 unique articles, of which 16 underwent full text review. No articles directly addressed the review question.

One cluster randomized trial compared EMS use of high-flow oxygen (defined as 8–10 L/min of oxygen) with use of titrated oxygen (titrated to an oxygen saturation of 88%–92%) for

patients with acute COPD exacerbations and found a lower mortality rate in patients treated with titrated oxygen (relative risk, 0.42 [95% CI, 0.20–0.89]).[488]

Task Force Insights

This ScopRev did not identify any direct evidence for or against the routine administration of oxygen in adults or children exhibiting signs or symptoms of shortness of breath, difficulty breathing, or hypoxia outside of a hospital.

The current review has yielded evidence that oxygen therapy at a rate of 8 to 10 L/minute is harmful in patients with acute exacerbations of COPD being treated by EMS, and oxygen needs to be titrated to the patient's oxygen saturation in this setting. This has implications for first aid providers given that the 2015 CoSTR did not identify harms associated with the use of oxygen in patients displaying symptoms of shortness of breath.[489]

We acknowledge that recognition of acute exacerbations of COPD and the use of pulse oximetry may be beyond the skill set of many first aid providers. However, some organizations teaching advanced first aid or first aid oxygen courses may include teaching on the use of pulse oximetry, so there may be circumstances where the administration of supplemental oxygen by first aid providers is common practice.

This review specifically excluded the use of supplemental oxygen in acute coronary syndrome,[486] suspected stroke,[490] drowning,[4] and after ROSC following cardiac arrest[58] because these indications have been covered in recent reviews.

Given the potential for harm with untitrated oxygen, we suggest a good practice statement that supplements the 2015 CoSTR and includes the aforementioned considerations around patients with COPD. There is inadequate evidence to pursue a systematic review on this topic at this time.

Prior Treatment Recommendations (2015)

No recommendation; the confidence in effect estimate is so low that the task force thinks a recommendation to change current practice is too speculative.

2023 Good Practice Statement

If first aid providers, trained to use oxygen, are administering supplemental oxygen to a person with known COPD, they should titrate the supplemental oxygen to maintain an oxygen saturation by pulse oximetry between 88% and 92% (good practice statement).

Recognition of Anaphylaxis (ScopRev)

Rationale for Review

Anaphylaxis is a time-sensitive condition for which early recognition and treatment with epinephrine are critical. It is unknown whether the presence or absence of any specific symptoms can assist first aid providers in appropriately identifying individuals with anaphylaxis. The full online CoSTR can be found on the ILCOR website.[491]

PICOST

- Population: Adults and children experiencing anaphylaxis
- Intervention: The description of any specific symptoms to the first aid provider
- Comparators: Absence of any specific description
- Outcomes: Recognition of anaphylaxis
- Study designs: RCTs and nonrandomized studies (nonrandomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies), case series or reports, gray literature, social media publications, non-peer reviewed studies, unpublished studies, conference abstracts and trial protocols were eligible for inclusion. All relevant publications in any language were included as long as there was an English abstract.

- Time frame: All years to September 19, 2022

Summary of Evidence

Our search identified 949 unique articles, of which 18 underwent full text review. No articles directly addressed the review question. Several of these studies reported an increase in knowledge of how to recognize anaphylaxis after educational interventions, viewing videos, health app use, and coaching.[492-501]

Other identified studies examined the effectiveness of action plans[502,503] and educational interventions to improve recognition of anaphylaxis,[504-507] and the relationship between education on anaphylaxis recognition and the use of epinephrine.[508]

Task Force Insights

Although none of the studies identified specific signs or symptoms that may be used by first aid providers in the identification of anaphylaxis, several surveys reported improvement in the ability to recognize anaphylaxis immediately following individual or community-level educational engagements.

New initiatives to improve recognition and management of anaphylaxis should be studied to evaluate their effectiveness and efficiency.

Previous literature has identified different factors associated with underuse of epinephrine in anaphylaxis.[509,510] Recognition of anaphylaxis is one of the identified factors that can reduce the delay in the administration of epinephrine when it is available, although evidence for this is limited. Recognition of anaphylaxis is not the only barrier to the first aid use of epinephrine autoinjectors. The high cost of epinephrine autoinjectors; lack of availability in some settings; lack of epinephrine use, even when it is available; and incorrect administration technique are also barriers.

There is inadequate evidence to pursue a systematic review of this topic at this time.

Previous Treatment Recommendation (2010), Unchanged

First aid providers should not be expected to recognize the signs and symptoms of anaphylaxis without repeated episodes of training and encounters with victims of anaphylaxis.[511]

Potential Harms From Bronchodilator Administration (ScopRev)

Rationale for Review

Persons with asthma exacerbations benefit from administration of bronchodilators. However, it is unknown whether first aid providers can appropriately identify asthma exacerbations, and it is unknown whether bronchodilators could result in harm if administered to individuals with undifferentiated respiratory symptoms. The full online CoSTR can be found on the ILCOR website.[512]

PICOST

- Population: Adults and children in any setting with acute undifferentiated respiratory problems
- Intervention: Administration of any type of inhaled bronchodilator (eg, beta agonists, anticholinergics)
- Comparators: No administration of an inhaled bronchodilator
- Outcomes: Survival, dysrhythmia, cardiac ischemia, hypokalemia, need for emergency department treatment, need for hospitalization, or time to treatment
- Study designs: RCTs and nonrandomized studies (nonrandomized controlled trials, interrupted time series, controlled before-and-after studies, cohort studies) and case series were eligible for inclusion. Only English language studies were included.
- Time frame: All years to November 2, 2022

Summary of Evidence

Our search identified 403 unique articles, of which 15 underwent full text review. Thirteen articles were identified that reported adverse effects of short-acting inhaled bronchodilators that could be available to first aid providers caring for patients with reactive airway disease; however, none directly addressed the PICOST. Examples of identified adverse effects were tachycardia, arrhythmias, tremor, dizziness, and a decrease in serum potassium concentrations. Bronchodilators included albuterol (salbutamol) via nebulizer, albuterol (salbutamol) via metered dose inhaler, fenoterol via metered dose inhaler, ipratropium via nebulizer, and metaproterenol via nebulizer.

Tachycardia was noted with albuterol; however, the increase in heart rate was less when albuterol was delivered through metered dose inhaler compared with delivery by nebulizer (MD, −6.47 beats per minute [95% CI, −11.69 to −1.25]; *P*=0.02).[513] Other studies noted palpitations (salbutamol)[514] and premature ventricular contractions (fenoterol and albuterol)[515] following the use of inhaled bronchodilators.

Multiple studies[515-518] documented a decrease in serum potassium concentration following the use of short-acting beta agonists, although these were typically mild (mean decrease of 0.54 mmol/L in 1 study and 0.52 mmol/L in another)[516,519] and of uncertain clinical significance.

Case reports[520-523] describe multiple side effects in patients exposed to short-acting bronchodilators. A case of unilateral mydriasis developed after nebulized ipratropium came into contact with one eye, resulting in the person receiving a CT scan of the brain to evaluate for intracranial abnormalities.[520] Severe bronchospasm occurred after exposure to an albuterol

inhaler and nebulizer treatment.[521] Finally, 1 patient developed Takotsubo cardiomyopathy, confirmed with angiography, that was associated with repetitive use of an albuterol inhaler.[523]

Task Force Insights

Most studies included patients with reactive airway diseases.

An increase in heart rate (eg, by an average of 13/min in 1 study of metaproterenol) could cause myocardial ischemia in a patient with cardiac disease or could exacerbate tachyarrhythmias such as supraventricular tachycardia.[524] Inhaled short-acting beta-agonists are associated with a decrease in plasma potassium values, typically by less than 1 mmol/L (eg, a mean decrease of 0.54 mmol/L in 1 study and 0.52 mmol/L in another).[516,519] Whether these adverse effects outweigh the potential benefit of bronchodilators is unknown.

There is inadequate evidence to undertake a systematic review on harm of bronchodilators and, therefore, inadequate evidence to amend the 2015 CoSTR on the use of bronchodilators in individuals with asthma.

Previous Treatment Recommendations (2015), Unchanged

When an individual with asthma is experiencing difficulty breathing, we suggest that trained first aid providers assist the individual with administration of a bronchodilator (weak recommendation, very low–certainty evidence).[525]

First Aid Topics Reviewed by Evidence Updates

Topics reviewed by evidence updates (EvUps) are summarized in Table 35, which provides the PICO, existing treatment recommendation, number of studies identified, key findings, and whether a SysRev was deemed worthwhile. Complete EvUps can be found in Appendix X.

Table 35. First Aid Topics Reviewed by EvUps

Topic/PICO	Year last updated	Existing treatment recommendation	RCTs since last review, n	Observational studies since last review, n	Key findings	Sufficient data to warrant SysRev?
Cervical Spinal Motion Restriction (FA7334)	2015	We suggest against the use of cervical collars by first aid providers (weak recommendation, very low–quality evidence).	3	5	Given limited additional information on spinal motion restriction identified in this evidence update, the task force did not feel there was sufficient information to pursue a systematic review or the reconsideration of current treatment recommendations.	No
Hemostatic agents for life-threatening external bleeding (FA7334)	2020	We suggest that first aid providers use a hemostatic dressing with direct pressure as opposed to direct pressure alone for severe, life-	None	None	Most new articles are on post-surgery bleeding or malignant ulcers.	No

		threatening external bleeding (weak recommendation, very low-certainty of evidence). For the treatment of severe, life-threatening external bleeding by first aid providers, due to very limited data and very low confidence in effect estimates, we are unable to recommend the use of any one specific type of hemostatic dressing compared with another.				

PICO indicates population, intervention, comparator, outcome; RCT, randomized controlled trial.

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