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ILCOR Summary Statement

2021 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations ★,★★,☆☆

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☆☆ Summary From the Basic Life Support; Advanced Life Support; Neonatal Life Support; Education, Implementation, and Teams; First Aid Task Forces; and the COVID-19 Working Group

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ABSTRACT

The International Liaison Committee on Resuscitation initiated a continuous review of new, peer-reviewed published cardiopulmonary resuscitation science. This is the fifth annual summary of the International Liaison Committee on Resuscitation International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations; a more comprehensive review was done in 2020. This latest summary addresses the most recently published resuscitation evidence reviewed by International Liaison Committee on Resuscitation task force science experts. Topics covered by systematic reviews in this summary include resuscitation topics of video-based dispatch systems; head-up cardiopulmonary resuscitation; early coronary angiography after return of spontaneous circulation; cardiopulmonary resuscitation in the prone patient; cord management at birth for preterm and term infants; devices for administering positive-pressure ventilation at birth; family presence during neonatal resuscitation; self-directed, digitally based basic life support education and training in adults and children; coronavirus disease 2019 infection risk to rescuers from patients in cardiac arrest; and first aid topics, including cooling with water for thermal burns, oral rehydration for exertional dehydration, pediatric tourniquet use, and methods of tick removal. Members from 6 International Liaison Committee on Resuscitation task forces have assessed, discussed, and debated the quality of the evidence, according to the Grading of Recommendations Assessment, Development, and Evaluation criteria, and their statements include consensus treatment recommendations or good practice statements. Insights into the deliberations of the task forces are provided in Justification and Evidence-to-Decision Framework Highlights sections. In addition, the task forces listed priority knowledge gaps for further research.

Keywords: AHA Scientific Statements, Advanced cardiac life support, Cardiopulmonary resuscitation, First aid, Health plan implementation, Infant, Newborn

Abbreviations

Abbreviations and Acronyms

ACS	acute coronary syndromes
AED	automated external defibrillator
ALS	advanced life support
ARD	absolute risk difference
BLS	basic life support
BPD	bronchopulmonary dysplasia
CAG	coronary angiography
CED	carbohydrate-electrolyte drink
CoSTR	International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations
COVID-19	coronavirus disease 2019
CPC	Cerebral Performance Category
CPR	cardiopulmonary resuscitation
DA-CPR	dispatcher-assisted CPR
ECMO	extracorporeal membrane oxygenation
ECPR	extracorporeal cardiopulmonary resuscitation
EIT	education, implementation, and teams
EMS	emergency medical services
EvUp	evidence update
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
ICU	intensive care unit
ILCOR	International Liaison Committee on Resuscitation
MD	mean difference
NIV	noninvasive ventilation
NLS	neonatal life support
OHCA	out-of-hospital cardiac arrest
OR	odds ratio
PCI	percutaneous coronary intervention
PEEP	positive end-expiratory pressure
PICO	population, intervention, comparator, outcome
PPE	personal protective equipment
PPV	positive-pressure ventilation
PROSPERO	International Prospective Register of Systematic Reviews
RCT	randomized controlled trial
ROSC	return of spontaneous circulation
RR	risk ratio
ScopRev	scoping review
SysRev	systematic review

This is the fifth in a series of annual International Liaison Committee on Resuscitation (ILCOR) International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations (CoSTR) summary publications that summarize the ILCOR task force analyses of published resuscitation evidence. This 2021 review includes 13 topics addressed with systematic reviews (SysRevs) by the 6 ILCOR task forces and an additional topic reviewed by the coronavirus disease 2019 (COVID-19) working group. Although only a SysRev can generate a full CoSTR and updated treatment recommendations, many other topics were reviewed via more streamlined approaches, detailed below.

Draft CoSTRs for all topics evaluated with SysRevs were posted on a rolling basis from November 2020 through March 2021 on the ILCOR website[1] and included the data reviewed and draft treatment recommendations, with comments accepted for at least 2 weeks after each posting date. The 9 draft CoSTR statements were viewed ≈11 000 times, and 154 comments were provided as feedback. These CoSTRs are now available online, adding to the existing CoSTR statements.

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This summary contains the final wording of the treatment recommendations and good practice statements as approved by the task forces and by the ILCOR member councils, but it differs in several respects from the online CoSTRs: The language used to describe the evidence in this summary is not restricted to standard Grading of Recommendations Assessment, Development, and Evaluation (GRADE) terminology, thereby making it more transparent to a wider audience; in some cases, only the high-priority outcomes are reported; the Justification and Evidence-to-Decision Framework Highlights sections are in some cases shortened but aim to provide insight into the rationale behind the treatment recommendations; and finally, the task forces have prioritized knowledge gaps requiring future research. Links to the published reviews and full online CoSTR are provided in the individual sections.

The CoSTRs are based on task force analysis of the data using the GRADE approach.[1] Each analysis has been detailed either in a SysRev conducted by a Knowledge Synthesis Unit or a systematic reviewer or as a task force–led SysRev, and always with input from ILCOR content experts. This GRADE approach rates the certainty of evidence supporting the intervention (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 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 reduce the detected effect.

In addition to the certainty of evidence, each statement includes the pertinent outcome data. The format for the data varies by what is available but ideally includes both risk ratio (RR) with 95% CI and risk difference with 95% CI. The 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 (number needed to treat=1/risk difference). In cases when the data do not enable absolute effect estimates to be determined, alternative measures of effect such as odds ratios (ORs) are reported.

Treatment recommendations are generated by the task forces after weighing 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 has not produced any guidance when the 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. To facilitate this goal and acknowledging that many PICO topics will not have sufficient new evidence to warrant a SysRev, ILCOR implemented 2 additional levels of evidence review in 2020, which were also used for 2021. Scoping reviews (ScopRevs) are undertaken when there is a lack of clarity on the amount and type of evidence on a broader topic. ScopRevs are broad searches done in multiple databases with a rigor similar to that of a SysRev but do not include bias assessments or meta-analyses. The third and least rigorous form of evidence evaluation is the evidence update (EvUp), in which a PubMed search is carried out to screen for significant new data and assess whether there has been sufficient new science to warrant a new ScopRev or SysRev. 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 evaluation, or meta-analyses. In some instances, ScopRevs done for the 2021 review did generate good practice statements. In this document, the results of ScopRevs are included in a more concise form than in the online version, similar to the SysRevs. EvUps are tabulated by topic at the end of each task force section, with the associated documents provided in the appendix.

The following topics are addressed in this CoSTR summary:

Basic Life Support

- Video-based dispatch system (new: SysRev)
- Head-up cardiopulmonary resuscitation (CPR) (new: SysRev)
- Bystander CPR in drowning (BLS 856: ScopRev)
- In-water resuscitation in drowning (BLS 856: ScopRev)
- Resuscitation on a boat after drowning (BLS 856: ScopRev)
- Airway management in drowning (BLS 856: ScopRev)
- Prehospital oxygen in drowning (BLS 856: ScopRev)
- Automated external defibrillator (AED) use in drowning (BLS 856: ScopRev)
- Mechanical ventilation in drowning (BLS 856: ScopRev)
- Extracorporeal membrane oxygenator (ECMO) in drowning (BLS 856: ScopRev)
- Criteria for discharge in drowning (BLS 856: ScopRev)
- Paddle size and placement for defibrillation (new: EvUp)
- CPR before call for help (BLS 1527: EvUp)
- Barrier devices (BLS 342: EvUp)
- Chest compression rate (BLS 343: EvUp)
- Rhythm check timing (BLS 345: EvUp)
- Timing of CPR cycles (2 minutes versus other) (BLS 346: EvUp)
- Public-access AED programs (BLS 347: EvUp)
- Check for circulation during basic life support (BLS) (BLS 348: EvUp)
- Rescuer fatigue in chest compression–only CPR (BLS 349: EvUp)
- Harm from CPR to victims not in arrest (BLS 353: EvUp)
- Harm to rescuers from CPR (BLS 354: EvUp)
- Hand position during compressions (BLS 357: EvUp)
- Dispatcher instructions (BLS 359: EvUp)
- Emergency medical services (EMS) chest compression–only CPR versus conventional CPR (BLS 360: EvUp)
- Feedback for CPR quality (BLS 361: EvUp)
- Compression-to-ventilation ratio (BLS 362: EvUp)
- CPR before defibrillation (BLS 363: EvUp)
- Chest compression depth (BLS 366: EvUp)
- Chest wall recoil (BLS 367: EvUp)
- Foreign body airway obstruction (BLS 368: EvUp)
- Firm surface for CPR (BLS 370: EvUp)
- Analysis of rhythm during chest compression (BLS 373: EvUp)
- Alternative compression techniques (cough, precordial thump, fist pacing) (BLS 374: EvUp)

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- Tidal volumes and ventilation rates (BLS 546: EvUp)
- Lay rescuer chest compression–only CPR versus standard CPR (BLS 547: EvUp)
- Starting CPR (compression-airway-breathing compared with airway-breathing-compression) (BLS 661: EvUp)
- Dispatcher recognition of cardiac arrest (BLS 740: EvUp)
- Resuscitation care for suspected opioid-associated emergencies (BLS 811: EvUp)
- Drowning (BLS 856: EvUp)
- Dispatcher-assisted continuous chest compressions CPR versus conventional CPR (new: EvUp)

Advanced Life Support

- Early coronary angiography (CAG) after return of spontaneous circulation (ROSC) (ACS 340, 885: SysRev)
- CPR and defibrillation in the prone patient (new: SysRev)
- Consciousness during CPR (new: ScopRev)
- Transition from shockable to nonshockable rhythm (ALS 444: EvUp)
- Oxygen dose during CPR (ALS 889: EvUp)
- Steroids during CPR (ALS 433: EvUp)
- Confirmation of tracheal tube position (ALS 469: EvUp)
- Automatic ventilators versus manual ventilation during CPR (ALS 490: EvUp)
- Cardiac arrest and asthma (ALS 492: EvUp)
- Extracorporeal CPR (ECPR) versus manual or mechanical CPR (ALS 723: EvUp)
- Steroids after ROSC (ALS 446: EvUp)
- Oxygen dose after ROSC (ALS 448: EvUp)
- Neuroprognostication after ROSC (ALS 450, 458, 460, 484, 487, 713: EvUp)

Pediatric Life Support

The Pediatric Life Support Task Force did not complete any primary SysRevs before the deadline for publication of the 2021 CoSTR (although several reviews are in progress). The following SysRevs include children and were done in collaboration with the Pediatric Life Support Task Force members: duration of cooling with water for thermal burns as a first aid intervention (First Aid), pediatric tourniquets (First Aid), and CPR in the prone patient (ALS).

Neonatal Life Support

- Cord management at birth for preterm infants (NLS 787: SysRev)
- Cord management at birth for term and late preterm infants (NLS 1551: SysRev)
- Devices for administering positive-pressure ventilation (PPV) at birth (NLS 870: SysRev)
- Family presence during neonatal resuscitation (NLS 1590: SysRev)

Education, Implementation, and Teams

- Self-directed, digitally based BLS education and training in adults and children (EIT 647: SysRev)
- EMS practitioner's experience or exposure (EIT 437: EvUp)
- High-fidelity training (EIT 623: EvUp)
- Cardiac arrest centers (EIT 624: EvUp)
- Timing for retraining (EIT 628: EvUp)
- Cognitive aids during resuscitation (EIT 629: EvUp)
- Termination of resuscitation for in-hospital cardiac arrest (EIT 4002 EvUp)
- Precourse preparation for advanced courses (EIT 637: EvUp)
- System performance improvements (EIT 640: EvUp)
- Community initiatives to promote BLS implementation (EIT 641: EvUp)
- Prehospital termination of resuscitation rules (EIT 642: EvUp)
- CPR feedback devices during training (EIT 648: EvUp)
- BLS training in high-risk populations (EIT 649: EvUp)
- Technology to engage first responders (EIT 878: EvUp)
- Resuscitation team with advanced life support (ALS) course training (EIT 4000: EvUp)
- Opioid overdose first aid education (EIT 4001: EvUp)
- Facilitators and barriers to bystander CPR (EIT 4003: EvUp)
- Virtual reality, augmented reality, and gamified learning (EIT 4005: EvUp)
- In situ training (EIT 4007: EvUp)

First Aid

- Duration of cooling with water for thermal burns as a first aid intervention (FA 770: SysRev)
- Exertion-related dehydration and rehydration (FA 584: SysRev)
- Pediatric tourniquet types (FA 768: SysRev)
- Methods of tick removal (new: SysRev Adolopment)
- Use of cryotherapy for acute epistaxis in the first aid setting (new: ScopRev)
- Pressure immobilization bandaging for venomous snakebites (FA 1001: EvUp)
- Second dose of epinephrine for anaphylaxis (FA 500: EvUp)
- Dietary sugars for treatment of hypoglycemia (FA 795: EvUp)

COVID-19 Working Group

- COVID-19 infection risk to rescuers from patients in cardiac arrest (new: SysRev)

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

Video-Based Dispatch System (SysRev)

Rationale for Review

Because new communication technologies offer promising new avenues in emergency medical dispatch, the BLS Task Force considered it important to review any available evidence evaluating the use of video to enhance communication and improve lay-rescuer CPR in the out-of-hospital cardiac arrest (OHCA) setting. The SysRev was registered in the International Prospective Register of Systematic Reviews (PROSPERO; Registration CRD42020219112).

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The full text of this CoSTR can be found on the ILCOR website.[2]

PICO, Study Design, and Time Frame

- Population: Adults and children with presumed cardiac arrest in the out-of-hospital setting
- Intervention: Patients/cases or EMS systems through which dispatcher-assisted CPR (DA-CPR) is offered by video and audio communication between dispatcher center and scene
- Comparator: Patients/cases or EMS systems through which DA-CPR is offered by audio-only communication between dispatcher center and scene
- Outcome: Any clinical outcome (survival with favorable neurological outcome, survival, ROSC, and CPR quality)
- Study design: 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.
- Time frame: All years and all languages were included as long as there was an English abstract. Literature search was updated to February 8, 2021.

Consensus on Science

Only 1 observational study was identified.[3] For the critical outcome of good neurological function at discharge, we identified very low–certainty evidence from 1 observational study enrolling 1720 adult OHCAs, which showed benefit from the use of video-based dispatch compared with standard audio-based dispatch (OR, 1.89 [95% CI, 1.18–3.04]; $P<0.01$). However, the benefit was not observed after multivariable statistical adjustment (OR, 1.28 [95% CI, 0.73–2.26]) or propensity score–matching analysis (OR, 0.91 [95% CI, 0.51–1.64]). Similarly, the group receiving video-based dispatch had higher rates of survival to discharge and ROSC compared with the group receiving standard audio-based dispatch in unadjusted analysis, but there were no significant differences between the groups after multivariable statistical adjustment and propensity score–matching analysis.[3]

We also identified 13 manikin simulation studies that compared video-based with audio-based dispatch.[4–16] The simulation studies showed improved CPR quality parameters such as compression rate and time to compression in the video-based dispatch group but did not show any significant differences in chest compression depth, correct compression depth, correct hand position, correct chest release, or time to defibrillation.

Treatment Recommendations

We suggest that the usefulness of video-based dispatch systems be assessed in clinical trials or research initiatives (weak recommendation, very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplemental Appendix A1.

Only a single human observational study was identified, so the evidence informing the guideline is very uncertain. Despite limited evidence, the BLS Task Force considered it important to encourage research in this important area and therefore provided a conditional recommendation for video-based dispatch systems to be assessed in clinical trials or research initiatives.

Several manikin simulation studies were identified comparing video-based with audio-based dispatch. Lin et al[17] published a SysRev of simulation studies comparing the effect of video-based dispatch with the effect of audio-based dispatch on quality of DA-CPR. The review included 6 simulation studies that showed that video-based DA-CPR significantly improved the chest compression rate compared with audio-based dispatch, and a trend toward more correct hand position was also observed. However, video-based dispatch was associated with a delay in the start of bystander-initiated CPR.[17] Although not directly informing clinical practice, these simulation studies provide important information about the aspects that need to be addressed and evaluated in future clinical studies evaluating video-based dispatch.

Task Force Knowledge Gaps

- RCT evidence comparing video-based dispatch with audio-based dispatch in any patient population
- Further observational evidence evaluating the use of video communication in emergency medical dispatch
- Whether 2 rescuers are needed to effectively process video-based DA-CPR: 1 to provide chest compressions and 1 to handle the mobile phone and assist with communication. This might lead to varying feasibility of implementing video-based dispatcher CPR according to location of arrest (crowded public place versus at home) and other variables.

Head-Up CPR (SysRev)

Rationale for Review

This topic was prioritized by the BLS Task Force because of increasing interest and debate surrounding head-up CPR within the resuscitation community. Head-up CPR has been suggested as an alternative CPR method, potentially improving cerebral perfusion by facilitating venous return from the brain. The BLS Task Force was aware of the growing body of animal research addressing head-up CPR[18–23] and that this strategy is currently being used in some EMS systems. The evidence review was performed in collaboration with the ALS Task Force. Because there was no intent to publish this SysRev outside of the 2021 CoSTR, PROSPERO registration was not done.

The full text of this CoSTR can be found on the ILCOR website.[24]

PICO, Study Design, and Time Frame

- Population: Adults in any setting (in hospital or out of hospital) with cardiac arrest
- Intervention: Head-up CPR
- Comparator: Standard or compression-only CPR in the supine position
- Outcome: Survival to hospital discharge with good neurological outcome and survival to hospital discharge were ranked as critical outcomes. ROSC was ranked as an important outcome.
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion.

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- 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. Literature search was updated to January 22, 2021.

Consensus on Science

Only 1 observational study was identified.[25] For the important outcome of survival to hospital admission, we identified very low–certainty evidence from 1 observational (before-and-after) study enrolling 1835 adult OHCAs; the study showed an increased rate of ROSC at hospital arrival in patients receiving −20° head-up CPR compared with standard care (RR, 1.90 [95% CI, 1.61–2.26]; *P*<0.001; absolute risk reduction, 16.1% [95% CI, 20.0%–12.2%], or 161 [95% CI, 109–225] more patients per 1000 survived with the intervention more). Notably, both head-up CPR and standard resuscitation in this study were bundled with mechanical CPR and the use of an impedance threshold device. Head-up CPR, but not standard care, was also accompanied by deferred PPV for several minutes and the deployment of a pit-crew approach for more efficient placement of the mechanical CPR device. No studies were identified that compared head-up CPR alone with standard care.

This technique has also been evaluated in animal laboratory studies (also in concert with mechanical CPR and an impedance threshold device) with mixed outcomes, but those studies were not included in this review, which focused on clinical data.[18–23]

Treatment Recommendations

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).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplemental Appendix A1.

The limited observational evidence identified in this review suggests that head-up CPR might have the potential to improve short-term outcome from cardiac arrest, but the certainty of evidence is very low with very high risk of bias. Head-up CPR was assessed only as a bundle with mechanical CPR with active decompression and the use of an impedance threshold device, making the generalizability of the results to other systems questionable. With a before-and-after design, the study findings may have been influenced by unrelated and unreported changes in practice over time—in particular, a change in ventilation strategy and potentially more efficient deployment of the mechanical CPR that accompanied the intervention. Outcome measures were also limited to ROSC at the time of hospital arrival, without any information on longer-term survival or functional outcomes.

Implementation of the head-up CPR bundle requires purchase of equipment (mechanical CPR and the impedance threshold device), along with education and training in the use of this equipment and the technique for deploying head-up CPR. Without a demonstrable improvement in longer-term outcomes, it is unlikely to be an acceptable strategy for key stakeholders. The BLS Task Force does not find the current evidence sufficient to recommend routine use of this strategy and encourages further research before its clinical deployment.

Task Force Knowledge Gaps

- Comparisons of head-up CPR alone with standard care
- RCT evidence evaluating the effect of head-up CPR either alone or as part of a bundle of care
- The effect of head-up CPR on longer-term outcomes such as survival and neurologically intact survival to hospital discharge or 30 days

Bystander CPR in Drowning (BLS 856: ScopRev)

Rationale for Review

Drowning is the third leading cause of unintentional injury death worldwide, accounting for >360 000 deaths annually.[26] Submersion in water leads to the rapid onset of hypoxemia. If someone who has drowned is left untreated, cardiac arrest occurs within minutes. The initiation of CPR by a bystander allows treatment to be delivered before EMS arrives, but its effects on outcomes after drowning are uncertain. The BLS Task Force, in collaboration with several experts on drowning, considered it timely to undertake a ScopRev of the literature to identify any new evidence on multiple BLS topics in the context of drowning.[27]

The full text of this ScopRev can be found on the ILCOR website.[28]

PICO, Study Design, and Time Frame

- Population: Adults and children who are submerged in water
- Intervention: Bystander CPR
- Comparator: No bystander CPR
- Outcome: Any clinical outcome (eg, survival, survival with a favorable neurological outcome, hospitalization)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Manikin studies were included only if no human studies were available.
- Time frame: From 2000 onward. All languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols), narrative reviews, and animal studies were excluded. Literature search was updated to October 2019.

Summary of Evidence

Eighteen studies were identified that discussed bystander CPR as an intervention for 16 303 adults and children after drowning.[29–46] There were 2 prospective observational studies,[36,41] 9 retrospective observational studies,[30–32,37,38,43–46] and 7 retrospective case reviews.[29,33–35,39,40,42] All studies reported survival status after OHCA caused by drowning, and 13 reported neurological outcomes.[29,31–33,36,39–45]

Only 2 cohort studies were designed to directly assess the impact of bystander CPR, and both found statistically significant associations between bystander CPR and improved outcomes.[43,45] One study documented improved neurologically favorable survival (RR, 2.19; *P*=0.0076), 1-month survival (RR, 1.55; *P*=0.0150), and prehospital ROSC (RR, 1.30; *P*=0.0296).[45] The second study also documented an association between bystander CPR and neurologically favorable survival (adjusted OR, 3.02; *P*<0.001).[43]

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Four other studies found significant associations with bystander CPR and survival.[32,38,41,44] Five studies found a positive trend toward survival,[29,34,36,39,42] and 3 found no association between bystander CPR and good outcomes.[29,30,33,40] One of those studies did find a significant association between survival and the time from witnessing arrest to BLS initiation (P<0.001).[33] Several studies compared the effect on survival of conventional CPR by bystanders with the effect on survival of compression-only CPR by bystanders.[36,41,46] One study documented a highly positive association with bystander ventilation and survival (OR, 6.742; P=0.002),[41] and another documented a trend favoring conventional CPR for both survival (adjusted OR, 1.87 [95% CI, 0.83–4.20]) and neurologically favorable outcome (adjusted OR, 2.35 [95% CI, 0.52–10.62]).[36] Another study documented similar outcomes for conventional CPR and compression-only CPR: Both were better than no CPR.[46] A more recent study, published after the literature search was conducted, reported that compared with compression-only CPR, conventional CPR improved survival to discharge (all patients, adjusted OR, 1.54 [95% CI, 1.01–2.36]; P=0.046) and neurological outcomes in children (adjusted OR, 2.68 [95% CI, 1.10–6.77]; P=0.03).[48]

Task Force Insights

The evidence identified suggests that bystander CPR for drowning is feasible and appears effective. The apparent superiority of conventional CPR, which includes ventilation, has biological plausibility because cardiac arrest attributable to drowning is caused primarily by hypoxemia. The findings of this review are consistent with the 2020 ILCOR recommendation that chest compressions be performed for all patients in cardiac arrest.[49] ILCOR suggests that those who are trained, able, and willing to give rescue breaths and chest compressions do so for all adult patients in cardiac arrest.[49] Rescue breaths are likely to be particularly important in patients who sustain a cardiac arrest attributable to hypoxemia after drowning. The evidence base identified in this ScopRev suggests that a SysRev on this topic should be considered.

Treatment Recommendations

There was no previous treatment recommendation on bystander CPR in drowning, and a SysRev will be pursued by the BLS Task Force.

In the meantime, we highlight our 2020 recommendation and 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).

In-Water Resuscitation in Drowning (BLS 856: ScopRev)

Rationale for Review

The 2005 ILCOR treatment recommendation stated that in-water, expired-air resuscitation may be considered by trained rescuers, preferably with a flotation device, but chest compressions should not be attempted in the water.[50]

The full text of this ScopRev can be found on the ILCOR website.[51]

PICO, Study Design, and Time Frame

- Population: Adults and children who are submerged in water
- Intervention: Starting resuscitation while the person is still in the water
- Comparator: Delaying resuscitation until the person is rescued from the water
- Outcome: Any clinical outcome (eg, survival, survival with a favorable neurological outcome, hospitalization), CPR quality, physiological end points
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Manikin studies were included only if no human studies were available.
- Time frame: From 2000 onward. All languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols), narrative reviews, and animal studies were excluded. Literature search was updated to October 2019.

Summary of Evidence

Five studies evaluating in-water resuscitation were identified. A single retrospective observational study reported the outcomes of adults and children who were rescued unconscious and not breathing from the ocean in Brazil.[52] The other 4 studies were manikin studies conducted in swimming pools[53,54] and open water.[55,56]

The clinical study reported survival status and neurological outcome of 19 patients who received in-water resuscitation compared with 27 patients who did not.[52] The in-water resuscitation protocol recommended performing up to 1 minute of ventilation before attempting to bring the unconscious and not-breathing patient to the shore. For patients in deep water, in-water resuscitation required the availability of rescue flotation equipment or at least 2 rescuers. In the prehospital setting, initial survival was significantly higher in the in-water resuscitation group (94.7% versus 37.0%; P<0.001). The rate of survival at hospital discharge was higher in the in-water resuscitation group (87.5% versus 25%; P<0.005), as was favorable neurological outcome (52.6% versus 7.4%; P<0.001).[52]

All other studies were crossover trials that evaluated the capacity of lifeguards[53–56] and laypeople[54] to perform in-water resuscitation while simulating a water rescue with a manikin. In-water resuscitation was technically difficult and physically demanding, particularly in open water. Some trained lifeguards[55] and laypeople[54] were unable to complete the rescue. In-water resuscitation increased rescue time and the number of submersions and aspiration of water by the manikin.[54–56] The use of ventilation adjuncts by well-trained lifeguards might facilitate in-water resuscitation.[55,56]

Task Force Insights

From the available evidence, in suitable water conditions, in-water resuscitation by highly trained rescue teams with water rescue equipment seems feasible.

The evidence base identified in this ScopRev suggests that a SysRev on this topic should be considered.

Treatment Recommendations

The 2005 treatment recommendation is unchanged: In-water, expired-air resuscitation may be considered by trained rescuers, preferably with a flotation device, but chest compressions should not be attempted in the water.[50]

Resuscitation on a Boat After Drowning (BLS 856: ScopRev)

Rationale for Review

Starting resuscitation on a rescue boat is one approach to enable early initiation of resuscitation. However, the feasibility and effectiveness of CPR on a boat have not previously been explored.

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The full text of this ScopRev can be found on the ILCOR website.[57]

PICO, Study Design, and Time Frame

- Population: Adults and children who are submerged in water
- Intervention: Delivering resuscitation on a boat
- Comparator: Delaying resuscitation until on dry land
- Outcome: Any clinical outcome (eg, survival, survival with a favorable neurological outcome, hospitalization), CPR quality, physiological end points
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Manikin studies were included only if no human studies were available.
- Time frame: From 2000 onward. All languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols), narrative reviews, and animal studies were excluded. Literature search was updated to October 2019.

Summary of Evidence

Six studies evaluating resuscitation on a boat were identified. Two were clinical studies undertaken in the Netherlands[58] and Hawaii,[59] and 4 were manikin studies.[60–63] A case series from the Royal Dutch Lifeboat Institution reported 37 patients who had received resuscitation from lifeboat crews.[58] Among these, 24 cases included resuscitation on a lifeboat or another ship. There were only 3 survivors, none of whom received resuscitation on a boat. An AED was used on 12 patients (7 drowned, 4 not drowned, 1 unknown), and 3 shocks were delivered. CPR quality was reported as suboptimal (high compression frequency and long pauses in chest compressions). In the other case series, 6 resuscitations were attempted on a boat or lifeboat; there was only 1 survivor after 1 month who received BLS, ALS, and tracheal intubation on board.[59]

Three simulation crossover studies evaluated the capacity of lifeguards[61,62] and fishermen[60] to perform CPR on inflatable rescue boats or traditional fishing boats. These studies showed that resuscitation on a boat was feasible; however, the quality of the resuscitation was affected by boat speed[60,61] and sea conditions.[62] CPR was physically demanding.[60–62] The motion-induced interruptions and early fatigue affected mainly ventilation.[62] A further simulation study showed that AED use on rigid inflatable rescue boats on calm water was feasible.[63]

Task Force Insights

From the available evidence, resuscitation on a boat seems feasible if safety conditions, number of crew, and deck space allow, but those who are providing resuscitation need to focus on high-quality CPR and be alert to the development of fatigue.

The evidence base identified in this ScopRev suggests that a SysRev on this topic should be considered.

Treatment Recommendations

There was no previous treatment recommendation on resuscitation on a boat after drowning; a SysRev will be pursued by the BLS Task Force.

In the meantime, we highlight our 2020 recommendation and suggest that bystanders who are trained, able, and willing to give rescue breaths and chest compressions do so for all adults patients in cardiac arrest (weak recommendation, very low–certainty evidence).

Airway Management in Drowning (BLS 856: ScopRev)

Rationale for Review

Airway management in drowning is pivotal to effective resuscitation, but the optimal strategy is unclear.

The full text of this ScopRev can be found on the ILCOR website.[64]

PICO, Study Design, and Time Frame

- Population: Adults and children who are submerged in water
- Intervention: Advanced airway management
- Comparator: No advanced airway management
- Outcome: Any clinical outcome (eg, survival, survival with a favorable neurological outcome, hospitalization), CPR quality, physiological end points
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Manikin studies were included only if no human studies were available.
- Time frame: From 2000 onward. All languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols), narrative reviews, and animal studies were excluded. Literature search was updated to October 2019.

Summary of Evidence

No studies specifically examining the effect of any particular airway management strategy over another in the management of a submerged casualty were identified. Five observational studies indirectly examined airway management strategies in 699 adults and children after drowning events.[40,41,65–67] One study reported outcomes in adults and children,[41] whereas the other 4 studies reported only pediatric cases.[40,65–67] Some studies reported only those who sustained cardiac arrest attributable to drowning.[41,67] All studies reported survival—specifically, survival with good neurological outcome,[65] survival to hospital admission,[41] and good outcome versus bad outcome (death or neurological sequelae).[40]

In all studies, tracheal intubation was an indication of the severity of the injury, with the most severely injured being intubated during cardiac arrest or facilitated with anesthesia, without comprehensive adjustment for confounders. Two studies showed that tracheal intubation was associated with worse outcome (OR for good outcome, 0.25 [95% CI, 0.08–0.83][67]; OR, 0.04 [95% CI, 0.01–0.2]).[40] One study showed that mobile medical team ventilation was associated with better outcomes (44% versus 17% survival to admission).[65]

Task Force Insights

The studies reviewed show that tracheal intubation is a feasible intervention after a water submersion incident. The association between tracheal intubation and poor outcomes is almost certainly confounded by the fact that tracheal intubation is limited to more severe drowning.

The limited evidence base identified in the ScopRev suggests little benefit from a full SysRev to evaluate advanced airway management compared with no advanced airway management after drowning. In the absence of data supporting an alternative strategy,

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there is no reason to deviate from the ALS Task Force recommendations for airway management.[68]

Treatment Recommendations

There was no previous treatment recommendation on advanced airway management after drowning. The lack of evidence in the drowning setting supports the use of standard ALS Task Force recommendations for airway management.[68]

Prehospital Oxygen in Drowning (BLS 856: ScopRev)

Rationale for Review

The use of prehospital oxygen has the potential to reverse hypoxemia and may improve outcomes. However, providing access to oxygen therapy has substantial resource implications to cover the costs of equipment and training. Without access to pulse oximetry or arterial blood gas analysis, identifying patients who may benefit from oxygen therapy can be difficult.

The full text of this ScopRev can be found on the ILCOR website.[69]

PICO, Study Design, and Time Frame

- Population: Adults and children who are submerged in water
- Intervention: Prehospital oxygen administration
- Comparator: No prehospital oxygen administration
- Outcome: Any clinical outcome (eg, survival, survival with a favorable neurological outcome, hospitalization), physiological end points
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Manikin studies were included only if no human studies were available.
- Time frame: From 2000 onward. All languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols), narrative reviews, and animal studies were excluded. Literature search was updated to October 2019.

Summary of Evidence

Indirect evidence from 4 observational studies found associations among hypoxemia, oxygen administration, and worse outcomes. One study documented a higher rate of hospital admission in patients with an initial oxygen saturation measured by pulse oximetry (Spo_2) no higher than 95% on arrival in the emergency department (92% versus 52%; adjusted OR, 6.8 [95% CI, 1.07–43.8]).[70] Hospital admission rates were also higher (91% versus 34%) among 71 children with an initial Spo_2<92% at the scene or on arrival in the emergency department in univariate but not multivariate analysis.[71] In contrast, another study did not find an association between Pao_2/fraction of inspired oxygen (F_{IO_2}) ratio and the duration of hospital stay among 43 adults and children.[72] In an observational study involving 31 adults, lower blood oxygen saturations (87% versus 76%; P=0.007) and Pao_2/F_{IO_2} ratios (255 versus 133; P=0.004) were associated with reduced survival with favorable neurological outcome.[73]

Task Force Insights

The review found no direct evidence to guide the prehospital use of oxygen therapy in drowning. Yet, the primary cause of death from drowning is insufficient oxygen delivery to the heart and brain, and prompt restoration of oxygen delivery is of paramount importance. The indirect evidence identified in this review suggests frequent need for supplemental oxygen in patients who have drowned. Work in other domains of resuscitation science has identified adverse outcomes associated with both sustained hypoxia and hyperoxia. Pulse oximetry can be unreliable, particularly after cold-water immersion,[74] but when feasible can enable continuous titration of F_{IO_2} after restoration of spontaneous circulation.

Treatment Recommendations

There was no previous treatment recommendation on prehospital use of oxygen therapy in drowning. The lack of evidence for a different approach to prehospital oxygen therapy in the drowning setting supports the use of standard ALS Task Force recommendations to avoid hypoxemia and hyperoxia by using 100% inspired oxygen until arterial oxygen saturation or the partial pressure of arterial oxygen can be measured, after which oxygen can be titrated to maintain an arterial oxygen saturation in the normal range.[68]

AED Use in Drowning (BLS 856: ScopRev)

Rationale for Review

Although the most common cause of cardiac arrest associated with drowning is hypoxemia, in some cases, a primary cardiac arrythmia may be the precipitating event. The use of an AED in such cases may be lifesaving, but this needs to be balanced against the risk of harm from interruptions to CPR for patients with nonshockable rhythms. Although ILCOR recommends the use of AEDs, their role in the setting of resuscitation from drowning is not clearly defined.

The full text of this ScopRev can be found on the ILCOR website.[75]

PICO, Study Design, and Time Frame

- Population: Adults and children who are submerged in water
- Intervention: AED use
- Comparator: No AED use
- Outcome: Any clinical outcome (eg, survival, survival with a favorable neurological outcome, hospitalization), CPR quality, physiological end points
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Manikin studies were included only if no human studies were available.
- Time frame: From 2000 onward. All languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols), narrative reviews, and animal studies were excluded. Literature search was updated to October 2019.

Summary of Evidence

There were no interventional, observational, or case series showing direct evidence on the outcome from on-site AED use in OHCA attributable to drowning before the arrival of EMS. Indirect evidence of AED use was found from 15 observational studies. Four studies involving 1044 patients showed a range of AED use in cases of suspected drowning before the arrival of EMS of 5% to 32%.[37,43,58,76] In 12 studies involving 14 920 patients, a shockable rhythm in OHCA attributable to drowning was uncommon, with a reported range of

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ventricular fibrillation/ventricular tachycardia between 2% and 14%.[30,33,35,37–39,43,45,58,67,76,77] Among 7 observational studies involving 1846 patients in cardiac arrest after drowning, a shockable rhythm was not associated with better survival.[30,33,43,58,67,76,77] In 1 study with 776 drowning survivors, only 0.4% were defibrillated at the emergency department.[78] In 1 study involving 529 patients in a multivariable analysis, although a shockable rhythm did not improve survival to hospital admission, there was an association between shockable rhythm and increased 30-day survival (OR, 4.12 [95% CI, 1.13–13.71]).[38]

In 1 simulation study testing 6 AEDs on 3 different boats in moderate sea conditions, use of AEDs seemed feasible.[63] In 1 simulation study with 616 lifeguards, mean time from arrival to defibrillation was 62 seconds (SD, 20 seconds).[79] In 1 study, a case of inappropriate shock delivered to a patient in asystole with artifacts on the ECG resulting from movements was described, with no obvious consequences.[58]

No adverse events were reported in the studies identified in this review.

Task Force Insights

Studies reviewed showed that using AEDs in cardiac arrest in the drowning setting appears to be feasible and safe, although the chances of a shockable rhythm may be lower (2%–14%) than for a primary cardiac cause. The current ILCOR treatment recommendation suggests a short period of CPR until the defibrillator is ready for analysis or until defibrillation in unmonitored cardiac arrest. This may be particularly important in situations in which the cardiac arrest was caused by drowning.[49]

Treatment Recommendations

There was no previous treatment recommendation on AED use after drowning; a SysRev will be pursued by the BLS Task Force.

In the meantime, we highlight our 2020 recommendation suggesting that delivery of a shock with an AED during BLS is safe.

Mechanical Ventilation in Drowning (BLS 856: ScopRev)

Rationale for Review

Patients with severe lung injury after submersion may require support from a mechanical ventilator, but the optimal ventilation strategy is unclear.

The full text of this ScopRev can be found on the ILCOR website.[80]

PICO, Study Design, and Time Frame

- Population: Adults and children who are submerged in water
- Intervention: Mechanical ventilation
- Comparator: No mechanical ventilation
- Outcome: Any clinical outcome (eg, survival, survival with a favorable neurological outcome, hospitalization), physiological end points
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Manikin studies were included only if no human studies were available.
- Time frame: From 2000 onward. All languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols), narrative reviews, and animal studies were excluded. Literature search was updated to October 2019.

Summary of Evidence

Four studies were identified that examined the use of ventilation strategies in 93 adults or children after drowning.[81–84] The studies included 1 retrospective observational study with 88 patients,[84] 1 case series comprising 3 children,[81] and 2 case reports.[82,83] All articles reported survival status at hospital discharge. Two articles reported neurological outcome (Glasgow Coma Scale) and severity of oxygen impairment.[82,84] Three studies reported the feasibility of noninvasive ventilation (NIV) use in patients with respiratory failure after drowning.[81,82,84]

In a multicenter, retrospective observational study across 7 French intensive care units (ICUs), 48 adults received NIV (both continuous positive airway pressure and bilevel positive airway pressure; average positive end-expiratory pressure [PEEP], 8±2 cm H_2O) to treat moderate to severe lung injury (mean $Pa_{O_2}/F_{I_{O_2}}$ ratio, 156 mm Hg).[84] Compared with patients treated with invasive mechanical ventilation, those receiving NIV had a better initial neurological and hemodynamic status. NIV was successful in 92% (44 of 48), with an average duration of ventilation of 1.4 days. Both mechanical ventilation and NIV were associated with rapid improvement of oxygenation (within 6 hours) and short ICU length of stay. Two further articles reported successful use of NIV to treat drowning-related acute lung injury in hemodynamically stable adults[82,83] and children.[81]

Task Force Insights

NIV appears feasible as a treatment for moderate to severe lung injury caused by drowning. The published experience involves mostly patients with higher Glasgow Coma Scale scores who were hemodynamically stable. Patients appear to respond within 12 to 24 hours. The indications for the optimal time to transition to invasive ventilation if NIV is unsuccessful require further research.

Treatment Recommendations

There was no previous treatment recommendation on mechanical ventilation after drowning. The lack of evidence in the drowning setting supports the use of standard general recommendations for the management of acute respiratory distress syndrome.[85]

ECMO in Drowning (BLS 856: ScopRev)

Rationale for Review

ECMO and ECPR have been used in the treatment of severe drowning with refractory hypoxia or cardiac arrest.

The full text of this ScopRev can be found on the ILCOR website.[86]

PICO, Study Design, and Time Frame

- Population: Adults and children who are submerged in water
- Intervention: ECMO
- Comparator: No ECMO
- Outcome: Any clinical outcome (eg, survival, survival with a favorable neurological outcome, hospitalization), CPR quality, physiological end points
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Manikin studies were included only if no human studies were available.
- Time frame: From 2000 onward. All languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols), narrative reviews, and ani-

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mal studies were excluded. Literature search was updated to October 2019.

Summary of Evidence

Thirteen studies were identified that examined the use of extracorporeal support in 658 adults and children after drowning.[87–99] The studies included 2 retrospective observational studies[88,89] and 11 case series.[87,90–99] Some articles reported overlapping data: 1 study[91] reported cases from 3 other case series,[90,92,98] whereas 2 studies appear to report the same cases.[90,92] All 13 articles reported survival status, and 9 reported neurological outcomes.[87,89–92,94,96–99] Outcome measures reported for neurological outcome were the Glasgow Coma Scale[98,99] or the Cerebral Performance Category (CPC)[89] or were undefined.

Most studies reported the use of venoarterial ECMO for patients who were in cardiac arrest,[89–93,95–99] whereas 3 studies reported using venoarterial ECMO for patients in cardiac arrest and venovenous ECMO for respiratory failure.[87,88,94] Most uses of ECMO appeared in the context of patients who had been submerged in cold water leading to hypothermia (core temperature range, 13 °C–31 °C).[89,90,92,95,96,99] When reported, the duration of submersion ranged between 15 and 90 minutes.[89,90,92,93,95,96,99] The duration of ECMO treatment was between 2 and 260 hours.[89,90,98,99]

The Extracorporeal Life Support Organization registry reported the use of ECMO among 251 patients treated for drowning from multiple centers around the world between 1986 and 2015.[88] Survival to discharge (71.4%) was highest for patients who did not have a cardiac arrest. Survival was 57% for patients who required CPR before ECMO and 23.4% in patients who received ECPR. Survival rates across the other studies for patients with cardiac arrest ranged from 10% to 100%. Survival with a favorable neurological outcome was between 5% and 57%. Outcomes were better for patients who required ECMO for respiratory support rather than conventional ECPR.[94]

Factors reported as associated with worse outcomes were the requirement for ECPR,[88] hyperkalemia,[91,96] hypoxemia as the primary cause of cardiac arrest,[91,97] asystole as an initial rhythm,[90] submersion duration of >10 minutes,[96] low pH,[90] renal failure,[88] and requirement for CPR while on ECMO.[88] Factors associated with good outcomes were profound hypothermia (core body temperature <26 °C) and normal potassium.[89]

Task Force Insights

Extracorporeal oxygenation to treat cardiac arrest or severe respiratory failure caused by drowning is feasible, but further research is required to refine the indications and optimal timing for initiating ECMO in adults and children who develop cardiac arrest or severe lung injury after drowning. The evidence identified supports the existing ILCOR treatment recommendation.[68] Similarly, the evidence identified for severe respiratory failure is consistent with guidelines suggesting the use of ECMO in select patients with severe acute respiratory distress syndrome (weak recommendation, very low–certainty evidence).[85]

Treatment Recommendations

There was no previous treatment recommendation on ECMO after drowning. The evidence identified supports the ILCOR treatment recommendation that states "ECPR may be considered as a rescue therapy for selected patients with cardiac arrest when conventional CPR is failing in settings in which it can be implemented (weak recommendation, very low–certainty evidence)."[68] A SysRev will be pursued by the BLS and ALS Task Forces.

Criteria for Discharge in Drowning (BLS 856: ScopRev)

Rationale for Review

Submersion leads to a spectrum of presentations from no or mild symptoms to severe hypoxemia or cardiac arrest. Patients with milder symptoms may not require hospitalization. Some investigators have suggested discharge criteria that can be used to guide the decision about whether to admit or discharge from the scene or emergency department.

The full text of this ScopRev can be found on the ILCOR website.[86]

PICO, Study Design, and Time Frame

- Population: Adults and children who are submerged in water
- Intervention: Criteria for discharge after submersion
- Comparator: Other criteria for discharge after submersion
- Outcome: Any clinical outcome (eg, survival, survival with a favorable neurological outcome, hospitalization)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Manikin studies were included only if no human studies were available.
- Time frame: From 2000 onward. All languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols), narrative reviews, and animal studies were excluded. Literature search was updated to October 2019.

Summary of Evidence

Five studies were identified for final data abstraction,[70,71,100–102] all of which were retrospective observational studies, including 1 with both derivation and validation arms.[102] Four studies were performed in the United States,[70,100–102] and 1 was performed in Israel.[71] In total, 834 patients were analyzed, all of whom were <18 years of age.

All studies correlated objective clinical findings to determine factors that could predict safe discharge early in the clinical phase. These factors include pulmonary examination (744 patients),[71,100–102] oxygen saturation in air (834 patients),[70,71,100–102] pulse rate (673 patients),[100–102] blood pressure (673 patients),[100–102] mental status (744 patients),[71,100–102] need for airway support (535 patients),[70,102] and dyspnea (744 patients).[71,100–102] Three studies evaluated specific safe discharge times, specifically 6 hours[71,100] and 8 hours,[102] with the remaining studies solely comparing discharged patients to admitted patients. Additional objective factors that were analyzed were chest radiography (341 patients)[70,71,101] and arterial blood gas results (161 patients).[70,71]

Pooled together, these studies found that for drowning patients <18 years of age presenting to the emergency department with normal mentation, an observation period of at least 6 hours appears to be sufficient to allow any clinical deterioration to be revealed. Patients who remain with normal mentation, no need for supplemental oxygen, and normal age-adjusted vital signs can be considered for discharge at that time.

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Task Force Insights

This small body of evidence demonstrated associations between clinical and physiological factors and the likelihood of hospital admission after a submersion incident. Of the studies identified, none prospectively tested a clinical decision rule to identify patients who can be safely discharged. Future studies should consider creating and validating clinical decision rules.

Treatment Recommendations

There was no treatment recommendation on criteria for discharge after submersion; a SysRev will be pursued by the BLS Task Force.

Topics Reviewed by EvUps

The topics reviewed by EvUps are summarized in Table 1, and complete EvUps are provided in Supplemental Appendix B1.

Advanced Life Support

Early CAG After ROSC (SysRev)

Rationale for Review

In 2015, ILCOR recommended early CAG for patients with ROSC after cardiac arrest and ST-segment elevation on ECG.[103,104] For select post-ROSC patients without ST-segment elevation but with suspected cardiac cause of cardiac arrest, early CAG was suggested, although the evidence was acknowledged to be of very low–certainty and at high risk of bias. It was also acknowledged that it was very unclear which patients might benefit, and the evidence at that time was primarily observational. Because of the recent publication of additional evidence, including RCTs, on the question of CAG after ROSC after cardiac arrest, this SysRev was undertaken to evaluate the impact of early CAG on key clinical outcomes in patients who remain comatose after ROSC following cardiac arrest of presumed cardiac origin. The review was registered on PROSPERO (CRD42020160152).

The full text of this CoSTR can be found on the ILCOR website.[105]

PICO, Study Design, and Time Frame

- Population: Unresponsive* adults (>18 years of age) with ROSC after cardiac arrest
- Intervention: Emergency or early CAG with percutaneous coronary intervention (PCI) if indicated; early CAG defined as within 2 to 6 hours
- Comparator: Delayed CAG defined as within 24 hours; both time intervals start at hospital arrival or from ROSC
  Outcome: Any clinical outcome prioritized as critical or important by the ALS Task Force
- Study design: 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.
- Time frame: The original SysRev search included dates from January 1990 through July 18, 2019, and the literature search was updated on April 20, 2020. All languages were included as long as there was an English abstract.

Consensus on Science

Because of the known importance of the presence or absence of ST-segment elevation in determining the need for emergency CAG in the absence of cardiac arrest, the evidence is presented by the 3 patient populations of most clinical relevance: (1) no ST-segment elevation and any initial rhythm, (2) no ST-segment elevation and initial shockable rhythm, and (3) ST-segment elevation. We have included the cohort of undifferentiated ECG and all rhythms as well as an undifferentiated ECG and initial shockable rhythm because this addressed the original PICO, study design, time frame. Because of variation in the timing and occurrence of angiography in the comparator groups in the studies identified, the comparator group was changed to late (>6 hours after ROSC) or no angiography.

Data from observational studies with a serious or very serious risk of bias are included as supplementary material in Supplemental Appendix C1, and a table summarizing the characteristics for every study or trial included in this CoSTR is provided in Supplemental Appendix C2.

After ROSC, Without ST-Segment Elevation on ECG, and All Initial Rhythms

For this patient population, 2 small RCTs[106,107] were identified, only 1 of which[106] reported outcomes considered critical by the ALS Task Force. No significant difference was found between groups for any of these outcomes in the 99 patients included. Evidence was deemed low certainty for all outcomes, and key data are presented in Table 2.

Very low–certainty evidence from the second pilot RCT[107] enrolling 78 patients with ROSC after OHCA found no improvement in the important outcome of 24-hour survival with early CAG compared with late or no CAG (OR, 2.06 [95% CI, 0.48–8.90]; RR, 1.08 [95% CI, 0.92–1.27]; absolute survival difference, 0.07 [95% CI, −0.08 to 0.22], or 71 of 1000 more patients survived at 24 hours [95% CI, 80 fewer–221 more]).

After ROSC, Without ST-Segment Elevation on ECG, and Shockable Initial Rhythm

A single RCT[108] enrolling 538 patients was identified for patients without ST-segment elevation after ROSC with an initial shockable rhythm. The outcomes and certainty of evidence for this RCT are presented in Table 3.

For the critical outcome of survival with favorable neurological outcome at hospital discharge (CPC 1), 1 observational study[109] including 4029 patients provided low-certainty evidence of benefit with early CAG compared with late or no CAG (adjusted OR, 1.60 [95% CI, 1.14–2.26], no raw data provided). An additional study[110] including 203 patients also provided very low–certainty evidence of benefit for favorable neurological outcome (CPC 1–2) at ICU discharge associated with early CAG (adjusted OR, 2.77 [95% CI, 1.31–5.85], no raw data provided).

After ROSC, With ST-Segment Elevation on ECG

For the critical outcome of survival to hospital discharge, we identified very low–certainty evidence from 1 observational study[110] of 112 patients that found no effect with early CAG compared with late or no CAG (OR, 1.89 [95% CI, 0.48–7.40]).

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Table 1 – BLS Topics Reviewed by EvUps

Topic/PICO	Year(s) last updated	Existing treatment recommendation	RCTs since last review, n	Observational studies since last review, n	Sufficient data to warrant SysRev?
Paddle size and placement for defibrillation (new)	2010 CoSTR; 2020 ScopRev	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 for optimal external defibrillation in adults. However, it is reasonable to use a pad size >8 cm.	0	0	No
CPR before call for help (BLS 1527)	2020 CoSTR	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
Barrier devices (BLS 342)	2005 CoSTR	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	4	No
Chest compression rate (BLS 343)	2015 CoSTR; 2020 ScopRev	We recommend a manual chest compression rate of 100–120/min (strong recommendation, very low–quality evidence).	0	0	No
Rhythm check timing (BLS 345)	2020 CoSTR	We suggest against the checking of cardiac rhythm immediately after defibrillation (weak recommendation, very low–certainty evidence).	0	0	No
Timing of CPR cycles (2 min vs other) (BLS 346)	2020 CoSTR	We suggest pausing chest compressions every 2 min to assess the cardiac rhythm (weak recommendation, low-certainty evidence).	0	0	No
Public-access AED programs (BLS 347)	2020 CoSTR	We recommend the implementation of public-access defibrillation programs for patients with OHCAs (strong recommendation, low-certainty evidence).	0	2	No
Check for circulation during BLS (BLS 348)	2015 CoSTR; 2020 EvUp	Outside of the ALS environment where invasive monitoring is available, there are insufficient data on the value of a pulse check while performing CPR. We therefore do not make a treatment recommendation on the value of a pulse check.	0	0	No
Rescuer fatigue in chest compression–only CPR (BLS 349)	2010 CoSTR	No treatment recommendation	3 (simulation)	1 (simulation)	No
Harm from CPR to victims not in cardiac arrest (BLS 353)	2020 CoSTR	We recommend that laypersons initiate CPR for presumed cardiac arrest without concerns of harm to patients not in cardiac arrest (strong recommendation, very low–certainty evidence).	0	2	No
Harm to rescuers from CPR (BLS 354)	2010 CoSTR; 2020 ScopRev	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 defibrillator shock with an AED during BLS is also safe. The incidence and morbidity of defibrillator-related injuries in the rescuers are low.	0	0	No

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Table 1 (continued)

Topic/PICO	Year(s) last updated	Existing treatment recommendation	RCTs since last review, n	Observational studies since last review, n	Sufficient data to warrant SysRev?
Hand position during compressions (BLS 357)	2020 CoSTR	This treatment recommendation is unchanged from 2015: We suggest performing chest compressions on the lower half of the sternum on adults in cardiac arrest (weak recommendation, very low–certainty evidence).	0	2	No
Dispatcher instructions in CPR (BLS 359)	2019 CoSTR	We recommend that emergency medical dispatch centers have systems in place to enable call handlers to provide CPR instructions for adult patients in cardiac arrest (strong recommendation, very low–certainty evidence). We recommend that emergency medical call takers provide CPR instructions (when deemed necessary) for adult patients in cardiac arrest (strong recommendation, very low–certainty evidence).	0	8	No
EMS chest compression–only vs conventional CPR (BLS 360)	2017 CoSTR	We recommend that EMS providers perform CPR with 30 compressions to 2 breaths (30:2 ratio) or continuous chest compressions with PPV 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 OHCA (weak recommendation, very low–certainty evidence).	0	0	No
Feedback for CPR quality (BLS 361)	2020 CoSTR	We suggest the use of real-time audiovisual feedback and prompt devices during CPR in clinical practice as part of a comprehensive quality improvement program for cardiac arrest designed to ensure high-quality CPR delivery and resuscitation care across an EMS system (weak recommendation, very low–certainty evidence). We suggest against the use of real-time audiovisual feedback and prompt devices in isolation (ie, not part of a comprehensive quality improvement program) (weak recommendation, very low–certainty evidence).	0	3	Yes
CV ratio (BLS 362)	2017 CoSTR	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
CPR before defibrillation (BLS 363)	2020 CoSTR	We suggest a short period of CPR until the defibrillator is ready for analysis or defibrillation in unmonitored cardiac arrest (weak recommendation, low-certainty evidence).	0	0	No
Chest compression depth (BLS 366)	2015 CoSTR	We recommend a chest compression depth of ≈5 cm (2 in) (strong recommendation, low-quality evidence) while avoiding excessive chest compression depths (>6 cm [>2.4 in] in an average adult) (weak recommendation, low-quality evidence) during manual CPR.	0	0	No
Chest wall recoil (BLS 367)	2015 CoSTR	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	0	No
Removal of FBAO (BLS 368)	2020 CoSTR	We suggest that back slaps are used initially in adults and children with an FBAO and an ineffective cough (weak recommendation, very low–certainty evidence). We suggest that abdominal thrusts are used in adults and children (>1 y of age) with an FBAO and an ineffective cough when	0	4	No

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Table 1 (continued)

Topic/PICO	Year(s) last updated	Existing treatment recommendation	RCTs since last review, n	Observational studies since last review, n	Sufficient data to warrant SysRev?
		back slaps 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 an FBAO (weak recommendation, very low–certainty evidence). We suggest that appropriately skilled health care providers use Magill forceps to remove an FBAO in patients with OHCA from FBAO (weak recommendation, very low–certainty evidence). We suggest that chest thrusts be used in unconscious adults and children with an FBAO (weak recommendation, very low–certainty evidence). We suggest that bystanders undertake interventions to support FBAO 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).			
Firm surface for CPR (BLS 370)	2020 CoSTR	We suggest performing manual chest compressions on a firm surface when possible (weak recommendation, very low–certainty evidence). During IHCA, we suggest that when a bed has a CPR mode that increases mattress stiffness, it should be activated (weak recommendation, very low–certainty evidence). During IHCA, we suggest against moving a patient from a bed to the floor to improve chest compression depth (weak recommendation, very low–certainty evidence). The confidence in effect estimates is so low that the task force was unable to make a recommendation about the use of a backboard strategy.	0	1	No
Analysis of rhythm during chest compression (BLS 373)	2020 CoSTR	We suggest against the routine use of artifact-filtering algorithms for analysis of electrocardiographic rhythm during CPR (weak recommendation, very low–certainty evidence). 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).	0	2	Yes
Alternative compression techniques (cough CPR, precordial thump, fist pacing) (BLS 374)	2020 CoSTR	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 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) attributable to bradyasystole if such a nonperfusing rhythm is recognized promptly before loss of consciousness	0	0	No

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Table 1 (continued)

Topic/PICO	Year(s) last updated	Existing treatment recommendation	RCTs since last review, n	Observational studies since last review, n	Sufficient data to warrant SysRev?
		(weak recommendation, very low–certainty evidence). We recommend against the use of a precordial thump for cardiac arrest (strong recommendation, very low–certainty evidence).			
Tidal volumes and ventilation rates (BLS 546)	2010 CoSTR	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
Lay rescuer chest compression–only vs standard CPR (BLS 547)	2017 CoSTR	We continue to recommend that bystanders perform chest compressions for all patients in cardiac 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 adults in cardiac arrest (weak recommendation, very low–certainty evidence).	2 (simulation)	4	No
Starting CPR (C-A-B vs A-B-C) (BLS 661)	2020 CoSTR	We suggest starting CPR with compressions rather than ventilation (weak recommendation, very low–certainty evidence).	0	0	No
Dispatch diagnosis of cardiac arrest (BLS 740)	2020 CoSTR	We recommend that dispatch centers implement a standardized algorithm or standardized criteria to determine immediately if a patient is in cardiac arrest at the time of emergency call (strong recommendation, very low–certainty evidence). We suggest that dispatch centers monitor and track diagnostic capability. We suggest that dispatch centers look for ways to optimize sensitivity (minimize false-negatives). We recommend high-quality research that examines gaps in this area.	1	6	Yes
Resuscitation care for suspected opioid-associated emergencies (BLS 811)	2020 CoSTR	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 circulatory arrest (weak recommendation based on expert consensus).	0	0	No
Drowning (BLS 856)	2020 CoSTR	We recommend that submersion duration be used as a prognostic indicator when making decisions on search and rescue resource management/operations (strong recommendation, moderate-certainty evidence). We suggest against the use of age, EMS response time, water type (fresh or salt), water temperature, and witness status when making prognostic decisions (weak recommendation, very low–certainty evidence. We acknowledge that this review excluded exceptional and rare case reports that identify good outcomes after prolonged submersion in icy water.	0	0	No
Dispatcher-assisted continuous chest compressions vs conventional CPR (new)	2017 CoSTR	We recommend that dispatchers provide chest compression–only CPR instructions to callers for adults with suspected OHCA (strong recommendation, low-quality evidence).	0	0	No

A-B-C indicates airway-breaths-compressions; AED, automated external defibrillator; ALS, advanced life support; BLS, basic life support; CoSTR, Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations; C-A-B, compressions-airway-breaths; CPR, cardiopulmonary resuscitation; CV, compression-to-ventilation; EMS, emergency medical services; EvUps, evidence updates; FBAO, foreign body airway obstruction; HBV, hepatitis B virus; IHCA, in-hospital cardiac arrest; OHCA, out-of-hospital cardiac arrest; PICO, population, intervention, comparator, outcome; PPV, positive-pressure ventilation; RCT, randomized controlled trial; SARS, severe acute respiratory syndrome; ScopRev, scoping review; and SysRev, systematic review.

CoSTR documents are available at https://costr.ilcor.org/.

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Table 2 – RCT[106] Data for Effect of Early CAG Compared With No Early CAG on Critical Outcomes in Patients Without ST-Segment Elevation After ROSC, All Initial Rhythms

Outcome	OR (95% CI)	RR (95% CI)	Absolute difference, n patients/1000 (95% CI)
Survival at hospital discharge	1.33 (0.60–2.93)	1.15 (0.78–1.68)	71 more (122 fewer–257 more)
CPC 1–2* at hospital discharge	1.22 (0.56–2.69)	1.11 (0.74–1.67)	50 more (142 fewer–237 more)
Survival at 30 d	1.44 (0.65–3.18)	1.20 (0.81–1.77)	91 more (103 fewer–275 more)
CPC 1–2* at 30 d	1.35 (0.59–3.08)	1.21 (0.71–2.07)	68 more (117 fewer–247 more)
Survival at 180 d	1.50 (0.66–3.40)	1.25 (0.80–1.96)	100 more (98 fewer–288 more)
CPC 1–2* at 180 d	1.38 (0.58–3.29)	1.26 (0.68–2.33)	67 more (111 fewer–239 more)

Evidence was low certainty for all outcomes.

CAG indicates coronary angiography; CPC, Cerebral Performance Category; OR, odds ratio; RCT, randomized controlled trial; ROSC, return of spontaneous circulation; and RR, risk ratio.

* CPC 1 to 2 is considered a favorable neurological outcome in most studies.

Table 3 – RCT[108] Data for Effect of Early CAG Compared With Late or No CAG on Outcomes in Patients Without ST-Segment Elevation After ROSC, Initial Shockable Rhythm

Outcome	Certainty of evidence	OR (95% CI)	RR (95% CI)	Absolute difference, npatients/1000 (95% CI)
Survival at hospital discharge	Low	0.85 (0.60–1.22)	0.95 (0.84–1.07)	36 fewer (119 fewer–41 more)
Survival at 90 d	Low	0.89 (0.62–1.27)	0.96 (0.85–1.08)	26 fewer (113 fewer–50 more)
CPC 1–2* at ICU discharge	Low	0.80 (0.56–1.14)	0.90 (0.77–1.06)	55 fewer (144 fewer–32 more)
CPC 1–2* at 90 d	Low	0.94 (0.66–1.33)	0.98 (0.86–1.11)	14 fewer (97 fewer–60 more)
Percutaneous intervention frequency†	High	1.54 (1.06–2.25)	1.37 (1.04–1.79)	88 more (11–176 more)
Coronary artery bypass grafting	Moderate	0.87 (0.45–1.67)	0.88 (0.48–1.60)	10 fewer (46 fewer–157 more)

CAG indicates coronary angiography; CPC, Cerebral Performance Category; ICU, intensive care unit; OR, odds ratio; RCT, randomized controlled trial; ROSC, return of spontaneous circulation; and RR, risk ratio.

* CPC 1 to 2 considered a favorable neurological outcome in most studies.

† Results are from intention-to-treat analysis. A per-protocol analysis was also performed and is included in the online CoSTR.

The same observational study[110] found no difference in the critical outcome of favorable neurological outcome at hospital discharge (CPC no greater than 2) (OR, 1.12 [95% CI, 0.3–4.19]).

After ROSC, All ECGs (Undifferentiated)

For the critical outcome of survival at 30 days, 1 observational study[111] enrolling 1722 patients provided low- certainty evidence of benefit from the use of early CAG compared with late or no CAG (OR, 1.43 [95% CI, 1.12–1.83]; absolute difference, 64 more patients of 1000 survived with the intervention [95% CI, 19–116]). The same observational study[111] provided very low–certainty evidence showing no difference in the critical outcome of survival at 1 to 3 years (adjusted OR, 1.79 [95% CI, 0.93–3.45]; absolute difference, 77 more patients of 1000 survived with the intervention [95% CI, 8 fewer–201 more]).

For the critical outcome of survival with favorable neurological outcome at discharge, we identified very low–certainty evidence from 3 observational studies[109,112,113] enrolling 8124 patients that found benefit from early CAG compared with late or no CAG (OR, 1.93 [95% CI, 1.20–3.10]).

For the critical outcome of survival with favorable neurological outcome at 3 to 6 months (CPC 1–2), we identified very low–certainty evidence from 1 observational study[114] including 544 patients that reported no effect of early CAG compared with late or no CAG (OR, 0.92 [95% CI, 0.69–1.18]).

For the important outcome of successful PCI, we identified very low–certainty evidence from 3 non-RCTs[114–116] including 1117 patients that found higher frequency of successful PCI in the intervention group compared with the control group (intention-to-treat analysis OR, 6.21 [95% CI, 4.45–8.67]; RR, 4.08 [95% CI, 3.09–5.40]; absolute risk difference [ARD], 0.31 [95% CI, 0.26–0.35], or 308 more patients/1000 had successful PCI in the intervention group [95% CI, 260–354 more]). A per-protocol analysis including only patients who underwent CAG is included in the online CoSTR.

After ROSC, All ECGs (Undifferentiated) With Initial Shockable Rhythm

For the critical outcome of survival with favorable neurological outcome at hospital discharge (CPC 1), we identified very low–certainty evidence from 1 observational study[109] of 4029 patients who identified benefit with early CAG (OR, 1.47 [95% CI, 1.36–1.72]).

Evidence for adverse events is reported in the online CoSTR.

Treatment Recommendations

When CAG is considered for comatose postarrest patients without ST-segment elevation, we suggest that either an early or a delayed approach for CAG is reasonable (weak recommendation, low-certainty evidence).

We suggest early CAG in comatose post–cardiac arrest patients with ST-segment elevation (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is provided in Supplemental Appendix A2.

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Without ST-Segment Elevation. In making the above recommendations, the task force weighed the fact that we did not find sufficient evidence to demonstrate improved outcomes with early CAG for post–cardiac arrest patients without ST-segment elevation regardless of presenting cardiac arrest rhythm (shockable or nonshockable). Patients in cardiogenic shock after cardiac arrest were excluded from all studies, and there is unlikely ever to be sufficient clinical equipoise to support a randomized trial of delayed intervention in the shock cohort. There may be subgroups of patients without ST-segment elevation with high-risk features who would benefit from earlier CAG.

It may be that survival and functional survival may not be the right outcomes to measure harm or benefit from an intervention that adjusts the timing of PCI in postarrest patients. For most patients admitted after CA who subsequently die, the cause of death is usually neurological injury rather than cardiac complications. There are no significant differences in adverse event rates with either time interval.

With ST-Segment Elevation. For comatose patients with ST-segment elevation, there is no randomized clinical evidence for the timing of CAG. The ALS Task Force acknowledges that early CAG, with PCI if indicated, is the current standard of care for patients with ST-segment–elevation myocardial infarction who did not have a cardiac arrest. We found no evidence to change this approach in patients with ST-segment elevation after cardiac arrest.

Task Force Knowledge Gaps

- Whether early CAG improves survival or survival with favorable neurological outcome for postarrest patients with ST-segment elevation
- Whether CAG compared with no CAG improves outcomes in postarrest patients
- Whether CAG and PCI improve outcomes in the no–ST-elevation cohort who present in shock
- Whether early CAG compared with late or no CAG is beneficial after cardiac arrest occurring in the in-hospital setting
- Whether CAG and PCI are beneficial compared with thrombolysis and what the impact of the treatment interval is on the outcome from these interventions
- Whether postarrest CAG and PCI have an effect on longer-term outcomes
- The effect of postarrest CAG and PCI on health-related quality-of-life outcomes
- Whether timing of CAG has an effect on more novel outcomes such as functional or biochemical measures

CPR and Defibrillation in the Prone Position (SysRev)

Rationale for Review

Evidence from clinical trials suggests that placing patients with severe hypoxemic respiratory failure in the prone position can improve oxygenation and survival.[117] Prone positioning has been used increasingly during the COVID-19 pandemic, both for patients requiring mechanical ventilation and for patients with hypoxemia not yet requiring mechanical ventilation. When a patient has a cardiac arrest while in the prone position, there is little guidance on whether it is preferable to begin CPR while the patient is still prone or to supinate the patient immediately and begin CPR in the more standard supine position. This task force–led SysRev was undertaken to attempt to answer this question, and the review was registered on PROSPERO (registration CRD42021230691).

The full text of this CoSTR is available on the ILCOR website.[118]

PICO, Study Design, and Time Frame

- Population: Adults and children with cardiac arrest occurring while in the prone position
- Intervention: Performing CPR or defibrillation while the patient remains in the prone position
- Comparator: Turning the patient supine before initiation of CPR or defibrillation
- Outcome: Arterial blood pressure during CPR, time to initiation of CPR, time to defibrillation for shockable rhythms during CPR, end-tidal capnography during CPR, ROSC, survival, and survival with favorable neurological outcome to discharge or $\geq$30 days
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies), case series, and case reports were eligible for inclusion. Case series and reports were included because the writing group is aware that the human data on prone CPR are extremely limited and there is a need for guidance, given the use of prone position for patients severely ill with COVID-19. Unpublished studies (eg, conference abstracts, trial protocols) and editorials were excluded, although case reports published in letter form could be included. ScopRevs and SysRevs were included for discussion and to ensure that no primary articles were missed, but data were not extracted primarily from these reviews.
- Time frame: All years and all languages were included as long as there was an English abstract. The literature search was conducted on December 9, 2020.

Consensus on Science

Of 20 adult case reports, 12 patients had chest compressions started in the prone position,[119–130] and 8 were supinated before chest compressions were started.[131–137] Of the 12 pediatric case reports, 11 children had chest compressions started while prone,[114,124–127,129–132,136] whereas 1 was supinated first.[128] Of all 32 case reports, 31 were of patients in a prone position in the operating room, most often with head fixation or other devices that could considerably hinder the ability to turn the patient supine safely and quickly. Only 1 adult case report involved a patient in the prone position in the ICU.[122]

Comparisons of the critical outcomes of survival to $\geq$30 days and survival to hospital discharge and the important outcome of ROSC from prone versus supine CPR are presented in Table 4 (adult case reports) and Table 5 (pediatric case reports). The critical outcome of survival with favorable neurological outcome was not explicitly or formally reported in any of the case reports.

The important outcome of time to CPR was reported in only a minority of case reports and, in those reports, usually as an estimate (eg, immediate), making comparisons difficult. Two simulation studies reported that the time to supinate to start chest compressions was 50±34 seconds[148] to 110 seconds.[121] Time to start of chest compressions (in supine position) of 77±31 seconds was reported in 1 simulation study of cardiac arrest in the prone position.[148]

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Table 4 – Commonly Reported Outcomes for CPR Started in Prone Versus Supine Position: 20 Adults

Outcome	Adult: CPR started prone (n=12), n[119–130]		Adult: patient supinated before CPR (n=8), n[131–137]	
	Cases reporting	Achieving outcome	Cases reporting	Achieving outcome
ROSC	12	12/12	8	3/8
Survival to hospital discharge	5	5/5	7	2/7
Survival to ≥30 d	1	1/1	6	2/6

CPR indicates cardiopulmonary resuscitation; and ROSC, return of spontaneous circulation.

Table 5 – Commonly Reported Outcomes for CPR Started in Prone Versus Supine Position: 12 Children

Outcome	Child: CPR started prone (n=11), n[129,138–146]		Child: patient supinated before CPR (n=1), n[147]	
	Cases reporting	Achieving outcome	Cases reporting	Achieving outcome
ROSC	11	10/11	1	1/1
Survival to hospital discharge	10	7/10	1	1/1
Survival to ≥30 d	5	2/5	0	NA

CPR indicates cardiopulmonary resuscitation; NA, not applicable; and ROSC, return of spontaneous circulation.

For the important outcome of time to defibrillation, 1 simulation study reported a time to prone defibrillation of 22 seconds (1 group) compared with an average time (13 groups) of 108±61 seconds when the patient was supinated before defibrillation.[148] Time to defibrillation was not reported in any case report.

For the important outcome of arterial blood pressure during CPR, we identified very low–certainty evidence from 2 small, nonrandomized studies enrolling a total of 17 patients who had already been declared dead after conventional supine CPR, comparing arterial blood pressure during CPR delivered with the patient prone with that obtained with the patient supine.[149,150] Both studies reported significantly higher systolic blood pressure during compressions in the prone position.[149,150]

The important outcome of end-tidal carbon dioxide ($ETCO_2$) during CPR was reported in 5 adult patients,[123–125,130,134] with values ranging from 15 mm Hg[130] to 33 mm Hg,[125] and 2 pediatric patients, both of whom had an $ETCO_2$ at least 10 mm Hg with prone compressions.[138,139]

Treatment Recommendations

For patients with cardiac arrest occurring while in the prone position with an advanced airway already in place and for whom immediate supination is not feasible or poses significant risk to the patient, initiating CPR while the patient is still prone may be a reasonable approach (good practice statement).

Invasive blood pressure monitoring and continuous $ETCO_2$ monitoring may be useful to ascertain whether prone compressions are generating adequate perfusion, and this information could inform the optimal time to turn the patient supine (good practice statement).

For patients with cardiac arrest occurring while in the prone position without an advanced airway already in place, we recommend turning the patient supine as quickly as possible and beginning CPR (strong recommendation, very low–certainty evidence).

For patients with cardiac arrest with a shockable rhythm who are in the prone position and cannot be supinated immediately, attempting defibrillation in the prone position is a reasonable approach (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is provided in Supplemental Appendix A2.

Although the task force would not usually generate treatment recommendations from extremely low–certainty evidence, the COVID-19 pandemic has resulted in many critically ill patients treated with prone positioning and has made this an important question for clinicians worldwide.

The task force weighed the risk of delaying chest compressions and defibrillation while a patient is supinated against the risk of CPR and defibrillation being less effective in the prone position and acknowledged that the balance of risks is unclear.

The task force considered that further studies would be feasible and useful. These could include larger case series from single or multiple centers or case reports on quality metrics such as $ETCO_2$ and arterial blood pressure during prone compressions. More data on patients in the ICU in particular are needed because virtually all published case reports on prone CPR concern patients positioned prone for spinal or brain surgery in the operating room.

In many ICU settings, patients receiving mechanical ventilation in the prone position are highly likely to have arterial lines and continuous $ETCO_2$ monitoring, thus enabling the effectiveness of prone compressions to be determined rapidly. The task force discussed that evidence of ineffective compressions ($ETCO_2$ or mean arterial pressure below the usual CPR targets) could indicate more urgency to supination.

The difficulty of supinating a patient will vary widely depending on patient size; personnel present; interventions in place such as chest tubes, advanced airways, and intravenous lines; personal protective equipment (PPE) and isolation requirements; potentially open wounds; exposed hardware; or unstable spine (in the case of patients having surgery). This may affect decisions on whether to perform CPR prone or to supinate a patient first.

The cause of the cardiac arrest will determine the urgency of supination. For example, a primary airway problem such as a dislodged tracheal tube will require immediate supination, whereas the need for hemorrhage control during surgery in the prone position may necessitate resuscitation in the prone position.

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Task Force Knowledge Gaps

There is almost no evidence beyond case reports on this topic. Some highlighted knowledge gaps include the following:

- The average time taken to supinate a critically ill patient or a patient in the operating room in a real clinical setting
- Data on outcomes in patients arresting in the prone position who receive CPR or defibrillation while prone compared with those who are supinated before CPR start or defibrillation
- Comparative data on CPR metrics such as $ETCO_2$ and arterial blood pressure during compressions done in the prone and supine positions, as well as time to CPR start and first defibrillation or dose of epinephrine
- The risk of aerosolization or infection transmission from supinating a patient in cardiac arrest
- Optimal hand placement and defibrillator pad placement for prone CPR and defibrillation

Consciousness During CPR (ScopRev)

Rationale for Review

CPR-induced consciousness is increasingly described. Rescuer and survivor experiences encompass multiple themes that can occur at different times relative to cardiac arrest, CPR, and recovery; reported experiences include transcendent mystical experiences, visual and auditory awareness with a perceived sense of bodily detachment, dream-like states, and CPR-induced consciousness, as well as conscious experiences related to emergence from coma. We aimed to describe reported experiences, assess whether any interventions could have been used to prevent them (eg, the use of sedatives), and determine whether a SysRev is warranted.

The full text of this ScopRev is available on the ILCOR website.[151]

PICO, Study Design, and Time Frame

- Population: Adults in any setting with consciousness during CPR
- Intervention: Sedation, analgesia, or other intervention to prevent consciousness
- Comparator: No specific intervention for consciousness
- Outcome: Any clinical outcome, including cardiac arrest outcomes and psychological well-being after arrest. Rescuer outcomes were also considered.
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were all eligible for inclusion. For the purpose of the ScopRev, we also included case reports and case series, gray literature, and unpublished studies (eg, conference abstracts, trial protocols). Articles based on the Lazarus phenomenon and cough CPR and narrative articles referring to near-death experiences and consciousness were excluded but noted for discussion.
- Time frame: All years and languages were included as long as there was an English title or abstract. The literature search was conducted on November 24, 2020.

Summary of Evidence

We identified observational studies looking at diverse aspects of consciousness and sedation in patients. In 143 survivors of in-hospital cardiac arrest or OHCA from the United States, sedation or analgesia immediately before, during, or after CPR was not associated with the development of posttraumatic stress disorder.[152] A UK study of awareness during CPR in 140 survivors of in-hospital cardiac arrest identified 2 patients who described awareness with explicit recall of seeing and hearing events during their resuscitation.[153] In interviews of Australian health care professionals (doctors, nurses, paramedics), 59 of 67 had witnessed CPR-induced consciousness during which the patient had not interfered with the CPR attempt, with 10 reporting having to pause CPR, 7 reassuring the patient, 16 using sedation or neuromuscular-blocking drugs, and 2 using physical restraints.[154] Consciousness during CPR interfering with resuscitation (eg, the patient preventing chest compressions or trying to pull out tubes and lines) was reported by 51 of 63 interviewees, with 7 pausing CPR, 23 using sedation or paralyzing drugs, and 7 using physical restraints. The interviews highlighted a need for further guidance on this issue. An observational study of 16 558 OHCAs in Victoria, Australia (2008–2014), identified 112 cases (0.7%) of CPR-induced consciousness, including eye opening (20.5%), speech (29.5%), body movement (87.5%), or a combination of these responses.[155] Forty-two patients (37.5%) were given drugs (midazolam, opioids, or neuromuscular-blocking drugs). Consciousness during CPR was associated with witnessed arrests and improved outcomes when no drugs were given. Another Australian study of 23 011 OHCAs in Queensland (2007–2018) identified 52 cases (0.23%) of CPR-induced consciousness with combativeness or agitation in 34.6% as the most common sign.[156] Consciousness was associated with witnessed cardiac arrest, EMS-witnessed arrest, and cardiac arrest in a public place with an initial shockable rhythm, which were in turn associated with improved ROSC and survival. Twenty-four case reports or series that described 31 cases of consciousness during CPR were published since 1962, with sedative drugs being used in ≈30%.[157–180] Existing drug regimens were identified that included the use of ketamine, midazolam, or fentanyl or a combination of these drugs.

Task Force Insights

The ALS Task Force concluded that there is insufficient evidence to warrant a formal SysRev. Distinguishing between overt physical signs of consciousness and transcendental cognitive experiences may be important because the psychological impact may vary greatly. Patients with physical signs of consciousness are more likely to experience pain and distress than those with out-of-body–type experiences; thus, optimal management may be different.

Evidence suggests that CPR-induced consciousness may have harmful effects on the rescuer and that CPR-induced consciousness probably signifies very recent sudden cardiac arrest and effective brain perfusion during CPR, thus being associated with better outcomes.

Some patient recall of events during CPR may relate to events that occurred before cardiac arrest, after ROSC, or during recovery. There needs to be a wider recognition of patient cognitive experiences among clinicians. Many patients are afraid to discuss these experiences because they feel that clinicians will not be receptive. There is a need for space to discuss these experiences and a need for awareness of resources available to manage ongoing problems such as posttraumatic stress disorder in both patients and rescuers.

There is an absence of standardized reporting criteria for the phenomena experienced by patients during CPR. In addition, the optimal drugs (including dosage) to manage CPR-induced consciousness

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(speed of effectiveness and impact on cardiac arrest outcomes) are unknown. Sedative drugs may have harmful cardiovascular effects, beneficial neuroprotective effects, or both. How sedative drugs given during CPR may affect post-ROSC consciousness and thus decision-making on the indication for targeted temperature management is unknown. In the absence of evidence to the contrary, drug regimens should be extrapolated from experience of sedation and analgesia in critically ill patients and using the smallest possible drug dose to achieve a desired effect.

Treatment Recommendations

This is a new topic, and there is insufficient evidence to warrant progressing to a SysRev of interventions for CPR-induced consciousness. Given the interest in this topic, the task force considered the available evidence and made the following good practice statements:

In settings in which it is feasible, rescuers may consider using sedative or analgesic drugs (or both) in very small doses to prevent pain and distress to patients who are conscious during CPR (good practice statement).

Neuromuscular-blocking drugs alone should not be given to conscious patients (good practice statement).

The optimal drug regimen for sedation and analgesia during CPR is uncertain. Regimens can be based on those used in critically ill patients and according to local protocols (good practice statement).

Evidence Updates

The topics reviewed by EvUps are summarized in Table 6, and complete EvUps are provided in Supplemental Appendix B2.

Neonatal Life Support

Cord Management at Birth for Preterm Infants (SysRev)

Rationale for Review

Clamping the umbilical cord at birth has a significant impact on a newborn's cardiovascular system. In the seconds and minutes immediately after birth, placental venous return and its contribution to systemic blood pressure and flow remain critical.[181] When breathing begins, inflation of the lung increases pulmonary blood flow, enabling pulmonary venous return to replace umbilical venous return as the primary source of preload for the left ventricle. Cardiac output markedly increases, and the heart rate stabilizes. In contrast, for infants who are apneic and hypoxic at birth, immediate cord clamping decreases cardiac output. Because increased cardiac output counteracts the effects of hypoxemia, limiting the increase in cardiac output exposes the infant to the combination of ischemia and hypoxia.[182] Such instability can be avoided if the infant's lungs are aerated and pulmonary blood flow increases before the umbilical cord is clamped. Large swings in arterial pressure and flow are reduced, leading to a more stable circulatory transition.[182]

For many years, the umbilical cord was routinely clamped immediately after birth. However, improved understanding of the potentially negative effects of immediate cord clamping led to investigation and use of many different cord-management strategies for preterm infants. In 2015, the ILCOR Neonatal Life Support Task Force published 2 CoSTRs summarizing the evidence comparing later (delayed) cord clamping (≥30 seconds) with earlier cord clamping (<30 seconds) and comparing intact-cord milking with early cord clamping for preterm newborn infants.[183,184] Additional evidence has accumulated, and alternative techniques have been studied. Thus,

Table 6 – ALS Topics Reviewed by EvUps

Topic/PICO	Year(s) last updated	Existing treatment recommendation	Relevant studies since last review, n	Sufficient data to warrant SysRev?
Transition from nonshockable to shockable rhythm (ALS 444)	2010 CoSTR	None	No studies	No
Oxygen dose during CPR (ALS 889)	2015 CoSTR; 2020 EvUp	We suggest using the highest possible inspired oxygen concentration during CPR (weak recommendation, very low–certainty evidence).	No studies	No
Steroids during CPR (ALS 433)	2015 CoSTR; 2020 EvUp	For IHCA, the task force was unable to reach a consensus recommendation for or against the use of steroids during cardiac arrest. We suggest against the routine use of steroids during CPR for OHCA (weak recommendation, very low–certainty evidence).	2 SysRevs, 3 RCTs registered with trial registries yet to report	Consider after publication of ongoing RCTs
Confirmation of correct tracheal tube position (ALS 469)	2015 CoSTR	We recommend using waveform capnography to confirm and continuously monitor the position of a tracheal tube during CPR in addition to clinical assessment (strong recommendation, low-quality evidence).	1 SysRev, 2 observational studies	No

(continued on next page)

Table 6 (continued)

Topic/PICO	Year(s) last updated	Existing treatment recommendation	Relevant studies since last review, n	Sufficient data to warrant SysRev?
Automatic ventilators vs manual ventilation during CPR (ALS 490)	2010 CoSTR	There is insufficient evidence to support or refute the use of an automatic transport ventilator over manual ventilation during resuscitation of the patient with cardiac arrest with an advanced airway.	2 RCTs (simulation studies), 2 observational studies	No
Cardiac arrest caused by asthma (ALS 492)	2010 CoSTR	There is insufficient evidence to suggest any routine change to cardiac arrest resuscitation treatment algorithms for patients with cardiac arrest caused by asthma.	1 observational study	No
ECPR vs manual or mechanical CPR (ALS 723)	2019 CoSTR	We suggest that ECPR may be considered as a rescue therapy for selected patients with cardiac arrest when conventional CPR is failing in settings in which it can be implemented (weak recommendation, very low–certainty evidence).	1 RCT	No
Postresuscitation steroids (ALS 446)	2010 CoSTR; 2020 EvUp	There is insufficient evidence to support or refute the use of corticosteroids alone or in combination with other drugs after cardiac arrest.	1 SysRev, 1 RCT not yet reported, 2 further RCTs ongoing	Consider after publication of ongoing RCTs
Oxygen dose after ROSC in adults (ALS 448)	2020 CoSTR	We recommend avoiding hypoxemia in adults with ROSC after cardiac arrest in any setting (strong recommendation, very low–certainty evidence). We suggest avoiding hyperoxemia in adults with ROSC after cardiac arrest in any setting (weak recommendation, low-certainty evidence).	1 SysRev, 1 RCT subgroup analysis, 12 observational studies	Consider after publication of ongoing RCTs
Neuroprognostication after ROSC (ALS 450, 458, 460, 484, 487, 713)	2020 CoSTR	We recommend that neuroprognostication always be undertaken with a multimodal approach because no single test has sufficient specificity to eliminate false positives (strong recommendation, very low–certainty evidence). Clinical examination: We suggest using PLR at $\geq$72 h after ROSC for predicting neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence). We suggest using quantitative pupillometry at $\geq$72 h after ROSC for predicting neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, low-certainty evidence).We suggest using bilateral absence of corneal reflex at $\geq$72 h after ROSC for predicting poor neurological outcome in adults who are comatose after cardiac arrest (weak recommendation, very low-certainty evidence).We suggest using presence of myoclonus or status myoclonus within 7 d after ROSC, in combination with other tests, for predicting poor neurological outcome in adults who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence). We also suggest recording EEG in the presence of myoclonic jerks to detect any associated epileptiform activity (weak recommendation, very low–certainty evidence). Electrophysiology: We suggest using a bilaterally absent N20	1 SysRev, 10 observational studies	No

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Table 6 (continued)

Topic/PICO	Year(s) last updated	Existing treatment recommendation	Relevant studies since last review, n	Sufficient data to warrant SysRev?
		wave of SSEP in combination with other indices to predict poor outcome in adult patients who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence). We suggest against using the absence of EEG background reactivity alone to predict poor outcome in adult patients who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence). We suggest using the presence of seizure activity on EEG in combination with other indices to predict poor outcome in adult patients who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence).		
		We suggest using burst suppression on EEG in combination with other indices to predict poor outcome in adult patients who are comatose and effects of sedation after cardiac arrest have cleared (weak recommendation, very low–certainty evidence). Serum biomarkers: We suggest using NSE within 72 h after ROSC, in combination with other tests, for predicting neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence). There is no consensus on a threshold value. We suggest against using S-100B protein for predicting neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, low-certainty evidence). We suggest against using serum levels of glial fibrillary acidic protein, serum tau protein, or neurofilament light chain for predicting poor neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence) Neuroimaging: We suggest using GWR on brain computed tomography for predicting neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence). However, no GWR threshold for 100% specificity can be recommended. We suggest using diffusion-weighted brain MRI for predicting neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence). We suggest using ADC on brain MRI for predicting neurological outcome of adults who are comatose after cardiac arrest (weak recommendation, very low–certainty evidence).		

ADC indicates apparent diffusion coefficient; ALS, advanced life support; CoSTR, International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations; CPR, cardiopulmonary resuscitation; ECPR, extracorporeal cardiopulmonary resuscitation; EEG, electroencephalogram; EvUp, evidence update; GWR, gray matter–to–white matter ratio; IHCA, in-hospital cardiac arrest; MRI, magnetic resonance imaging; NSE, neuron-specific enolase; OHCA, out-of-hospital cardiac arrest; PICO, population, intervention, comparator, outcome; PLR, pupillary light reflex; RCT, randomized controlled trial; ROSC, return of spontaneous circulation; SSEP, somatosensory evoked potential; and SysRev, systematic review.

CoSTR documents are available at https://costr.ilcor.org/.

ILCOR prioritized scientific review of all umbilical cord-management strategies for preterm births (PROSPERO registration CRD42019155475).[186]

The full text of this CoSTR can be found on the ILCOR website.[187]

PICO, Study Design, and Time Frame

- Population: Moderate, very, and extremely preterm infants (or equivalent birth weight) <34 (+0) weeks (plus days) gestation
- Intervention: (1) Later (delayed) cord clamping, (2) intact-cord milking, and (3) cut-cord milking
- Comparator:
  - A. Early clamping of the cord (at <30 seconds after birth)
  - B. Between-intervention comparisons
  - C. Delayed cord clamping at ≥30 seconds to <60 compared with ≥60 seconds
  - D. Delayed cord clamping based on time since birth compared with physiological approach to cord clamping (until cessation of pulsation or based on vital signs monitoring)
    - Definitions used in PROSPERO submission:
      - Early cord clamping, defined as application of a clamp to the umbilical cord at <30 seconds after birth of the infant without cord milking
      - Later (or delayed) cord clamping, defined as application of a clamp to the umbilical cord ≥30 seconds after birth or based on physiological parameters (such as when cord pulsation has ceased or breathing has been initiated), without cord milking
      - Intact-cord milking (also referred to as stripping), defined as repeated compression of the cord from the placental side toward the infant with the connection to the placenta intact at any time point immediately after birth
      - Cut-cord milking (also referred to as stripping), defined as drainage of the cord by compression from the cut end toward the infant after clamping and cutting of a long segment
- Outcome: Additional details on outcomes and prioritization are provided in the full online CoSTR.[187]
  - A. Survival; neurodevelopmental outcomes (with age-appropriate, validated tools); inpatient morbidities (eg, intraventricular hemorrhage, necrotizing enterocolitis, retinopathy of prematurity, chronic lung disease); hematological and cardiovascular status (in hospital), hyperbilirubinemia treated with phototherapy; maternal complication (postpartum hemorrhage, infection); resuscitation (need for PPV±intubation±chest compressions±medications)
- Study design: RCTs and cluster RCTs in preterm infants (<34 weeks' gestational age) or low–birth-weight infants (<2500 g) were included. For those studies that reported a broad population of infants (including both preterm infants of <34 weeks' gestation, late preterm infants, and term infants), studies recruiting a preponderance of preterm infants (defined as a mean gestational age <34 weeks or reported >80% of infants as preterm <34 weeks' gestational age) were included. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: All years and all languages were included if there was an English abstract. Literature search was last conducted on July 26, 2019.

Consensus on Science

Comparison 1: Later (Delayed) Cord Clamping (≥30 Seconds) Compared With Early Cord Clamping (<30 Seconds). The SysRev[186] identified 23 trials (3513 infants) for this comparison. Most studies included infants of <34 weeks' gestational age, and most were done in high-income countries.[188–210]

Data relating to the key critical and important infant and maternal outcomes for this comparison are summarized in Table 7. Evidence for additional outcomes evaluated is included in the full online CoSTR.[187]

Comparison 2: Intact-Cord Milking Compared With Early Cord Clamping. The SysRev identified 13 trials including 1170 infants for this comparison.[196,211–222]

Data relating to the key critical and important infant and maternal outcomes for this comparison are summarized in Table 8. Evidence for additional outcomes evaluated is included in the full online CoSTR.[187]

Comparison 3: Cut-Cord Milking Compared With Early Cord Clamping (Based on Timing of Delay Clamping <30 Seconds). For this comparison, a single study enrolling 60 patients[223] provided very low–certainty evidence that could not exclude benefit or harm for any of the included outcomes except hematocrit in the first 24 hours after birth, for which a benefit from cut-cord milking compared with early cord clamping was suggested.

Comparison 4: Later (Delayed) Cord Clamping (≥30 Seconds) Compared With Intact-Cord Milking. The SysRev identified 7 trials (1073 infants) for this comparison.[196,224–229] For the critical outcome of survival to discharge, moderate-certainty evidence from 5 trials involving 1000 infants could not exclude benefit or harm from later cord clamping.[224–226,228,229] For all other outcomes evaluated, results were similarly inconclusive.

Comparisons 5 Through 8. For comparisons 5 (later [delayed] cord clamping [≥30 seconds] compared with cut-cord milking), 6 (intact-cord milking compared with cut-cord milking), 7 (later [delayed] cord clamping ≥60 seconds versus later [delayed] cord clamping [≥30 and <60 seconds]), and 8 (later [delayed] cord clamping [≥30 seconds] versus physiological approach), no studies were identified that met inclusion criteria.

Subgroup Analyses

There were many prespecified subgroup analyses and comparisons. If subgroup data were not available, we performed subgroup analyses according to study characteristics when applicable. These subgroup analyses are exploratory and must be interpreted with caution, especially for interaction tests between studies and by strata that were not used in randomization.

Subgroup Comparison: Later (Delayed) Cord Clamping Compared With Early Cord Clamping (Based on Gestational Age). This subgroup comparison found significant improvements in survival to discharge for preterm infants of <30 weeks' gestational age (moderate-certainty evidence from 3 trials[190,206,210] involving 1639 infants) but not 30 to 34 weeks (very low–certainty evidence from 1 trial[192] involving 461 infants). Moderate-certainty evidence

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Table 7 – Meta-Analysis for Comparison 1: Later (Delayed) Cord Clamping (≥30 Seconds) Compared With Early Cord Clamping (<30 Seconds) for Preterm Infants

Outcome	Included studies	Total, n	Certainty of evidence	RR (95% CI); I^2	Absolute difference (95% CI) or mean difference (95% CI); I^2
Survival to discharge	Armanian et al,[189] 2017 Backes et al,[190] 2016 Baenziger et al,[191] 2017 Das et al,[192] 2018 Duley et al,[195] 2018 Finn et al,[196] 2019 Hofmeyr et al,[198] 1988 Hofmeyer et al,[199] 1993 Kazemi et al,[200] 2017 Kinmond et al,[201] 1993 Kugelman et al,[202] 2007 McDonnell and Henderson-Smart,[205] 1997 Mercer et al,[203] 2003 Mercer et al,[204] 2006 Oh et al,[206] 2011 Rabe et al,[208] 2000 Ruangkit et al,[209] 2019 Tarnow-Modri et al,[210] 2017	2988	Moderate	1.02 (1.00–1.04); 0%	18/1000 more infants (0–36 more per 1000) survived when later cord clamping was intended than when early cord clamping was intended
Severe IVH	Armanian et al,[189] 2017 Backes et al,[190] 2016 Das et al,[192] 2018 Dong et al,[194] 2016 Duley et al,[195] 2018 Finn et al,[196] 2019 Kazemi et al,[200] 2017 Kugelman et al,[202] 2007 Mercer et al,[203] 2003 Mercer et al,[204] 2006 Rabe et al,[208] 2000 Rana et al,[207] 2018 Ruangkit et al,[209] 2019 Tarnow-Modri et al,[210] 2017	2972	Low	0.98 (0.67–1.42); 0%	1/1000 fewer infants (10 fewer–10 more per 1000) developed severe IVH when later cord clamping was intended than when early cord clamping was intended
Hb concentration within 24 h after birth	Baenziger et al,[191] 2007 Dong et al,[194] 2016 Finn et al,[196] 2019 Gokmen et al,[197] 2011	196	Moderate		MD, 1.24 g/dL (0.01–2.47); 79%
Hct within 24 h after birth	Armanian et al,[189] 2017 Backes et al,[190] 2016 Baenziger et al,[191] 2007 Das et al,[192] 2018	1022	High		MD, 2.63% (1.85–3.42); 5%

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Table 7 (continued)

Outcome	Included studies	Total, n	Certainty of evidence	RR (95% CI); I^2	Absolute difference (95% CI) or mean difference (95% CI); I^2
	Dipak et al,[193] 2017 Gokmen et al,[197] 2011 Kinmond et al,[201] 1993 Kugelman et al,[202] 2007 McDonnell and Henderson-Smart,[205] 1997 Mercer et al,[203] 2003 Mercer et al,[204] 2006 Oh et al,[206] 2011 Rabe et al,[208] 2000 Ruangkit et al,[209] 2019				
Hct within 7 d after birth	Tarnow-Mordi et al,[210] 2017	1550	High		MD, 2.70% (1.88–3.52)*
Inotropic support for hypotension within 24 h after birth	Dong et al,[194] 2016 Gokmen et al,[197] 2011 McDonnell and Henderson-Smart,[205] 1997 Oh et al,[206] 2011 Rabe et al,[208] 2000 Ruangkit et al,[209] 2019	351	Moderate	0.36 (0.17–0.75); 0%	91/1000 fewer infants (30–143 fewer per 1000) received inotropic support in 24 h after birth when later cord clamping was intended
Lowest MAP in the first 12 h after birth	Baenziger et al,[191] 2007 Finn et al,[196] 2019 Gokmen et al,[197] 2011 Kugelman et al,[202] 2007 Mercer et al,[203] 2003 Mercer et al,[204] 2006 Ruangkit et al,[209] 2019	374	Low		MD, 1.79 mm Hg (0.53–3.05); 0%
No. of infants receiving any blood transfusions	Armanian et al,[189] 2017 Das et al,[192] 2018 Dipak et al,[193] 2017 Dong et al,[194] 2016 Duley et al,[195] 2018 Finn et al,[196] 2019 Kugelman et al,[202] 2007 Mercer, et al,[204] 2006 Rabe et al,[208] 2000 Rana et al,[207] 2018 Ruangkit et al,[209] 2019 Tarnow-Mordi et al,[210] 2017	2910	Low	0.83 (0.77–0.90); 36%	71/1000 fewer infants (40–111 fewer per 1000) received any blood transfusions when later cord clamping was intended than when early cord clamping was intended
Maternal PPH (≥500 mL)	Duley et al,[195] 2018 Ruangkit et al,[209] 2019 Tarnow-Mordi et al,[210] 2017	1477	Low	0.93 (0.54–1.62); 52%; random effects	7/1000 fewer mothers (8 fewer–12 more per 1000) developed a PPH (≥500 mL) when later cord clamping was intended than when early cord clamping was intended

Hb indicates hemoglobin; Hct, hematocrit; IVH, intraventricular hemorrhage; MAP, mean arterial blood pressure; MD, mean difference; PPH, postpartum hemorrhage; and RR, risk ratio.

* There was only 1 trial, so no I^2 was available.

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Table 8 – Meta-Analysis for Comparison 2: Intact-Cord Milking Compared With Early Cord Clamping for Preterm Infants

Outcome	Included studies	Total, n	Certainty of evidence	RR (95% CI); I^2	Absolute difference (95% CI) or mean difference (95% CI); I^2
Survival to discharge	Alan et al,[211] 2014 Elimian et al,[212] 2014 El-Naggar et al,[213] 2019 Hosono et al,[214] 2018 Katheria et al,[215] 2014 Li et al,[218] 2018 March et al,[219] 2013 Mercer et al,[220] 2016 Silahli et al,[221] 2018 Song et al,[222] 2017	945	Moderate	1.02 (0.98–1.06); 24%	20/1000 more infants (10 fewer–50 more per 1000) survived to discharge with intact-cord milking than with early cord clamping
Hb within 24 h after birth	Elimian et al,[212] 2014 El-Naggar et al,[213] 2019 Finn et al,[196] 2019 Hosono et al,[214] 2008 Kildag et al,[216] 2016 Li et al,[218] 2018 March et al,[219] 2013 Mercer et al,[220] 2016 Silahli et al,[221] 2018	914	Moderate		MD, 1.18 g/dL (0.65–1.71); 71%; random effects
Hct within 24 h after birth	Elimian et al,[212] 2014 Katheria et al,[215] 2014 Kildag et al,[216] 2016 Li et al,[218] 2018 March et al,[219] 2013 Mercer et al,[220] 2016 Silahli et al,[221] 2018	774	Moderate		MD, 3.04% (1.28–4.80); 69%; random effects
Inotropic support for hypotension within 24 h after birth	Elimian et al,[212] 2014 El-Naggar et al,[213] 2019 Hosono et al,[214] 2018 Katheria et al,[215] 2014 Song et al,[222] 2017	439	Moderate	0.61 (0.44–0.84); 0%	125/1000 fewer infants (50–200 fewer per 1000) received inotropic support for hypotension within the first 24 h after birth when intact-cord milking was intended than when early cord clamping was intended
No. of infants receiving any blood transfusion	Alan et al,[211] 2014 Elimian et al,[212] 2014 Finn et al,[196] 2019 Hosono et al,[214] 2018 Katheria et al,[215] 2014 Li et al,[218] 2018 March et al,[219] 2013	545	Very low	0.73 (0.56–0.94); 56%; random effects	167/1000 fewer infants (40–333 fewer per 1000) received any blood transfusions when intact-cord milking was intended than when early cord clamping was intended
Severe maternal PPH (≥1000 mL)	Elimian et al,[212] 2014 Song et al,[222] 2017	266	Very low	2.83 (0.12–67.01); not applicable	10/1000 more mothers (20 fewer–30 more per 1000) developed a PPH (≥1000 mL) with intact-cord milking than with early cord clamping

Hb indicates hemoglobin; Hct, hematocrit; MD, mean difference; PPH, postpartum hemorrhage; and RR, risk ratio.

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from 12 trials involving 846 infants from both gestational age strata showed improved survival or no difference from later (delayed) clamping (≥30 seconds) compared with early cord clamping (<30 seconds)[189,191,195,198,199,201–205,208,209]

Subgroup Comparison: Later (Delayed) Cord Clamping Compared With Early Cord Clamping (Based on Setting Defined According to World Bank Country Classifications). This subgroup comparison found significant improvements in the critical outcome of survival to discharge from later (delayed) clamping (≥30 seconds) compared with early cord clamping (<30 seconds) in high-income countries[190,191,195,201–206] but not low- and middle-income countries.[189,192,198,199,209]

Subgroup Comparison: Intended Management in the Late Cord Clamping Group if Resuscitation Required: Resuscitation Before Cord Clamping Compared With Clamping and Cutting of Cord Followed by Resuscitation. One trial involving 270 infants stipulated an intention to provide respiratory support before delayed cord clamping.[195] Both this and the 5 included trials involving 331 infants with cord cut before respiratory support[195,199,203,204,208,209] and the 10 trials involving 2174 infants from studies that were unclear about whether respiratory support was given with intact or cut cord could not exclude benefit or harm from later clamping at ≥30 compared with <30 seconds.[189–192,198,201,202,205,206,210]

Subgroup Comparison: Later (Delayed) Cord Clamping Compared With Early Cord Clamping (Based on Duration of Clamping [30–<60, 60–120, >120 Seconds]). The results of this comparison did not show a linear dose response for the interval until intended cord clamping. For the critical outcome of survival to discharge, moderate-certainty evidence from 12 trials involving 1075 infants could not exclude benefit or harm from clamping at 30 to <60 compared with <30 seconds (RR, 1.00 [95% CI, 0.97–1.04]; I^2=0%).[189,190,192,199,201–206,208,209] Low-certainty evidence from 3 trials involving 1643 infants showed improved survival or no difference from clamping at 60 to 120 compared with <30 seconds (RR, 1.03 [95% CI, 1.00–1.10]; number needed to treat to benefit, 45 [95% CI, 21–>1000]; I^2=40%).[191,198,210] Low-certainty evidence from 1 trial involving 270 infants could not exclude benefit or harm from clamping at ≥2 minutes compared with <30 seconds (RR, 1.07 [95% CI, 0.99–1.15]).[195]

Treatment Recommendations

In infants born at <34 weeks' gestational age who do not require immediate resuscitation after birth, we suggest deferring clamping the cord for at least 30 seconds (weak recommendation, moderate-certainty evidence).

In infants born at 28+0 to 33+6 weeks' gestational age who do not require immediate resuscitation after birth, we suggest intact-cord milking as a reasonable alternative to deferring cord clamping (weak recommendation, moderate-certainty evidence).

We suggest against intact-cord milking for infants born at <28 weeks' gestational age (weak recommendation, very low–certainty evidence).

In infants born at <34 weeks' gestational age who require immediate resuscitation, there is insufficient evidence to make a recommendation with respect to cord management.

There is also insufficient evidence to make recommendations on cord management for maternal, fetal, or placental conditions that were considered exclusion criteria in many studies (in particular, multiple fetuses, congenital anomalies, placental abnormalities, alloimmunization, fetal anemia, fetal compromise, and maternal illness). In these situations, we suggest individualized decisions based on severity of the condition and assessment of maternal and neonatal risk (weak recommendation, very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is provided in Supplemental Appendix A3.

Our suggestions/recommendations were based on several inferences. First, the critical outcome of survival with later (delayed) clamping versus early clamping suggests benefit or neutrality from delaying clamping, and there are no significant differences in other critical outcomes for all comparisons. There is improvement in important cardiovascular (blood pressure), therapeutic (inotropic support or transfusions), and hematological outcomes with delayed (later) clamping or intact-cord milking versus early clamping. These beneficial effects may have a clinically important impact on inpatient care. Together with the potential benefit for survival to discharge, they influenced us to suggest either later (delayed) cord clamping or intact-cord milking (in the case of infants born at 28 to <34 weeks' gestational age) over early clamping, despite the lack of evidence for benefit for other critical outcomes.

One large clinical trial comparing intact-cord milking with later (delayed) cord clamping closed recruitment before completion because of an increased rate of severe intraventricular hemorrhage in infants born at <28 weeks' gestational age who received intact-cord milking.[224] However, meta-analysis of 4 trials involving 761 infants could not exclude benefit or harm from later (delayed) cord clamping compared with intact-cord milking (RR, 0.60 [95% CI, 0.32–1.12]; I^2=23%).[196,224,225,228] There was only 1 small study on cut-cord milking.

Post hoc and subgroup analyses did not conflict with our suggestions or recommendations. We do not have sufficient confidence in these findings to make separate recommendations for cord management by country income, gestational age, or interval from birth to cord clamping (>30 seconds). We consider that the beneficial effect of delayed clamping in high-income countries is likely to be widely generalizable and therefore should be offered in all settings.

There is very little evidence to make recommendations for cord management in the preterm infant needing immediate resuscitation.

Our suggestions and recommendations are provided in the context of both immediate and deferred clamping being commonly practiced after preterm delivery and in light of historical and regional changes in cord-management practices over past decades.[230] We acknowledge the perception of immediate clamping as a medical intervention and of deferring clamping as a natural, or physiological, approach and the paradox that many studies defined immediate clamping as the control.[231]

We were influenced by current cord-management practices with respect to preterm delivery. If our current norm were delayed clamping, we would have rejected early clamping and recommended further study of cord milking as an alternative in infants born at ≥28 weeks' gestational age. However, if our current norm were early clamping, our recommendations to change current practice would have to be more cautious, given the weak evidence.

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Some animal studies suggest that cardiorespiratory transition after birth occurs more effectively when cord clamping is deferred.[232] There are also societal, maternal, and practitioner preferences for the timing of cord clamping.

With respect to equity, acceptability, accessibility, and cost, deferring cord clamping for ≥30 seconds and intact-cord milking are inexpensive, readily available, universally applicable interventions that can be performed regardless of setting.[233] The beneficial effect of delayed clamping in high-income countries is likely to be generalizable; therefore, it should be offered in all settings. Although differences in maternal safety outcomes were not found, the data on maternal outcomes were limited.

Most trials allowed infants perceived to require resuscitation to have early cord clamping, even if they were assigned to late clamping in an RCT. Therefore, their optimal cord management remains unresolved. Several studies of resuscitation with the cord intact are planned or underway. Until they are completed, we consider we should defer our recommendation for this population.

With more studies and more options for comparisons, with or without resuscitation, the "Systematic Review and Network Meta-Analysis With Individual Participant Data on Cord Management at Preterm Birth (iCOMP): Study Protocol" may help identify the optimal cord-management strategy.[234] Similarly, individual patient meta-analyses may improve our ability to determine the most effective interventions.

The task force debated the certainty of evidence for the overall recommendation of delayed cord clamping. Although evidence for survival was of moderate certainty, the doubt raised by the post hoc analysis of mortality justified downgrading our primary recommendation to low-certainty evidence.

Task Force Knowledge Gaps

- Effect of cord management on long-term neurodevelopment outcomes or any other postdischarge outcomes
- The impact of cord management as a public health strategy on child health and development
- The best approach to cord management among preterm infants who require immediate resuscitation
- The best approach to cord management among preterm infants with specific conditions such as congenital heart or lung disease
- The long-term neurodevelopmental outcomes after intact-cord milking in extremely preterm infants
- The optimal timing of cord clamping and how it should be determined with different maternal or fetal conditions
- Few studies of cut-cord milking as a management strategy
- The impact of cord management on vertical transmission of infectious diseases
- Widely agreed-on nomenclature and definitions of different interventions, including delayed, deferred, later, optimal, and physiological cord clamping, as well as milking, stripping, intact cord, and cut cord

Cord Management at Birth for Term and Late Preterm Infants (SysRev)

Rationale for Review

Umbilical cord management affects every 1 of the 130 million babies born in the world each year. At the time of birth, ≈30% of the fetal-placental circulation is outside the fetus. Cord management affects the volume of placental transfusion to the newborn infant and the cardiovascular transition around the onset of breathing or ventilation.[235] Thus, early cord clamping before onset of breathing may have major hemodynamic consequences not only for preterm newborn infants but also for term and near-term, nonvigorous newborn infants. Cord management at birth also influences iron status and possibly neurodevelopment of full-term infants.[236,237] Iron deficiency in young children is associated with impaired motor development, behavioral problems, and cognitive delays.[238–240] Cord management and placental transfusion at birth may help to reduce iron deficiency.

The topic of later (delayed) cord clamping for late preterm and term infants was last reviewed by ILCOR in 2010.[241–243] The 2010 recommendation stated, "Delay in umbilical cord clamping for at least 1 minute is recommended for newborn infants not requiring resuscitation. There is insufficient evidence to support or refute a recommendation to delay cord clamping in babies requiring resuscitation." The publication of further important data led ILCOR to prioritize a review of umbilical cord–management strategies for all term and late preterm births (PROSPERO registration CRD4202015549).[235]

The full text of this CoSTR can be found on the ILCOR website.[244]

PICO, Study Design, and Time Frame

- Population: Term and late preterm infants (≥34 weeks' gestation) or equivalent birth weight
- Intervention:
  - Later (delayed) cord clamping: Cord clamping after a delay of at least 30 seconds
  - Intact-cord milking: Repeated compression of the cord from the placental side toward the baby with the connection to the placenta intact
  - Cut-cord milking: Drainage of the cord by compression from the cut end toward the baby after clamping and cutting a long segment
- Comparator:
  - Early clamping of the cord (clamping at <30 seconds after birth) without cord milking or initiation of respiratory support compared with each of the above interventions
  - Between-intervention comparisons
  - Later (delayed) cord clamping at <60 compared with ≥60 seconds
  - Later (delayed) cord clamping based on time since birth compared with physiological approach to cord clamping (until cessation of pulsation of the cord or based on vital signs monitoring/initiation of breathing)
- Outcome (Additional details on outcomes and prioritization are provided in the full online CoSTR[244]):
  - Primary outcomes:
    - Infant: Survival without moderate to severe neurodevelopmental impairment; anemia by 4 to 6 months after birth
    - Maternal: Postpartum hemorrhage
  - Secondary outcomes:
    - Neonatal: Mortality; moderate to severe hypoxic ischemic encephalopathy; resuscitation (PPV±intubation ±chest compressions); respiratory distress; admission to neonatal ICU or special care nursery; hemoglobin; hematocrit; hyperbilirubinemia treated with phototherapy; polycythemia; partial or full exchange transfusion

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■ Infant: Moderate to severe neurodevelopmental impairment; ferritin

■ Maternal: Death or severe morbidity; severe postpartum hemorrhage; manual removal of the placenta; postpartum infection

– A priori subgroups: Details about a priori subgroup comparisons are provided in the full online CoSTR.[244]

- Study design: RCTs, quasi-RCTs, and cluster RCTs. For studies that reported on a broad population of infants (including preterm infants of <34 weeks' gestation, late preterm infants, and term infants), we considered studies that had a preponderance of late preterm and term infants (defined as study populations comprising >80% late preterm or term infants). 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 was updated to July 26, 2019.

Consensus on Science

Comparison 1: Later (Delayed) Cord Clamping at ≥30 Seconds Compared With Early Cord Clamping at <30 Seconds After Birth. The SysRev identified 33 studies (5263 mothers and their infants) in this category. Data relating to key critical and important infant and maternal outcomes for this comparison are summarized in Table 9. Evidence for additional outcomes evaluated is included in the full online CoSTR.[244]

Comparison 2: Intact-Cord Milking Compared With Early Cord Clamping. The SysRev identified 1 small study of 24 infants that documented higher hemoglobin and hematocrit values in the intact-cord milking group compared with early cord clamping.[273]

Comparison 3: Cut-Cord Milking Compared With Early Cord Clamping. The SysRev identified 1 study (200 infants) in this category. Data related to key critical and important outcomes for this comparison are summarized in Table 10. Evidence for additional outcomes evaluated is included in the full online CoSTR.[244]

Comparison 4: Later (Delayed) Cord Clamping Versus Intact-Cord Milking. The SysRev identified 1 study.[275] No reliable assessment of treatment effects could be drawn because of serious methodological concerns about the study.

Comparison 5: Later (Delayed) Cord Clamping At ≥30 Seconds Compared With Cut-Cord Milking. The SysRev identified 3

Table 9 – Meta-Analysis of Comparison 1: Later (Delayed) Cord Clamping at ≥30 Seconds Compared With Early Cord Clamping at <30 Seconds After Birth for Term and Late Preterm Infants

Outcome	Included studies	Total, n	Certainty of evidence	RR (95% CI); I^2	Absolute difference (95% CI) or mean difference (95% CI); I^2
Neonatal mortality	Backes et al,[245] 2015 Ceriani Cernadas et al,[246] 2006 Chopra et al,[247] 2018 Datta et al,[248] 2017	537	Very low	2.54 (0.50–12.74); 0%	8/1000 more infants (10 fewer–30 more per 1000) died when later (delayed) cord clamping was intended than when early cord clamping was intended
Hb concentration within 24 h after birth	Al Tawil et al,[249] 2012 Chaparro et al,[250] 2006 De Paco et al,[251] 2016 Emhamed et al,[252] 2004 Fawzy et al,[253] 2015 Mohammad et al,[254] 2021 Salari et al,[255] 2014 Ultee et al,[256] 2008 Yadav et al,[257] 2015	1352	Very low		MD, 1.17 g/dL (0.48–1.86; corresponds to MD of 11.7 g/L [4.8–18.6]); 89%, random effects
Hct within 24 h after birth	Al Tawil et al,[249] 2012 Ceriani Cernadas et al,[258] 2006 Chaparro et al,[250] 2006 Chen et al,[259] 2018 Chopra et al,[247] 2018 Emhamed et al,[252] 2004 Jahazi et al,[260] 2008 Philip,[261] 1973 Salari et al,[255] 2014 Ultee et al,[256] 2008 Vural et al,[262] 2019 Yadav et al,[257] 2015	2183	Very low		MD, 3.38% (2.08–4.67); 81%, random effects
Polycythemia (Hct >65%)	Backes et al,[245] 2015 Ceriani Cernadas et al,[258] 2006 Chaparro et al,[250] 2006 Chopra et al,[247] 2018 Emhamed et al,[252] 2004 Grajeda et al,[263] 1997	1335	Low	2.26 (1.56–3.28); 0%	50/1000 more infants (30–80 more per 1000) had polycythemia in the later cord-clamping group compared with early cord clamping

Table 9 (continued)

Outcome	Included studies	Total, n	Certainty of evidence	RR (95% CI); I^2	Absolute difference (95% CI) or mean difference (95% CI); I^2
	Krishnan et al,[264] 2015 Mercer et al,[265] 2017 Saigal et al,[266] 1972 Salari et al,[255] 2014 Salea et al,[267] 2016 Ultee et al,[256] 2008 Van Rheenen et al,[268] 2007				
Hb concentration within 7 d after birth	Andersson et al,[269] 2011 Mercer et al,[265] 2017 Yadav et al,[257] 2015	695	Very low		MD, 1.11 g/dL (0.4–1.82); 82%, random effects
Hct within 7 d after birth	Cavallin et al,[270] 2019 Mercer et al,[271] 2018 Philip,[261] 1973 Salae et al,[267] 2016 Yadav et al,[257] 2015	590	Very low		MD, 5.84% (2.74–8.95); 91%, random effects
Anemia at 4–6 mo of age	Al-Tawil, 2012 et al,[249]Andersson et al,[269] 2011 Chaparro et al,[250] 2006 Van Rheenen et al,[268] 2007	937	Very low	1.01 (0.75–1.37); 0%	An equal number of infants (40 fewer–40 more per 1000) had anemia at 4–6 mo of age when later cord clamping was intended than when early cord clamping was intended
Maternal PPH (≥1000 mL)	Andersson et al,[272] 2015 Backes et al,[245] 2015 Ceriani Cernadas et al,[258] 2006 Chaparro et al,[250] 2006 Chen et al,[259] 2018	1828	Very low	0.75 (0.42–1.35); 0%	10/1000 fewer mothers (20 fewer–10 more per 1000) had a PPH (≥1000 mL) when later cord clamping was intended than when early cord clamping was intended

Hb indicates hemoglobin; Hct, hematocrit; MD, mean difference; PPH, postpartum hemorrhage; and RR, risk ratio.

Table 10 – Meta-Analysis of Comparison 3: Cut-Cord Milking Compared With Early Cord Clamping for Term and Late Preterm Infants

Outcome	Included studies	Total, n	Certainty of evidence	RR (95% CI)	Absolute difference (95% CI) or mean difference (95% CI); I^2
Neonatal mortality	Upadhyay et al,[274] 2013	200	Very low	0.20 (0.01–4.11)	20/1000 fewer infants (50 fewer–10 more per 1000) died when cut-cord milking was intended than when early cord clamping was intended
Hb concentration within 24 h after birth	Upadhyay et al,[274] 2013	200	Very low		MD, 1.60 g/dL (0.96–2.24); not available*
Hct within 24 h after birth	Upadhyay et al,[274] 2013	200	Very low		MD, 4.30% (2.36–6.24); not available*
Hb concentration within 7 d after birth	Upadhyay et al,[274] 2013	200	Very low		MD, 1.10 g/dL (0.74–1.46); not available*
Hct within 7 d after birth	Upadhyay et al,[274] 2013	200	Very low		MD, 4% (2.29–5.71); not available*

Hb indicates hemoglobin; Hct, hematocrit; MD, mean difference; and RR, risk ratio.

* Only 1 trial available.

studies[257,276,277] (740 infants) in this category. Data relating to key critical and important infant outcomes for this comparison are summarized in Table 11. Evidence for additional outcomes evaluated is included in the full online CoSTR.[244]

Comparison 6: Intact-Cord Milking Compared With Cut-Cord Milking. No trials were identified.

Comparison 7: Later (Delayed) Cord Clamping at ≥60 Seconds Compared With Later (Delayed) Cord Clamping at <60 Seconds. The SysRev identified 7 studies[278–284] (2745 mothers and their infants) in this category.

Data relating to key critical and important outcomes are summarized in Table 12. Evidence for additional outcomes evaluated is included in the full online CoSTR.[244]

Comparison 8: Later (Delayed) Cord Clamping at ≥30 Seconds Compared With Physiological Approach to Cord Clamping (Until Cessation of Pulsation of the Cord or Based on Vital Signs Monitoring/Initiation of Breathing). The SysRev identified 3

Table 11 – Meta-Analysis of Comparison 5: Later (Delayed) Cord Clamping at ≥30 Seconds Compared With Cut-Cord Milking for Term and Late Preterm Infants

Outcome	Included studies	Total, n	Certainty of evidence	RR (95% CI)	Absolute difference (95% CI) or mean difference (95% CI); I^2
Neonatal mortality	Yadav et al,[257] 2015	300	Very low	1.00 (0.09 to 10.90)	An equal number of infants (20 fewer–20 more per 1000) died when later (delayed) cord clamping was intended than when cut-cord milking was intended
Hb concentration within 24 h after birth	Jaiswal et al,[276] 2015 Yadav et al,[257] 2015	500	Very low		MD, –0.56 g/dL (–0.92 to –0.21); 9%
Hct within 24 h after birth	Jaiswal et al,[276] 2015 Yadav et al,[257] 2015	500	Very low		MD, –1.60% (–3.11 to –0.09); 45%
Hb concentration within 7 d after birth	Jaiswal et al,[276] 2015 Yadav et al,[257] 2015	500	Very low		MD, –0.47 g/dL (–0.81 to –0.13); 0%
Hct within 7 d after birth	Jaiswal et al,[276] 2015 Yadav et al,[257] 2015	500	Very low		MD, –1.11% (–2.12 to –0.09); 0%

Hb indicates hemoglobin; Hct, hematocrit; MD, mean difference; and RR, risk ratio.

Table 12 – Meta-Analysis of Comparison 7: Later (Delayed) Cord Clamping ≥60 Seconds Versus Later (Delayed) Cord Clamping <60 Seconds for Term and Late Preterm Infants

Outcome	Included studies	Total, n	Certainty of evidence	RR (95% CI); I^2	Absolute difference (95% CI) or mean difference (95% CI); I^2
Neonatal mortality	Andersson et al,[278] 2019	231	Very low	0.10 (0.01–1.98)	30/1000 fewer infants (70 fewer–10 more per 1000) died when later (delayed) cord clamping ≥60 s was intended than when later (delayed) cord clamping <60 s was intended
Hb concentration within 24 h after birth	Katheria et al,[282] 2017	60	Very low		MD, 1.30 g/dL (0.14–2.46); not available**
Hyperbilirubinemia treated with phototherapy	Kc et al,[279] 2017 Nouraie et al,[283] 2019	906	Very low	1.93 (1.00–3.72); 60%	70/1000 more infants (0–204 more per 1000) had hyperbilirubinemia treated with phototherapy when later cord clamping ≥60 s was intended compared with when later cord clamping <60 s was intended
Neurodevelopmental outcomes in early childhood	Rana et al,[285] 2019	540	Very low	2.3 (1.44–3.78)	103/1000 more infants (34–216 more per 1000) would have ASQ-3 scores >279 when later cord clamping for ≥60 s was intended compared with when later cord clamping for <60 s was intended

ASQ-3 indicates Ages & Stages Questionnaire, Third Edition; Hb, hemoglobin; MD, mean difference; and RR, risk ratio.

* Only 1 study available.

studies[259,286,287] (1113 mothers and their infants) in this category. Data relating to several key critical and important outcomes for this comparison are shown in Table 13. Evidence for additional outcomes evaluated is included in the full online CoSTR.[244]

Subgroup Analyses

There were many prespecified subgroup analyses and multiple comparisons. The *P* values were not adjusted for multiple comparisons. If subgroup data were not available, we performed subgroup analysis according to study characteristics when applicable. These subgroup analyses are exploratory and must be interpreted with caution, especially for interaction tests between studies and by strata that were not used in randomization.

Subgroup: Later (Delayed) Cord Clamping at ≥30 Seconds Compared With Early Cord Clamping at <30 Seconds After Birth.

- A. Subgroups according to gestational age: For the important outcome of hyperbilirubinemia treated with phototherapy among term infants (≥37 weeks' gestation), low-certainty evidence from 13 trials involving 2691 infants[245,249,252,257,259,262,264,265,268–270,288,289] showed that more term infants in the later cord clamping group received phototherapy for hyperbilirubinemia (RR, 1.54 [95% CI, 1.01–2.34]; risk difference, 0.01 [95% CI, 0.00–0.03]; number needed to harm, 100; I^2=15%); 10 of 1000 more (95% CI, 0–30 more per 1000) term infants had hyperbilirubinemia treated with phototherapy after later cord clamping compared with early cord clamping. Among late preterm infants (34 to 36^{+6} weeks' gestation), low-certainty evidence from 2 trials involving

Table 13 – Meta-Analysis of Comparison 8: Later (Delayed) Cord Clamping at ≥30 Seconds Compared With Physiological Approach to Cord Clamping (Until Cessation of Pulsation of the Cord or Based on Vital Signs Monitoring/Initiation of Breathing) for Term and Late Preterm Infants

Outcome	Included studies	Total, n	Certainty of evidence	RR (95% CI); I^2	Absolute difference (95% CI) or mean difference (95% CI); I^2
Neonatal mortality	Sun et al,[287] 2017	338	Very low	5.00 (0.24 to 103.37)	12/1000 more infants (10 fewer–30 more per 1000) died when later (delayed) cord clamping was intended compared with when a physiological approach was intended
Hct within 24 h after birth	Chen et al,[259] 2018	540	Very low		MD, –1.40% (–2.79 to –0.01); not available**
Hb concentration within 7 d after birth	Sun et al,[287] 2017	338	Very low		MD, –1.70 g/dL (–1.97 to –1.43); not available**
Hct within 7 d after birth	Sun et al,[287] 2017	338	Very low		MD, –6.5% (–7.64 to –5.16); not available**
Severe PPH (≥1000 mL)	Chen et al,[259] 2018	540	Very low	1.82 (0.10 to 33.4); not available**	9/1000 more mothers (10 fewer–30 more per 1000) had a PPH (≥1000 mL) when later cord clamping was intended than when a physiological approach was intended

Hb indicates hemoglobin; Hct, hematocrit; MD, mean difference; PPH, postpartum hemorrhage; and RR, risk ratio.

* Only 1 study available.

123 infants[256,267] could not exclude benefit or harm from later cord clamping compared with early cord clamping (RR, 0.72 [95% CI, 0.37–1.40]; I^2=0%).

- B. Subgroups according to different resource settings based on World Bank country classifications: For the important outcomes of hematocrit values (percent) within the first 24 hours after birth, the evidence from 8 trials involving 1279 infants in low- or middle-income countries[247,250,252,255,257,258,260,262] and from 4 trials involving 904 infants in high-income countries[249,256,259,261] showed higher hematocrit values in the later cord clamping group compared with early cord clamping. The effect was greater in studies performed in high-income countries (*P* for interaction between subgroups=0.04).
- C. Subgroup analyses according to the timing of uterotonic medication administration and according to size for gestational age: The subgroup analyses for the timing of uterotonic medication administration and for size for gestational age did not reveal significant differences between subgroups.

Treatment Recommendations

For term and late preterm infants born at ≥34 weeks' gestation who are vigorous or deemed not to require immediate resuscitation at birth, we suggest later (delayed) clamping of the cord at ≥60 seconds (weak recommendation, very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is provided in Supplemental Appendix A3.

In making this recommendation, the Neonatal Life Support Task Force acknowledges that most studies comparing later cord clamping with early cord clamping in late preterm or full-term infants delayed clamping of the cord for ≥60 seconds. Later cord clamping facilitates postnatal cardiovascular transition,[181] increases hemoglobin and hematocrit in the neonatal period, and improves iron status in early infancy. Although there were no studies that showed that later cord clamping prevented the complications of iron deficiency anemia or associated developmental delay, we value the benefits of increased hemoglobin and the potential for improved iron status to benefit neurodevelopment during the critical periods of early infancy. These potential benefits may be greatest in settings where resources for evaluation of nutritional status are limited and iron deficiency and anemia are prevalent.

Later cord clamping is associated with increased rates of polycythemia and possible increase in the use of phototherapy for hyperbilirubinemia. Although there was no reported increase in the rates of exchange transfusions, these considerations are important in settings where resources for evaluation and treatment of hyperbilirubinemia are limited.

Only a few studies examined a physiological approach to cord clamping (delaying clamping until cessation of pulsation of the cord or on the basis of vital signs monitoring/initiation of breathing). Compared with early or time-based later cord clamping, this intervention improved neonatal hemoglobin and hematocrit. However, the effect on iron status, anemia in infancy, or neurodevelopment is uncertain.

Although cut-cord milking improves neonatal hemoglobin and hematocrit, it is unknown whether the intervention facilitates the postnatal cardiovascular transition in the same way as later cord clamping. There are only a few small studies, and no long-term outcomes were addressed, limiting assessment of safety. Although cut-cord milking may be useful when later cord clamping is contraindicated or not feasible, no included studies report its use in these situations.

There is insufficient evidence to recommend milking of the attached cord for term and late preterm infants.

Across all comparisons, there was no evidence that any of the studied cord-management strategies improved the primary infant outcome of survival without neurodevelopmental impairment. Likewise, there was no evidence that cord-management strategies altered important maternal outcomes, including postpartum hemorrhage. The small sample size of most trials and the associated risks of bias and imprecision limited the certainty of evidence for all outcomes of interest. Analysis of many outcomes could not exclude benefits or harm.

There have been historical and regional changes in cord-management practices over the past decades.[230] We acknowledge the perception of early clamping as a medical intervention and of later clamping as a natural, or physiological, approach and the paradox that many studies defined early clamping as the control.[231] As discussed with preterm cord clamping, current practices influence

the recommendations, animal studies provide evidence that cardiovascular transition after birth occurs more effectively when cord clamping is deferred,[181,290] and societal, maternal, and practitioner preferences influence decisions about the timing of cord clamping.

Later cord clamping is an inexpensive, readily available, universally applicable intervention that can be performed regardless of setting.[233] Many of the included studies did not record the exact time of cord clamping. The details of cord management, including the timing of clamping, should be routinely recorded in clinical practice and research studies.

Task Force Knowledge Gaps

- Whether the demonstrated reduction in early iron deficiency seen after later cord clamping improves long-term neurodevelopment. These studies need to be performed in low-resource and high-resource settings.
- The effects of cord-management practices on polycythemia and hyperbilirubinemia by using standardized protocols for diagnosis and management
- The optimal timing of later cord clamping and effects on important outcomes in the neonatal period, infancy, and childhood and for mothers
- Optimal cord-management practices (1) for infants who are not vigorous or are deemed to require immediate resuscitation at birth and (2) when there are contraindications to later cord clamping (eg, interrupted placental circulation). These studies should report the important outcomes in the neonatal period, infancy, and childhood and for mothers.
- Optimal cord-management practice in cesarean deliveries (under regional or general anesthesia), intrauterine growth restriction, multiple gestations, fetal anemia, fetal anomalies
- The impact of cord management on vertical transmission of infectious diseases
- The economic impact of different cord-management practices
- Parents' views about cord-management practices at birth

Finally, there is a need (in the settings of both clinical practice and research) to widely agree on nomenclature and definition of different interventions, including delayed, deferred, later, optimal, and physiological cord clamping, as well as milking, stripping, intact-cord and cut-cord.

Devices for Administering PPV at Birth (SysRev)

Rationale for Review

PPV is the most important step in neonatal resuscitation. Devices that can effectively deliver PPV are critical to successful resuscitation. In 2015, the ILCOR Neonatal Life Support Task Force published a CoSTR summarizing the evidence comparing the use of a T-piece resuscitator with the use of a self-inflating bag for newborns receiving ventilation during resuscitation.[183–185] The studies reviewed for the 2015 CoSTR noted that the use of T-piece resuscitators demonstrated marginal but not statistically significant benefits for the clinical outcome of achieving spontaneous breathing. The Neonatal Life Support Task Force reevaluated this topic with a ScopRev in 2020,[291] which identified sufficient new evidence to justify this new SysRev and reconsideration of current resuscitation guidelines (PROSPERO registration CRD42020200331).

The full text of this CoSTR can be found online.[292]

PICO, Study Design, and Time Frame

- Population: Newborn infants receiving PPV during resuscitation
- Intervention and comparator (shown in Table 14)
- Outcome: In-hospital mortality; severe intraventricular hemorrhage, Papile grade III to IV; intraventricular hemorrhage (any); bronchopulmonary dysplasia (BPD); CPR or medications in the delivery room; air leak; intubation in the delivery room; duration of PPV in the delivery room; length of stay; admission to neonatal ICU
- Study design: 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.
- Time frame: All years and all languages were included as long as there was an English abstract. Literature search was updated to December 30, 2020.

Consensus on Science

Comparison 1: T-Piece Resuscitator Compared With Self-Inflating Bag (With or Without PEEP Valve). The SysRev identified 4 RCTs[293–296] involving 1247 neonates and 1 prospective cohort study[297] involving 1962 neonates. Meta-analysis of RCT evidence for the critical outcomes of in-hospital mortality and BPD and the important outcome of duration of PPV is presented in Table 15.

For in-hospital survival, very low–certainty evidence from 1 prospective cohort study involving 1962 preterm infants[297] showed benefit from receiving PPV with a T-piece resuscitator compared with a self-inflating bag (RR, 0.71 [95% CI, 0.63–0.80]; $P<0.001$; $I^2=0\%$; ARD, −12.8% [95% CI, −16.4% to −8.9%]; number needed to treat, 8). For BPD, data from 1327 preterm infants in the same cohort study[297] also showed an association between PPV with a T-piece resuscitator and a reduction in BPD compared with a self-inflating bag (RR, 0.79 [95% CI, 0.65–0.96]; $P=0.02$; ARD, −6.6% [95% CI, −11.0% to −1.3%]; number needed to treat, 15).

For the critical outcome of severe intraventricular hemorrhage (grade III–IV), very low–certainty evidence from 1 prospective cohort

Table 14 – Comparison of PPV Devices in Newborns

Comparison	Intervention	Comparator
1	T-piece resuscitator	Self-inflating bag
2	T-piece resuscitator	Flow-inflating bag
3	Flow-inflating bag	Self-inflating bag
4	Self-inflating bag with PEEP valve	Self-inflating bag without PEEP valve

PEEP indicates positive end-expiratory pressure; and PPV, positive-pressure ventilation.

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Table 15 – Meta-Analysis of RCTs for Comparison 1: T-Piece Resuscitator Compared With Self-Inflating Bag (With or Without PEEP Valve)

Outcome	Included studies	Total, n	Certainty of evidence	RR (95% CI); I^2	Absolute risk difference (95% CI) or mean difference (95% CI); I^2
In-hospital mortality	Dawson et al,[293] 2011 Kookna et al,[294] 2019 Szyld et al,[295] 2014 Thakur et al,[296] 2015	1247	Very low	0.74 (0.40 to 1.34); 0%	10/1000 fewer infants (23 fewer–13 more per 1000) died in the T-piece resuscitator group than in the self-inflating bag group
BPD	Dawson et al,[293] 2011 Kookna et al,[294] 2019 Szyld et al,[295] 2014 Thakur et al,[296] 2015	1247	Very low	0.64 (0.43 to 0.95); 67%	32/1000 fewer infants (51 fewer–4 more per 1000) developed BPD in the T-piece resuscitator group than in the self-inflating bag group
Duration of PPV	Kookna et al,[294] 2019 Szyld et al,[295] 2014 Thakur et al,[296] 2015	1098	Moderate		MD, –19.8 s (–27.7 to –12)

ARD indicates absolute risk difference; BPD, bronchopulmonary dysplasia; MD, mean difference; PEEP, positive end-expiratory pressure; PPV, positive-pressure ventilation; RCT, randomized controlled trial; and RR, risk ratio.

study involving 1594 preterm infants[297] showed benefit from receiving PPV with a T-piece resuscitator compared with a self-inflating bag (RR, 0.75 [95% CI, 0.57–0.98]; *P*=0.04; ARD, −4.0% [95% CI, −6.9% to −0.3%]; number needed to treat, 24).

For the critical outcome of CPR or medications in the delivery room, very low–certainty evidence from 4 trials involving 1247 infants[293–296] could not exclude benefit or harm from receiving PPV with a T-piece resuscitator compared with a self-inflating bag. Very low–certainty evidence from 1 prospective cohort study involving 1962 preterm infants[297] also could not exclude benefit or harm for this outcome.

For the important outcome of intraventricular hemorrhage (all grades), very low–certainty evidence from 1 prospective cohort study involving 1594 preterm infants[297] showed benefit from receiving PPV with a T-piece resuscitator compared with a self-inflating bag (RR, 0.72 [95% CI, 0.63–0.83]; *P*<0.001; ARD, −12.9% [95% CI, −17% to −7.8%]; number needed to treat to benefit, 8). Evidence for the important outcomes of air leak, intubation in the delivery room, admission to a neonatal ICU, and length of hospitalization is provided in the full online CoSTR.[292]

Comparison 2: T-Piece Resuscitator Compared With Flow-Inflating Bag or Comparison 3: Flow-Inflating Bag Compared With Self-Inflating Bag. No studies were identified for these comparisons.

Comparison 4: Self-Inflating Bag With PEEP Valve Compared With Self-Inflating Bag Without PEEP Valve. For the critical outcome of in-hospital mortality, very low–certainty evidence from 2 trials involving 933 infants[295,298] could not exclude benefit or harm from receiving PPV with a self-inflating bag with a PEEP valve compared with one without a PEEP valve (RR, 0.99 [95% CI, 0.59–1.67]; *P*=0.97; ARD, 1 fewer patients per 1000 [95% CI, 24 fewer–39 more per 1000 patients] died when receiving PPV with a self-inflating bag with a PEEP valve).

For the critical outcome of BPD, low-certainty evidence from 1 trial involving 516 infants[295] could not exclude benefit or harm from receiving PPV with a self-inflating bag with a PEEP valve compared with one without a PEEP valve (RR, 1.03 [95% CI, 0.58–1.81]; *P*=0.93; ARD, 3 more patients per 1000 [95% CI, 35 fewer–68 more per 1000 patients] with BPD when receiving PPV with a self-inflating bag with a PEEP valve).

For the critical outcome of CPR or medications in the delivery room, very low–certainty evidence from 1 trial involving 516 infants[295] could not exclude benefit or harm from receiving PPV with a self-inflating bag with a PEEP valve compared with one without a PEEP valve (RR, 1.43 [95% CI, 0.54–3.80]; *P*=0.48; ARD, 11 fewer patients per 1000 [95% CI, 12 fewer–74 more] receive CPR or medications in the delivery room when receiving PPV with a self-inflating bag with a PEEP valve).

Evidence for several additional important outcomes (air leak, duration of PPV, intubation in the delivery room, admission to the neonatal ICU, length of hospitalization) is presented in the full online CoSTR.[292]

Subgroup Comparisons

Subgroup Analysis According to Gestational Age. The planned analyses by gestational age subgroups were not feasible because of limited data from the available studies.

Subgroup Analysis Comparing T-Piece Resuscitator With Self-Inflating Bag With or Without a PEEP Valve. The SysRev identified 1 RCT[295] involving 1027 infants.

T-Piece Resuscitator Compared With Self-Inflating Bag With PEEP Valve.. For the critical outcome of in-hospital mortality, low-certainty evidence from 1 trial involving 575 infants[295] could not exclude benefit or harm from receiving PPV with a T-piece resuscitator compared with a self-inflating bag with a PEEP valve (RR, 0.51 [95% CI, 0.15–1.67]; *P*=0.27; ARD, 14 fewer patients per 1000 [95% CI, 23 fewer–18 more] died when receiving PPV with a T-piece resuscitator).

For the critical outcome of BPD, moderate-certainty evidence from 1 trial involving 575 infants[295] showed benefit from receiving PPV with a T-piece resuscitator compared with a self-inflating bag with a PEEP valve (RR, 0.49 [95% CI, 0.25–0.95]; *P*=0.04; ARD, −4.4% [95% CI, −6.5% to −0.4%]; number needed to treat, 23).

For the critical outcome of CPR or medications in the delivery room, low-certainty evidence from 1 trial involving 575 infants[295] could not exclude benefit or harm from receiving PPV with a T-piece resuscitator compared with a self-inflating bag with a PEEP

valve (RR, 0.56 [95% CI, 0.21–1.48]; *P*=0.24; ARD, 17 fewer patients per 1000 [95% CI, 30 fewer–18 more] receive CPR or medications in the delivery room when receiving PPV with a T-piece resuscitator).

Evidence for important outcomes is presented in the full online CoSTR.[292]

T-Piece Resuscitator Versus Self-Inflating Bag Without a PEEP Valve.. For the critical outcomes of in-hospital mortality, need for CPR or medications in the delivery room, and BPD, low- to moderate-certainty evidence from 1 trial involving 452 infants[295] could not exclude benefit or harm from receiving PPV with a T-piece resuscitator compared with a self-inflating bag without a PEEP valve. Important outcomes are reported in the full online CoSTR.[292]

Treatment Recommendations

When resources permit, we suggest the use of a T-piece resuscitator over the use of a self-inflating bag in infants receiving PPV at birth (weak recommendation, very low–certainty evidence). A self-inflating bag should be available as a backup device for the T-piece resuscitator in case of gas-supply failure (technical remark).

There are no data to make a treatment recommendation for use of a T-piece resuscitator compared with a flow-inflating bag.

There are no data to make a treatment recommendation for use of a flow-inflating bag compared with a self-inflating bag.

The confidence in effect estimates is so low that the panel feels any recommendation for the use of a PEEP valve with a self-inflating bag versus a self-inflating bag without a PEEP valve is too speculative.

Subgroup considerations include the following:

- There are insufficient data for a recommendation based on gestational age because the planned subgroup analyses according to gestational age were not feasible.
- When resources permit, we suggest the use of a T-piece resuscitator over the use of a self-inflating bag either with or without a PEEP valve (weak recommendation, very low–certainty evidence). However, a self-inflating bag should be available as a backup for the T-piece resuscitator in the event of a gas-supply failure (technical remark).
- For the use of self-inflating bag with a PEEP valve versus the use of self-inflating bag without a PEEP valve, the data are too uncertain, so no recommendation can be made.

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table can be found in Supplemental Appendix A3.

Because the clinical evidence supporting the use of a T-piece resuscitator is of very low certainty, we have also considered evidence from animal studies showing that PEEP facilitates lung aeration. Animal studies suggest a benefit in using devices providing controlled levels of PEEP and peak inspiratory pressure to assist establishment of functional residual capacity during transition of a fluid-filled lung to an air-filled lung capable of supporting air breathing and to reduce lung damage secondary to barotrauma.[299–301] Benchtop and manikin studies demonstrate more consistent pressures and tidal volumes when a T-piece resuscitator is used than when a self-inflating bag is used.[302,303] However, the certainty of clinical evidence is not sufficient to recommend against using a self-inflating bag during neonatal resuscitation, particularly in regions where pressurized gases are not readily available.

Although subgroup analyses by gestation were not feasible, in contemporary neonatal practice, BPD is an outcome that affects mainly very preterm infants. Therefore, the reduction in the incidence of BPD suggests that the use of a T-piece resuscitator may be of greatest benefit for preterm infants.

Knowledge Gaps

- Evidence enabling comparison of benefits and risks of T-piece resuscitators with self-inflating bags by gestational age subgroups. Such studies should include outcomes relevant to each gestational age subgroup (eg, severe intraventricular hemorrhage, BPD, and neurodevelopmental impairment for very and extremely preterm infants; admission to neonatal intensive or special care unit, subsequent respiratory support, length of hospital stay, and air leaks for term and near-term infants).
- Cost-effectiveness of routine use of T-piece resuscitators compared with self-inflating bags
- Data on details of T-piece resuscitator and self-inflating bag use in practice (eg, pressures delivered, setup time, ease of use, adjustments to pressures made during use, perceived feedback from the device to the user)
- How these PPV devices perform with the use of different patient interfaces (eg, face masks, laryngeal masks, tracheal tubes)
- Evidence comparing the flow-inflating bag with either the T-piece resuscitator or the self-inflating bag (with or without PEEP) for neonatal resuscitation
- Trials comparing one T-piece device with another and one self-inflating bag with another, although benchtop experiments demonstrate variations in performance that are of potential clinical importance. The specific devices used in comparative studies should be reported.[304,305]

Family Presence During Neonatal Resuscitation (SysRev)

Rationale for Review

Infants are always born in the presence of their mother, although at times, a mother may be under general anesthesia and unaware of events involving her baby. Internationally, cultural norms and hospital policies vary as to whether partners or other family members (including siblings) or support people are encouraged or even allowed to attend the birth, especially if there is a high risk that the infant will need resuscitation.

The architecture of birthing areas also varies widely. In some locations, neonatal resuscitation always takes place in the birthing room. In others, separate rooms adjacent to birthing rooms or operating rooms are used to optimize ambient temperature for the infant and to provide adequate room for a neonatal resuscitation team and all the equipment that may be needed for an advanced resuscitation. In the case of an infant who needs more BLS measures at birth, there is concern that the parents or other family members present could experience short- or long-term psychological distress.

Concerns have also been raised about whether family presence could impede the performance of resuscitation team members and whether the neonatal resuscitation team members are present in sufficient numbers and have adequate training to support family members during a resuscitation. There is also concern that parents who are unaware of the circumstances of their infant's resuscitation may feel left out of a critical time in their infant's life and, in some sit-

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uations, of the opportunities to contribute to key decisions about the extent of resuscitation.

The Neonatal and Pediatric Life Support Task Forces conducted a combined SysRev of family presence during resuscitation (PROSPERO registration CRD42020140363).[306] The following summary describes the outcomes of the review applicable to newborn infants. The full CoSTR can be found on the ILCOR website.[307]

PICO, Study Design, and Time Frame

- Population: Neonates requiring resuscitation in any setting
- Intervention: Family presence during resuscitation
- Comparator: No family presence during resuscitation
- Outcome: Improved patient outcomes (short and long term), family-centered outcomes (short and long term, perception of the resuscitation), and health care provider–centered outcomes (perception of the resuscitation, psychological stress)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies, qualitative) 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 was updated to June 14, 2020.

Consensus on Science

The SysRev[306] identified 8 studies. For the critical outcome of improved patient outcomes (short and long term), there were no useful data to inform practice. Only 1 study reported Apgar scores in demographic data.[308] For the important outcome of family-centered outcomes, 7 articles reported 144 people, all from high-resource settings. The articles included 4 surveying parents or family members who were present during stabilization or resuscitation,[309–312] 2 surveying the opinions of health care providers,[313,314] and 1 surveying both health care providers and parents.[315] Overall, the findings in these mainly qualitative studies reflected a positive experience for families who were present during the stabilization or resuscitation of their newborn babies. Important themes included distinct aspects of fathers' experience, parents' feelings of reassurance and involvement if they were present, and concerns about the emotional toll of witnessing a resuscitation and the need for staff training in support of and debriefing for parents.

For the important outcome of health care provider outcomes, 4 articles were identified. Two surveyed health care providers who had participated in a resuscitation with family present or in a delivery with all immediate care provided beside the mother for delayed clamping of the umbilical cord[313,314] and expressed concern that less experienced professionals may feel under increased pressure while being observed. A survey of parental opinion[312] found that some were concerned about impact on staff performance. One survey of health care providers found that the presence of a family member reduced perceived workload.[308] Overall, health care provider participants were professionals who were used to having parents in attendance and did not report any major detrimental effects.

Treatment Recommendations

We suggest that it is reasonable for mothers/fathers/partners to be present during the resuscitation of neonates when circumstances, facilities, and parental inclination allow (weak recommendation, very low–certainty evidence).

There is insufficient evidence to indicate an interventional effect on patient or family outcome. Being present during the resuscitation of their baby seems to be a positive experience for some parents, but concerns about an adverse effect on performance exist among both health care providers and family members.

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table can be found in Supplemental Appendix A3.

In making these recommendations, the Neonatal Life Support Task Force considered that although family presence during neonatal resuscitation is practiced in some settings, it has never undergone a SysRev, and practice varies internationally. During the COVID-19 pandemic, some services have moved neonatal resuscitation sites to locations separated from parents, making this question a priority for the Neonatal Life Support Task Force.

All of the included articles originated in the United Kingdom, the United States, or Canada, and all were related to resuscitation and stabilization at birth.

Mothers are always present at birth, and it seems that most health care providers surveyed consider that the presence of a partner or support person should be offered but with the caveat that facilitation and support of the families require enough personnel with adequate training.

Of note, we did not identify any eligible RCTs or large cohort studies comparing family presence with no family presence during neonatal resuscitation. We acknowledge the lack of clinical trial data for this topic in our knowledge gaps. It is also notable that the evidence came from the opinions of only 144 parents and 350 health care providers in total, all sampled in tertiary centers in the United Kingdom, the United States, or Canada.

Task Force Knowledge Gaps

- No studies provided adequate comparative data to address this PICO question in the setting of a neonate receiving resuscitation at birth or within the first month of life. Most studies used retrospective survey or qualitative methods and included births at which resuscitation was not required. There would be serious ethical constraints in performing an RCT to address this question, among which would be the difficulty in obtaining informed consent. Therefore, larger-scale observational studies with appropriate quantitative and qualitative outcomes and experience measures are recommended.
- Whether family presence affects the outcome of a resuscitation
- Whether family presence affects decisions to continue or discontinue resuscitation
- Evidence from studies that recruit from different socioeconomic, cultural, and organizational settings

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Education, Implementation, and Teams

Self-Directed, Digitally Based BLS Education and Training in Adults and Children (SysRev)

Rationale for Review

Self-directed, digitally based resuscitation education programs (referred to below as digital training) are widely available and aim to teach BLS to the lay public at their own convenience. This SysRev intended to assess the evidence for the effectiveness of this educational approach in adults and children. Self-directed, digitally based BLS training was defined as any form of digital (eg, video, phone application [app] based, internet based, game based, virtual reality, augmented reality) education or training for BLS that can be completed without an instructor, except for mass media campaigns (eg, television, social media education). We defined instructor-led training as education or training (eg, lecture, skills demonstration, skills feedback) that occurred in the presence of a BLS instructor. Health care professional education was excluded, as were comparisons of different methods of digital training and BLS refresher courses (PROSPERO registration CRD42020199176).

The full text of this CoSTR can be found on the ILCOR website.[316]

PICO, Study Designs, and Time Frame

- Population: Adults and children undertaking BLS training
- Intervention: Self-directed, digitally based BLS training
- Comparator: Instructor-led BLS training
- Outcome: Patient outcomes: Good neurological outcome at hospital discharge/30 days; survival at hospital discharge/30 days; ROSC; rates of bystander CPR; bystander CPR quality during an OHCA arrest (any available CPR metrics); and rates of AED use. Educational outcomes at the end of training and within 12 months: CPR quality (chest compression depth and rate; chest compression fraction; complete chest recoil, ventilation rate, overall CPR competency) and AED competency; CPR and AED knowledge; and confidence and willingness to perform CPR
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies and case series in which n>5) were eligible for inclusion; unpublished studies (eg, conference abstracts, trial protocols), commentary, editorials, 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 was updated to July 1, 2020.

Consensus on Science

Overall, 41 studies (33 RCTs[317–349] and 8 non-RCTs[350–357]) reported short- and long-term outcomes of interest for self-directed digital BLS training compared with instructor-led training.

The overall certainty of evidence was rated as very low to moderate for all outcomes, primarily because of risk of bias. Most individual studies were at critical risk of bias, primarily because of missing outcome data (RCTs) and potential for confounding (non-RCTs). Because of this and the high degree of heterogeneity in the interventions and in the measurements of outcomes, we performed a narrative synthesis of the findings for each outcome overall and by the different mediums of digital training tested.

Critical Outcome: Subsequent Use of Skills and Patient Outcomes. Two RCTs[326,349] collected data on the use of BLS skills and patient outcomes after training. Only 1 of these[326] reported any OHCA events (n=13), but the data were insufficient to enable meaningful comparisons between groups.

Educational Outcomes (CPR and AED Skills Immediately and up to 1 Year). Testing of CPR and AED skills was conducted immediately and at 1 month after training in 36 studies (29 RCTs[317,319–325,328–345,347–349] and 7 non-RCTs[350–354,356,357]) and between 2 months and 1 year in 23 studies (18 RCTs[318–323,327–329,332,333,338,340,342,343,346,348,349] and 5 non-RCTs[350,352–355]).

We identified moderate-certainty evidence from 28 studies (22 RCTs[320,322–325,327–329,331,333–338,340,343–348] and 6 non-RCTs[350–353,355,356]) comparing instructor-led training with digital training using video or interactive computer programs with manikin practice, which demonstrated comparable educational outcomes for most CPR skills and knowledge gained immediately after training and up to 1 year.

We identified low-certainty evidence from 9 studies (7 RCTs[317–319,321,330,332,341] and 2 non-RCTs[354,357]) comparing instructor-led training with digital training using video only, which demonstrated comparable educational outcomes for most CPR skills and knowledge gained immediately after training and up to 1 year (3 RCTs[317–319]) and for overall CPR competency and knowledge immediately after training (7 RCTs[317–319,321,330,332,341] and 2 non-RCTs[354,357]).

We identified low-certainty evidence from 11 RCTs[318,320,321,323,324,337–340,342,344] comparing methods of digital training with instructor-led training for AED skills, suggesting that instructor-led training may be more effective immediately after training but not in the long term.

We identified low-certainty evidence from 3 RCTs[339,342,349] comparing gaming training with instructor-led training. Data were insufficient to be confident in the findings.

Treatment Recommendations

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 layperson adults and high school–aged (>10 years of age) children (strong recommendation, moderate-certainty 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 layperson adults and high school–aged (>10 years of age) children (strong recommendation, low-certainty evidence).

We suggest that BLS video education (without manikin practice) be used when instructor-led training or self-directed training with video kits (instructional video plus manikin with feedback device) is not accessible or when quantity over quality of BLS training is needed in adults and in children (weak recommendation, low-certainty evidence).

There was insufficient evidence to make a recommendation on gaming as a CPR or AED training method.

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There was insufficient evidence to suggest a treatment effect on bystander CPR rates or patient outcomes.

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in the Supplemental Appendix A4.

In making these recommendations, the Education, Implementation, and Teams Task Force acknowledges that instructor-led training was superior for the acquisition of some skills (eg, AED and compression depth) and in some groups of the population (namely, children). However, the task force considered the significant improvement compared with baseline or with groups with no training more important and questioned the clinical significance of some reported differences. Other methodological concerns included the wide variation in testing of educational outcomes and differences between groups within studies, differences in technical specifications of manikins with respect to delivery of CPR, and that some studies noted insufficient emphasis in digital materials for some skills (eg, AEDs[324]) or did not explain the use of feedback devices included in digital training kits.[356]

Task Force Knowledge Gaps

- Optimal methods to improve the achievement of guideline-recommended CPR metrics (compression rate and depth, chest recoil) and AED use
- Reporting and standardization of technical specifications of the manikin represent opportunities for future research.
- Evidence comparing outcomes from serious gaming with instructor-led training
- Evidence using objective methods (eg, sensor manikins) in CPR skill assessments, including important CPR metrics

Topics Reviewed by EvUps

The topics reviewed by EvUps are summarized in Table 16. The full documents can be found in Supplemental Appendix A4.

First Aid

Duration of Cooling With Water for Thermal Burns as a First Aid Intervention (SysRev)

Rationale for Review

This topic was prioritized by the ILCOR First Aid Task Force because of a lack of international consensus about the optimal duration of cooling of thermal burns with running water in the first aid setting and because of newly identified relevant studies since the topic was last reviewed in 2015. A SysRev was undertaken on behalf of the First Aid and Pediatric Task Forces.[358] No additional scientific literature has been published since the search date of August 6, 2020. All meta-analyses were done with unadjusted data. The SysRev was registered on PROSPERO (registration CRD42021180665).

The full text of this CoSTR can be found on the ILCOR website.[358]

PICO, Study Design, and Time Frame

- Population: Adults and children in first aid settings with a thermal burn
- Intervention: Active cooling using running water for ≥20 minutes as an immediate first aid intervention
- Comparator: Active cooling using running water for any other duration as an immediate first aid intervention
- Outcome: Size: defined as percentage of total body surface area at any reported time point; depth: any degree of deep partial or full thickness burn depth; pain: defined as any measurement of pain or administration of pain relief medications; adverse outcomes: defined as any adverse outcome, including hypothermia; wound healing: defined as time to re-epithelization in days; and complications within 24 hours: defined as organ dysfunction, ICU care, infections (within 7 days), bleeding, and rhabdomyolysis, as well as the need for surgical procedures such as skin grafting, fasciotomy, or escharotomy
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were included; animal studies, case series, unpublished studies, conference abstracts, and trial protocols were excluded.
- Time frame: All years and all languages were included as long as there was an English abstract. The literature was searched from database inception to August 6, 2020, and updated on February 10, 2021.

Consensus on Science

Four observational studies enrolling 5978 adults and children met inclusion criteria.[359–362]

For the critical outcome of burn size as a percentage of total body surface area, a meta-analysis of very low–certainty evidence from 3 studies[360–362] with 4616 adults and children showed no significant difference in the burn size for burns cooled with running water for ≥20 minutes compared with burns cooled for <20 minutes.

For the critical outcome of any degree of a full thickness burn depth, 2 studies including 4409 adults and children provided very low–certainty evidence.[361,362] Significant heterogeneity precluded meta-analysis. Results from a cohort study[361] including 2099 children (≤16 years of age) with a recorded duration of cooling favored cooling for <20 minutes compared with cooling for >20 minutes (RR, 0.90 [95% CI, 0.83–0.97]). Results from another study[362] including 2310 adults with a recorded duration of cooling favored cooling for ≥20 minutes over cooling for <20 minutes (RR, 1.11 [95% CI, 1.00–1.22]).

Sensitivity analysis for cooling times of <10 minutes compared with both ≥10 and ≥20 minutes showed no significant difference for any of the selected outcomes. There were no data for shorter durations.

For the important outcome of hypothermia as an adverse effect of cooling burns, unpublished data from a study including 117 children provided very low– certainty evidence.[360] Five of 117 children (4%) with a thermal burn cooled with water as a first aid intervention developed hypothermia to 34 °C to 36 °C tympanic (n=4) or were visibly cold with shivering (n=1). All 5 children were <4 years of age, and 4 of 5 received whole-body cooling in a shower.

Treatment Recommendations

We recommend the immediate active cooling of thermal burns with running water as a first aid intervention for adults and children (strong recommendation, very low–certainty evidence).

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Table 16 – EIT Topics Reviewed by EvUps

Topic/PICO	Year(s) last updated	Existing treatment recommendation	RCTs since last review, n	Observational studies since last review, n	Sufficient data to warrant SysRev?
EMS practitioner's experience or exposure (EIT 437)	2020 CoSTR	We suggest that EMS systems (1) monitor their clinical personnel's exposure to resuscitation and (2) implement strategies when possible to address low exposure or ensure that treating teams have members with recent exposure (weak recommendation, very low–certainty evidence).	None	None	No
High-fidelity training (EIT 623)	2015 CoSTR; 2020 EvUp	We suggest the use of high-fidelity manikins when training centers/organizations have the infrastructure, trained personnel, and resources to maintain the program (weak recommendations, very low-quality evidence). If high-fidelity manikins are not available, we suggest that the use of low-fidelity manikins is acceptable for standard ALS training in an educational setting (weak recommendations, low-quality evidence).	1 SysRev and 3 RCTs	1	No
CACs (EIT 624)	2019 CoSTR	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 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 either shockable or nonshockable initial cardiac rhythm, the current evidence is inconclusive, and the confidence in the effect estimates is currently too low to support an EIT and ALS Task Force recommendation.	1 SysRev and no RCTs	11	Yes
Timing for retraining (EIT 628)	2015 CoSTR; 2020 EvUp	There is insufficient evidence to recommend the optimum interval or method for BLS retraining for laypeople. Because there is evidence of skills decay within 3 to 12 mo after BLS training and evidence that frequent training improves CPR skills, responder confidence, and willingness to perform CPR, we suggest that individuals likely to encounter cardiac arrest consider more frequent retraining (weak recommendation, very low-quality evidence).	3	1	No
Cognitive aids during resuscitation (EIT 629)	2020 CoSTR	We recommend against the use of cognitive aids for the purposes of lay providers initiating CPR (weak recommendation, low-certainty evidence). We suggest the use of cognitive aids for health care providers during trauma resuscitation (weak recommendation, very low–certainty evidence). In the absence of studies on CPR, no evidence-based recommendation can be made. There are insufficient data to suggest for or against the use of cognitive aids in lay provider training. We suggest the use of cognitive aids for training of health care providers in resuscitation (weak recommendation, very low–certainty evidence).	8	2	Yes
TOR for in-hospital cardiac arrest (EIT 4002)	2020 CoSTR	We did not identify any clinical decision rule that was able to reliably predict death after in-hospital cardiac arrest. We recommend against using the UN10 rule as a sole strategy to terminate in-hospital resuscitation (strong recommendation, very low–certainty evidence).	None	None	No
Precourse preparation for advanced courses (EIT 637)	2020 CoSTR	We recommend distributing precourse learning formats preceding face-to-face training for participants of ALS courses (weak recommendation, very low- to low-certainty evidence). In addition, we strongly recommend providing the option of eLearning as part of a blended-learning approach to reduce face-to-face training time in ALS courses (strong recommendation, very low– to low-certainty evidence).	1	1	No
System performance improvements (EIT 640)	2020 CoSTR	We recommend that organizations or communities that treat cardiac arrest evaluate their performance and target key areas, with the goal of improving performance (strong recommendation, very low–certainty evidence).	1 SysRev	7	No

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Table 16 (continued)

Topic/PICO	Year(s) last updated	Existing treatment recommendation	RCTs since last review, n	Observational studies since last review, n	Sufficient data to warrant SysRev?
Community initiatives to promote BLS implementation (EIT 641)	2015 CoSTR; 2020 ScopRev	The treatment recommendation (below) remains unchanged from 2015. We recommend implementation of resuscitation guidelines within organizations that provide care for patients in cardiac arrest in any setting (strong recommendation, very low quality of evidence).	1 SysRev	2	No
Prehospital TOR rules (EIT 642)	2020 CoSTR	We conditionally recommend the use of TOR rules to assist clinicians in deciding whether to discontinue resuscitation efforts out of hospital or transport to hospital with ongoing CPR (conditional recommendation, very low–certainty evidence).	None	4	No
CPR feedback devices during training (EIT 648)	2020 CoSTR	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 (eg, music or metronome) during training to improve compression rate only (weak recommendation, low-certainty evidence).	5	None	No
BLS training in high-risk populations (EIT 649)	2015 CoSTR	We recommend the use of BLS training interventions that focus on high-risk populations on the basis of the willingness to be trained and the fact that there is low harm and high potential benefit (strong recommendation, low-quality evidence).	1 SysRev and no RCTs	11	Yes
Technology to engage first responders (EIT 878)	2020 CoSTR	We recommend that citizens/individuals who are in close proximity to a suspected OHCA event and are willing to be engaged/notified by a smartphone app with a mobile positioning system or text message–alert system should be notified (strong recommendation, very low–certainty evidence).	None	2	No
Resuscitation team with ALS course training (EIT 4000)	2020 CoSTR	We recommend the provision of accredited adult ALS training for health care providers (weak recommendation, very low–certainty evidence).	None	None	No
Opioid overdose first aid education (EIT 4001)	2015 CoSTR; 2020 ScopRev	We suggest offering opioid overdose response education, with or without naloxone distribution, to persons at risk for opioid overdose in any setting (weak recommendation, very low quality of evidence). In making these recommendations, we place greater value on the potential for lives saved by recommending overdose response education, with or without naloxone, and lesser value on the costs associated with naloxone administration, distribution, or education.	2 SysRevs and 2 RCTs	6	No
Facilitators and barriers to bystander CPR (EIT 4003)	2020 EvUp	NA; an evidence update was performed for 2020	None	5	No
Virtual reality, augmented reality, and gamified learning (EIT 4005)	2020 EvUp	NA; an evidence update was performed for 2020	1	2	No
In situ training (EIT 4007)	2021 EvUp	NA; an evidence update was performed for the first time in 2021	None	4	No

ALS indicates advanced life support; app, application; BLS, basic life support; CAC, cardiac arrest center; CPR, cardiopulmonary resuscitation; EIT, Education, Implementation, and Teams; EMS, emergency medical services; EvUps, evidence updates; NA, not applicable; OHCA, out-of-hospital cardiac arrest; PICO, population, intervention, comparator, outcome; RCT, randomized controlled trial; ScopRev, scoping review; SysRev, systematic review; and TOR, termination of resuscitation.

CoSTR documents are available at https://costr.ilcor.org/.

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Because no difference in outcomes could be demonstrated with the different cooling durations studied, a specific duration of cooling cannot be recommended.

Young children with thermal burns being actively cooled with running water should be monitored for signs or symptoms of excessive body cooling (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is provided in Supplemental Appendix A5.

Cooling of burns with running water is an established and beneficial intervention, although suggested durations of cooling are variable and based largely on expert opinion.[359,363–365] This has led to inconsistencies in international first aid guidance. The 2015 ILCOR CoSTR for cooling of burns provided a strong recommendation for active cooling of thermal burns with running water by first aid providers, but the duration of cooling was not specified.[366,367] It was suggested in task force insights that active cooling be started as soon as possible and continued for at least 10 minutes. Although several large human studies were identified in this 2021 SysRev, the evidence was found to be inconclusive to either support or refute the use of one duration compared with another. From an evidence-based perspective, the optimal technique (running water versus immersion) and the optimal temperature also remain unknown.

It is the task force consensus opinion that the optimal duration of cooling may vary by burn location, size, and depth; interval between the burn and the start of cooling; and the temperature of the water used for cooling. This is supported by the sensitivity analysis, which did not show a dose-response relationship for cooling duration and outcomes. Because most patients included in the current analysis had a small burn area (mean total body surface area <5%) and most burns were superficial, the reason for the lack of association between a longer duration of cooling and outcome may have been a skewed population. A scatterplot comparing burn size and duration of burn cooling suggests that larger burns are associated with longer cooling durations, and the task force considered that this may be attributable to pain or concern for worse outcomes. In the absence of science to guide duration of cooling, cooling until pain is relieved may be a commonly used first aid approach and one that deserves future research.

A concern was raised that cooling of burns in young children might result in hypothermia. Evidence of this complication supports the good practice statement. Even a short cooling duration, especially if full-body cooling is used, may result in hypothermia. Guideline organizations need to provide clear instructions on cooling techniques to minimize the risk of hypothermia.

Task Force Knowledge Gaps

- The optimal duration of cooling of burns with running water with similar temperatures
- Whether water immersion would be comparable to the use of running water
- The importance of the time from the burn event to the start of cooling and how this contributes to optimal cooling duration; future studies could estimate this by identifying who performed the burn cooling such as the patient or a bystander (likely very early cooling), the EMS (likely early cooling), or the emergency department or a burn center (likely later cooling).
- The optimal duration of cooling for minor burns that do not need assessment in burn centers or by advanced care providers
- Studies evaluating the duration of cooling of burns with running water as a first aid intervention from regions other than Australia
- Alternative optimal burn-cooling techniques when water is not available
- The effect of the duration of cooling of burns on patient-centered outcomes such as pain relief
- Whether circumstances such as environment, type, and location of burn change the time needed to cool a thermal burn

Exertion-Related Dehydration and Rehydration (SysRev)

Rationale for Review

Dehydration associated with exertion is a commonly encountered condition in the first aid setting, particularly at sporting events. This SysRev was undertaken to compare water with the myriad sports drinks that are promoted for rehydration after prolonged exercise. A SysRev and CoSTR were last completed in 2015,[366,367] and the topic was prioritized on the basis of knowledge of newly published studies. The 2021 SysRev was registered on PROSPERO (registration CRD42020153077).[368]

The full text of this CoSTR can be found on the ILCOR website.[368]

PICO, Study Design, and Time Frame

- Population: Adults and children with exertion-related dehydration
- Intervention: Drinking oral carbohydrate-electrolyte or alternative rehydrating liquids
- Comparator: Drinking water
- Outcome: Volume/hydration status (measured as cumulative urine volume, net fluid balance, hematocrit, hemoglobin, plasma volume change), vital signs (measured as heart rate), development of hyponatremia (measured as serum sodium concentration, serum/plasma osmolality), need for advanced medical care, and patient satisfaction (thirst perception, perceived intensity of stomach fullness, nausea, stomach upset, abdominal discomfort)
- Study design: 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.
- Time frame: All years and all languages were included as long as there was an English abstract. Literature search was performed April 17, 2020, and updated February 15, 2021.

Consensus on Science

Comparisons with water were completed for 4% to 9% carbohydrate-electrolyte drinks (CEDs), 0% to 3.9% CEDs, skim or low-fat milk, coconut water (fresh or from concentrate), regular beer, low-alcohol beer, and nonalcoholic beer. Across all comparisons and outcomes, marked heterogeneity in study design and outcomes precluded meta-analysis. Overall certainty of evidence was rated as low to very low, primarily because of serious risk of bias, imprecision, or suspected publication bias. A summary of the direction of evidence from the 22 included studies is provided in Table 17.

The 4% to 9% CEDs Compared With Water. For the critical outcome of volume/hydration status, 9 RCTs[369–377] and 4 non-RCTs[378–381] including a total of 200 subjects conducted 17 comparisons of varying percentages of CEDs with water. No difference in volume/hydration status was shown in 12 of 17 of these compar-

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Table 17 – Summary of Studies Showing Effectiveness of Various Rehydration Solutions

Rehydration solutions	Outcome	Studies (RCT/non-RCT), n	Subjects, n	Benefit intervention, n	No difference could be demonstrated, n	Benefit water, n
4%–9% CED	Volume/hydration status	13 (9/4)	200	7	21	
4%–9% CED	Vital signs	2 (2/0)	53		3	
4%–9% CED	Hyponatremia	7 (3/4)	86	3	9	
4%–9% CED	Patient satisfaction	6 (5/1)	95		36	
0%–3.9% CED	Volume/hydration status	6 (5/1)	53	3	13	
0%–3.9% CED	Vital signs	1 (1/0)	10		1	
0%–3.9% CED	Hyponatremia	5 (4/1)	45	4	6	
0%–3.9% CED	Patient satisfaction	3 (3/0)	25		16	1
Skim or low-fat cow's milk	Volume/hydration status	4 (3/1)	68	12		
Skim or low-fat cow's milk	Hyponatremia	2 (1/1)	19	1	2	
Skim or low-fat cow's milk	Patient satisfaction	4 (3/1)	68		26	6
Fresh coconut water	Volume/hydration status	4 (4/0)	42		6	
Fresh coconut water	Vital signs	1 (1/0)	12		1	
Fresh coconut water	Hyponatremia	3 (3/0)	30	2	3	
Fresh coconut water	Patient satisfaction	4 (4/0)	42	4	24	1
Coconut water from concentrate	Vital signs	1 (1/0)	12		1	
Coconut water from concentrate	Hyponatremia	1 (1/0)	12	1		
Coconut water from concentrate	Patient satisfaction	1 (1/0)	12		5	1
Beer with 4.5%–5% alcohol	Volume/hydration status	3 (3/0)	38		7	1
Beer with 4.5%–5% alcohol	Hyponatremia	1 (1/0)	16		1	
Beer with 0.5%–2% alcohol	Volume/hydration status	2 (2/0)	22		4	
Beer with 0% alcohol	Volume/hydration status	1 (1/0)	11		3	

CED indicates carbohydrate-electrolyte drink; and RCT, randomized controlled trial.

isons. One RCT reported a significant decrease in cumulative urine output with 4% CEDs (mean difference [MD], −289 mL [95% CI not calculable]).[371] Decreased cumulative urine output was associated with rehydration with 6% CEDs[378,380] (MD, −160 and −465 mL, respectively) and 6.6% CEDs[370,381] (MD, −241 and −277 mL, respectively [95% CI not calculable]) compared with water. For the outcome of net fluid balance, no significant difference was shown at 60 and 120 minutes after rehydration with 6% CEDs,[372] 7% CEDs,[376] or 8% CEDs[375] and at 60 minutes for 6.9% CEDs[377] compared with water. Similarly, no differences were reported in plasma volume or plasma volume change at 120 minutes after rehydration with any of the CED concentrations tested compared with water. One study[379] did not show a difference in hematocrit at 30 minutes after rehydration with 8.75% CEDs compared with water.

For the critical outcome of vital signs, 2 RCTs[369,382] and 1 non-RCT[381] including 53 subjects observed no difference in heart rate at time points from 60 to 120 minutes after rehydration with any tested CED concentration compared with water.[369,381,382]

For the critical outcome of hyponatremia, 3 RCTs[369,377,382] and 4 non-RCTs[378–381] including 86 subjects were included. A significant increase was reported in serum sodium concentration 1 hour after rehydration with 6.9% CEDs[377] compared with water, whereas no difference was reported after rehydration with 6% CEDs[378] and 8.75% CEDs.[379] Two studies found a significant increase in serum osmolality at 60[380] and 75 minutes[378] after rehydration with 6% CEDs compared with water (MD, 5.9 and 4.5 mOsm/kg, respectively), whereas no difference was reported at 120 minutes after 6% CEDs,[380] at 60 minutes after 6.9% CEDs,[377] and at 30 minutes after 8.75% CEDs.[379] Two studies failed to show a significant difference in plasma osmolality at 60 and 90 minutes after rehydration with 5% to 6.6% CEDs.[369,382]

The 0% to 3.9% CEDs Compared With Water. For the critical outcome of volume/hydration status, we identified low-certainty evidence from 5 RCTs[369,383–386] and 1 non-RCT[387] including 53 subjects. Of 12 comparisons of rehydration using 0% to 3.9% CEDs compared with water, only 2 demonstrated a difference.

A significant decrease in cumulative urine output was shown in 2 RCTs after rehydration with 0% CEDs (saline)[383] and 3.7% CEDs[384] compared with water (MD, −416 mL [95% CI, −786 to −46] and −174.5 mL [95% CI not calculable], respectively).

For the critical outcome of hyponatremia, low-certainty evidence was included from 4 RCTs[369,384–386] and 1 non-RCT[387] including 45 subjects. A significant increase in serum sodium concentration was shown at 60 minutes after rehydration with 1.83% CEDs[387] or

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3.7% CEDs[384] compared with water, whereas a third study[385] did not find a significant difference with 3.2% CEDs. Significant increases in serum osmolality were found in 2 studies at 60 minutes after rehydration with 1.83% CEDs[387] or 3.7% CEDs[384] compared with water (MD, 9.0 and 4 mOsm/kg, respectively [95% CI not calculable]), whereas 1 RCT[385] did not find a difference with 3.2% CEDs. Significant differences in plasma osmolality were not shown at 120 minutes after rehydration with 2% CEDs[369] or 3.9% CEDs[386] compared with water.

Skim or Low-Fat Cow's Milk Compared With Water. For the critical outcome of volume/hydration status, we identified 3 RCTs[372,375,386] and 1 non-RCT[388] including 68 subjects. Four of 5 studies[372,375,386,388] showed a significant decrease in cumulative urine output after rehydration with skim or low-fat cow's milk compared with water (MD, −368, −635, −594, and −175 mL, respectively [95% CI not calculable]). A significant increase in net fluid balance was shown in 3 studies[372,375,386] at 60 minutes after rehydration with skim milk compared with water (MD, 655, 368, and 111 mL, respectively [95% CI not calculable]) and in 1 study,[388] at 30 to 90 minutes after rehydration (MD, 0.26 L [95% CI not calculable]) and 90 to 150 minutes after rehydration (MD, 0.36 L [95% CI not calculable]).

For the critical outcome of hyponatremia, we identified 1 RCT[386] and 1 non-RCT[388] including 19 subjects, reporting conflicting results.

Coconut Water (as Fresh Coconut Water or Coconut Water From Concentrate) Compared With Water. For the critical outcome of volume/hydration status, 3 RCTs with 30 subjects were included.[371,384,385] In these 3 studies of rehydration with fresh coconut water compared with water, no significant differences were found in cumulative urine output,[371,384,385] net fluid balance,[384,385] or plasma volume change at 60 minutes.[384] One small study[382] did not observe a difference in heart rate at 120 minutes after rehydration with fresh or coconut water from concentrate compared with water.

For the critical outcome of hyponatremia, we identified 3 RCTs with a total of 30 subjects.[382,384,385] One study[384] showed a significant increase in serum sodium concentration and serum osmolality 60 minutes after rehydration with fresh coconut water compared with water (MD, 2 mmol/L and 3 mOsm/kg, respectively [95% CI not calculable]), whereas a second study[385] found no difference. A third study[382] reported a significant increase in plasma osmolality at 120 minutes after rehydration with coconut water from concentrate compared with water (MD, 1.5 mOsm/kg [95% CI not calculable]) but did not find a difference in plasma osmolality after rehydration with fresh coconut water.

Regular Beer (4.5%–5% Alcohol) Compared With Water. For the critical outcome of volume/hydration status, we identified 3 RCTs with 38 subjects.[376,389,390] One study[390] showed a statistically significant increase in cumulative urine output (MD, 444 mL [95% CI not calculable]) after rehydration with regular beer compared with water, whereas 2 studies[376,389] found no difference. No difference was found in net fluid balance at 60[376] or 120 minutes[376,389] after rehydration with regular beer compared with water. A single study[389] found no significant difference in change in hematocrit, plasma volume, or serum sodium concentration after rehydration with beer compared with water.

Low-Alcohol Beer (0.5%–2% Alcohol) Compared With Water. Two RCTs enrolling 22 subjects[376,390] reported no significant difference in net fluid balance at 60 and 120 minutes after rehydration with low-alcohol beer (2%) compared with water.

Nonalcoholic Beer (0% Alcohol) Compared With Water. One RCT with 11 subjects[376] reported no significant difference in cumulative urine output or net fluid balance at 60 and 120 minutes after rehydration with nonalcoholic beer compared with water.

Treatment Recommendations

We recommend the use of any readily available rehydration drink or water for treating exertion-related dehydration in the first aid setting (good practice statement).

We suggest rehydration for exertion-related dehydration with a 4% to 9% CED. Alternative rehydration options include 0% to 3.9% CEDs, water, coconut water, or skim or low-fat cow's milk (weak recommendation, very low–certainty evidence).

There is insufficient evidence to recommend for or against rehydration with beer (0%–5% alcohol).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is provided in Supplemental Appendix A5.

First aid providers are commonly recruited to assist at first aid stations located at sporting events, where exercise-induced dehydration is a common problem. It may not be possible to determine the exact quantity or percent of fluid loss in the first aid setting. The First Aid Task Force acknowledges that in cases of exertional dehydration, it is most important to rehydrate as soon as possible and emphasizes this priority as a good practice statement. The choice of what to drink will often be based on what the dehydrated person is willing to drink and what is palatable.

We further acknowledge that all included trials conducted exercise in a controlled environment and duration. Extreme events such as ultramarathons were not included in the evidence evaluation.

Although there is variability among the identified studies, we identified a beneficial effect with use of CEDs for many of the reviewed outcomes. Differences in cumulative urine output between beverages were discussed by the task force and are likely a result of beverage composition. Drinks with high energy content (ie, from carbohydrates, fat, protein, or alcohol) will empty from the stomach more slowly than drinks containing no energy. Therefore, they will potentially reduce or delay diuresis compared with water.

Numerous studies were sponsored and financed by the manufacturers of the tested drinks. In many of these studies, a statement was included noting that the funders did not influence the study or results. In these cases, we did not downgrade for publication bias. In cases when such a statement was not provided, we downgraded for publication bias.

Findings related to milk as a rehydration drink were also discussed at length by the task force. Skim or low-fat cow's milk appears to have a water, energy, and macronutrient content similar to that of sports drinks. Milk, however, generally requires refrigeration and may not be readily accessible. In some regions, the prevalence of lactose intolerance is higher than in other regions, making milk a less suitable rehydration drink. There may also be more issues with patient satisfaction or compliance compared with water. The use of alcoholic beverages may have other unwanted effects, including a diuretic effect, and is not recommended for athletes in competition.

Excessive fluid consumption may lead to an electrolyte imbalance. However, if clean, potable water is available, its cost, relative

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to CEDs, makes it an acceptable alternative, although water may require longer times to rehydrate and, in some cases, may be associated with hyponatremia.

Task Force Knowledge Gaps

- Whether medical conditions such as diabetes and hypertension affect recommendations for rehydration drinks after exercise and dehydration
- The ideal means of determining goals for rehydration in the first aid/sports setting

Pediatric Tourniquet Types (SysRev)

Rationale for Review

The continuous evidence evaluation process for the production of this CoSTR started with a SysRev of first aid interventions for control of life-threatening bleeding[391] and a ScopRev of the use of tourniquets in the pediatric population (<19 years of age).[392,393] These reviews led to a recommendation for a SysRev, which was done on behalf of the First Aid and Pediatric Task Forces after registration on PROSPERO CRD42021229767.[391]

The full text of this CoSTR can be found on the ILCOR website.[394]

PICO, Study Design, and Time Frame

- Population: Children (<19 years of age) with severe, life-threatening bleeding from an extremity wound
- Intervention: Commercial elastic wrap tourniquet or commercial ratcheting tourniquet
- Comparator: Commercial windlass rod-type tourniquet
- Outcome: Mortality, control of bleeding (including surrogate outcome of obliteration of Doppler pulses), blood loss, shock/hypotension, and adverse events
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) and case series were eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols), modeling studies, studies of tourniquets applied solely to maintain a bloodless surgical field, or those relating only to education were excluded.
- Time frame: All years and all languages were included as long as there was an English abstract. Database searches were performed on October 1, 2020.

Consensus on Science

Two cohort studies including 73 patients 2 to 16 years of age met our eligibility criteria. Evidence from both studies was of very low certainty. Additional experimental studies using models and manikins were considered by the task force within the context of the GRADE evidence-to-decision process.

For the critical outcome of control of bleeding, no studies were identified that compared the use of one tourniquet type with another tourniquet type. Two cohort studies enrolling a total of 73 children between 2 and 16 years of age and using a manufactured windlass rod tourniquet were identified.[395,396] The first study was conducted on 60 uninjured volunteers in an orthopedic office (6–16 years of age)[395] with researchers applying a windlass rod tourniquet to an uninjured extremity. The second study was conducted on 13 volunteers (2–7 years of age) with the same manufactured windlass rod tourniquet on an uninjured extremity while under anesthesia in an operating room.[396] Pooled data showed cessation of pulses in 71 of 71 upper extremities (100%) and in 69 of 73 lower extremities (94.5%). Tourniquet failures were attributable to an inability to continue secondary to pain in the unanesthetized group (n=1) and to an inability to occlude the distal pulse after a prespecified maximum of 3 windlass turns in the anesthetized group (n=3).[395]

No evidence was identified for the outcomes of mortality, blood loss, and shock/hypotension.

Treatment Recommendations

We suggest the use of a manufactured windlass tourniquet for the management of life-threatening extremity bleeding in children (weak recommendation, very low–certainty evidence).

We are unable to recommend for or against the use of other tourniquet types in children because of a lack of evidence.

For infants and children with extremities that are too small to allow the snug application of a tourniquet before activating the circumferential tightening mechanism, we recommend the use of direct manual pressure with or without the application of a hemostatic trauma dressing (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is provided in Supplemental Appendix A5.

This topic was prioritized by the First Aid Task Force after a ScopRev[392,393] identified emerging evidence from human studies of tourniquet use in children. Previous reviews of adult and pediatric literature identified experimental studies of tourniquet use in pediatric models such as polyvinyl chloride pipes that demonstrated failure of adult tourniquets on smaller pipes.[397]

In making this recommendation, the First Aid Task Force weighed the lack of direct evidence to show that tourniquets are a lifesaving intervention for life-threatening extremity bleeding in children against the previously established role of a manufactured windlass tourniquet in reducing mortality in adults with life-threatening extremity bleeding.[391] The Combat Application Tourniquet Generation 7 was the specific brand of windlass rod tourniquet used in both included studies, and the minimum limb circumference of the children included was 13 cm. Other windlass rod tourniquets may vary in their ability to tighten successfully on limbs with small circumferences. Although some data are available from studies using manikins or models such as polyvinyl chloride pipes and stair rails, these studies were felt to be too indirect to be included.[397,398] Review of these studies in the evidence-to-decision process suggested that the rigid mechanism of some tourniquets can preclude successful application on limbs with small circumferences.

It is the consensus of the task force that for children <2 years of age, body size and a lower relative pressure would likely make direct manual pressure more effective for control of life-threatening extremity bleeding. Although it may be difficult for providers to determine whether a child is ≥2 years of age, the task force discussed that the typical habitus of a toddler, rather than an infant, could be used to help make this determination.

Task Force Knowledge Gaps

- Urgent need for RCTs in the prehospital setting to determine which tourniquet designs produce beneficial outcomes in children
- Younger age and size limits for manufactured tourniquets and which tourniquets can be applied to both upper and lower extremities to control hemorrhage

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- Data on complications of tourniquet use in children
- Data on efficacy and speed of application of tourniquets on children by first aid providers

Methods of Tick Removal (SysRev Adolopment)

Rationale for Review

This topic was prioritized by the First Aid Task Force because of a lack of international consensus in guidelines for removal of an attached tick in the first aid setting and a lack of prior SysRevs of this topic by ILCOR. This CoSTR was created with the adolopment process by using a recent SysRev.[399] Additional scientific literature published after the completion of the published SysRev was identified by a subsequent search of the relevant literature. The totality of this identified evidence was considered by the First Aid Task Force and used to create and update bias assessment tables and evidence profile tables.

The full text of this CoSTR can be found on the ILCOR website.[400]

PICO, Study Design, and Time Frame

- Population: Individuals in the first aid setting with a tick attached to the skin
- Intervention: Any tick-removal method, including heat, chemical, commercial tick-removal apparatus, or tweezers/forceps
- Comparator: Any other method of tick removal
- Outcome: Transmission of disease, removal of (parts of) the tick, damaged or broken-off mouthparts
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies, cross-sectional studies, and animal studies) were eligible for inclusion. Conference abstracts, conference papers, (clinical) trial registrations, dissertations, case series, ex vivo or in vitro studies, studies reporting no quantitative data, and studies reporting only means without standard deviation, effect sizes, or *P* values were excluded.
- Time frame: All languages were included as long as there was an English abstract. Searches were conducted from 2017 (date of the adoloped SysRev) to June 23, 2020, and updated February 14, 2021.

Consensus on Science

Three RCTs[401–403] and 5 observational studies[404–408] were identified, 2 of which were not in the original (adoloped) SysRev.[404,407] For the critical outcome of tick (or tick part) removal and the important outcome of damaged or broken-off mouthparts, an overview of studies, certainty of evidence, and key outcomes are presented in Table 18. For the critical outcome of disease transmission, no evidence was identified.

Treatment Recommendations

We recommend against the use of chemicals, heat, or ice compared with mechanical methods for the removal of a tick (strong recommendation, very low–certainty evidence).

We suggest either pulling with tweezers or using commercial devices according to the manufacturer's instructions to remove a tick rather than removal by hand (weak recommendation, very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is provided in Supplemental Appendix A5.

In making these recommendations, the First Aid Task Force considered that early removal of a tick is likely the most important aspect of preventing infection. We prioritized methods of tick removal that would be safe and effective while promoting early tick removal.

Although studies differentiated adult and nymph ticks, different species of ticks, and time of tick attachment/engorgement, the task force acknowledged that it is impractical for lay providers to differentiate their features or the potential need for different devices for removal of each stage. Therefore, these studies were combined in this review.

Tweezers are likely more readily available, have more first aid uses, and are less expensive than commercial tick-removal devices. They are therefore more practical for earlier tick removal than a commercial tick-removal device is.

Although no study evaluated the proper grasp of the tick with tweezers, in the included studies, when described, ticks were grabbed as close to the skin as possible. The tweezers or forceps that were used were described as having a thin jaw, similar to Adson forceps, which would allow gripping of the tick near the skin without crushing the body.

No studies evaluated disease transmission. Removal of a tick does not guarantee lack of disease transmission, and first aid guideline writers should consider including signs and symptoms of local and systemic illness after tick bites. All techniques of tick removal are subject to user error and could result in retained tick mouthparts in the skin.

Task Force Knowledge Gaps

- The most effective methods of tick removal by first aid providers
- The effect of method of tick removal on clinical outcomes such as transmission of disease and local infection

Use of Cryotherapy for Acute Epistaxis in the First Aid Setting (ScopRev)

Rationale for Review

Epistaxis is typically managed in the first aid setting with direct manual pressure by pinching the nasal alae. Cryotherapy with ice/cold packs or ice collars is commonly recommended as adjunctive therapy for epistaxis on self-care web pages but is not recommended in first aid guidelines by ILCOR member organizations and has not been reviewed previously by ILCOR. The goal of this ScopRev is to identify any literature evaluating the use of cryotherapy as an adjunct to direct pressure and to assess the need for a SysRev.

The full text of this ScopRev is available on the ILCOR website.[409]

PICO, Study Design, and Time Frame

- Population: Adults and children receiving first aid for acute epistaxis
- Intervention: Cryotherapy alone or cryotherapy with nose pinching
- Comparator: Nose pinching/pressure alone
- Outcome: Time to hemostasis control, hemostasis, reduction of nasal blood volume, reduction of pain, need for follow-up care, adverse events, recovery time, reduction of swelling

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Table 18 – Overview of Studies and Key Outcomes for Methods of Tick Removal

Study	Study design	Certainty of evidence	Population	Outcome	Comparison	Results
Akin Belli et al,[404] 2016	NR	Low	160 tick removals by health care providers using tweezers or 3 different commercial devices; if tweezers, grabbed close to mouthparts and pulled straight out	Tick removal	Freezing (Tickner) vs pulling with tweezers	0/40 vs 40/40 RR, not estimable
				Intact tick removal	Pulling with a slit-and-traction device (Zeckenkarte) vs pulling with tweezers	3/40 vs 33/40 RR, 0.09 (95% CI, 0.03–0.27)
					Pulling with a lasso device (Trix Ticklasso) vs pulling with tweezers	19/40 vs 33/40 RR, 0.58 (95% CI, 0.40–0.83)
Bowles et al,[401]1992	RCT	Very low	299 adult ticks removed on 8 stray dogs by researchers using 1 removal device and 3 types of forceps	Ticks with damaged mouthparts	Rotation with opposing jaw device (Tick Solution) vs pulling with economy forceps	2/81 vs 2/73 RR, 0.90 (95% CI, 0.13–6.25)
					Pulling with jeweler's forceps vs economy forceps	2/72 vs 2/73 RR, 0.90 (95% CI, 0.15–7.00)
					Pulling with angled forceps vs pulling with economy forceps	1/73 vs 2/73 RR, 0.50 (95% CI, 0.05–5.40)
de Boer et al,[405] 1993	NR	Very low	175 ticks applied on skin of 6 animals were treated chemically; 149 ticks applied on skin of 6 animals were used for pulling vs rotation comparison	Tick removal	Application of gasoline	Removals: 0/72
					Application of nail polish	Removals: 0/46
					Application of methylated spirit	Removals: 0/57
				Tick mouthparts remaining in the skin	Pulling straight out with blunt forceps vs rotation with opposing jaw device (Tick Solution)	59/80 vs 14/69 RR, 3.63 (95% CI, 2.24–5.91)
Duscher et al,[402] 2012	RCT	Very low	527 ticks removed from animals by 22 veterinarians and 4 lay volunteers; 4 different commercial devices and Adson forceps were tested	Ticks with damaged mouthparts	Rotating mechanical removal vs pulling mechanical removal	37/337 vs 60/190 RR, 0.35 (95% CI, 0.24–0.50)
					Pulling with Adson forceps vs pulling with slit-and-traction device (TickPic)	36/90 vs 24/100 RR, 1.67 (95% CI, 1.08–2.56)
					Rotation with lasso device (Trix Ticklasso) vs pulling with Adson forceps	20/108 vs 36/90 RR, 0.46 (95% CI, 0.29–0.74)
					Rotation with slit-and-rotation device (Tick Twister) vs pulling with Adson forceps	7/108 vs 36/90 RR, 0.16 (95% CI, 0.08–0.35)
					Rotation with opposing jaw device (pen-tweezers) vs pulling with Adson forceps	10/121 vs 36/90 RR, 0.21 (95% CI, 0.11–0.39)
					Rotation with lasso device (Trix Ticklasso) vs pulling with slit-and-traction device (TickPic)	20/108 vs 24/100 RR, 0.77 (95% CI, 0.46–1.31)

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Table 18 (continued)

Study	Study design	Certainty of evidence	Population	Outcome	Comparison	Results
					Rotation with slit-and-rotation device (Tick Twister) vs pulling with slit-and-traction device (TickPic)	7/108 vs 24/100 RR, 0.27 (95% CI, 4(0.12–0.60)
					Rotation with opposing jaw device (pen-tweezers) vs pulling with slit-and-traction device (TickPic)	10/121 vs 24/100 RR, 0.34 (95% CI, 0.17–0.69)
					Rotation with lasso device (Trix Ticklasso) vs rotation with slit-and-rotation device (Tick Twister)	20/108 vs 7/108 RR: 2.86 (95% CI, 1.26–6.48)
Duscher et al,[402] 2012 continued					Rotation with lasso device (Trix Ticklasso) vs rotation with opposing jaw device (pen-tweezers)	20/108 vs 10/121 RR, 2.24 (95% CI, 1.10–4.57)
					Rotation with slit-and-rotation device (Tick Twister) vs rotation with opposing jaw device (pen-tweezers)	7/108 vs 10/121 RR, 0.78 (95% CI, 0.31–1.99)
Needham,[406] 1985	NR	Very low	29 ticks attached to sheep were treated with chemicals or a hot match; 22 ticks attached to sheep were pulled with forceps using various traction techniques	Tick removal	Application of petroleum jelly	Removals: 0/14
					Application of clear fingernail polish	Removals: 0/8
					Application of 70% isopropyl alcohol	Removals: 0/8
					Application of a hot kitchen match	Removals: 0/8
				Ticks with broken mouthparts	Pulling straight up with a quick motion with forceps vs rotating clockwise with forceps	7/7 vs 0/5 RR, 11.25 (95% CI, 0.79–160.81)
					Pulling straight up with a steady pressure with forceps vs rotating clockwise with forceps	5/5 vs 5/5 RR, 1.0 (95% CI, 0.71–1.41)
					Pulling parallel with the skin with forceps vs rotating clockwise with forceps	5/5 vs 5/5 RR, 1.0 (95% CI, 0.71–1.41)
Şahin et al,[407] 2020	NR	Very low	93 participants who presented to an emergency department for tick removal; ticks were removed either by the participants themselves by hand or by health care providers using a lasso technique with suture material or with tweezers	Ticks with broken mouthparts	Pulling with tweezers or removal by hand	4/22 vs 11/21 RR, 0.35 (95% CI, 0.13–0.92)
Stewart et al,[408] 1998	NR	Very low	342 ticks were removed from laboratory rabbits by untrained individuals using 4 different commercial removal devices or tweezers	Ticks with damaged mouthparts	Pulling with slit-and-traction device (Ticked Off) vs pulling with medium-tipped tweezers	9/104 vs 20/79 RR, 0.34 (95% CI, 0.16–0.71)
					Pulling with slit-and-traction device (Pro-Tick Remedy) vs pulling with medium-tipped tweezers	13/82 vs 20/79 RR, 0.63 (95% CI, 0.33–1.17)

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Table 18 (continued)

Study	Study design	Certainty of evidence	Population	Outcome	Comparison	Results
					Pulling with opposing jaw device (Tick Plier or Tick Nipper) vs pulling with medium-tipped tweezers	10/77 vs 20/79 RR, 0.51 (95% CI, 0.26–1.02)
Zenner et al,[403] 2006	RCT	Very low	Veterinarians and pet owners removed 236 ticks (various species) from 178 dogs and 46 cats using 3 commercial tick-removal devices or Adson forceps in random order	Ticks with damaged mouthparts	Rotation with slit-and-rotation device (Tick Twister) vs rotation with opposing jaw device (Buster Tick forceps) or Adson forceps	$P<0.01$ in favor of slit-and-rotation device; raw data not given

NR indicates nonrandomized study; RCT, randomized controlled trial; and RR, risk ratio.

- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies), case series, gray literature reports, reviews, or webpage articles 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. Initial literature search (Embase, MEDLINE, and Cochrane) was completed on July 13, 2020, and was updated on January 14, 2021. Literature search on PubMed was completed on December 19, 2020. Gray literature searches were completed on December 21, 2020. ILCOR member organization website guidelines were searched on December 28, 2020. Hand searching of references from reviewed manuscripts was included.

Summary of Evidence

No studies were identified that directly addressed the PICO, study design, and time frame question. Six indirect experimental studies (all including adults without epistaxis) examined the effects of cryotherapy on nasal mucosal blood flow,[410,411] nasal submucosal temperature,[412] nasal blood volume,[413] nasal congestion and nasal cavity volume,[414] nasal airflow and patency,[411] and nasal airway volume.[415] An overview of all study characteristics and findings is presented in Supplemental Appendix C3. One randomized crossover study[410] of 16 adults reported a significant decrease in nasal mucosal blood flow (23% versus 5%; $P<0.05$) with ice packs inside the mouth compared with an ice pack applied to the forehead. A second randomized crossover study[412] of 13 adults reported a lower nasal submucosa temperature with sucking ice cubes compared with the application of ice packs to the forehead. The combination of sucking ice cubes and an ice pack to the forehead was reported to cause a greater drop in nasal submucosal temperature than an ice pack alone.

An observational study of 56 healthy adults[411] reported no change in nasal mucosal microcirculatory blood flow or inspiratory airflow after 5 minutes of ice packs around the neck. A before-and-after study of 15 healthy adults also reported no significant change in nasal blood volume after a 10-minute application of an ice collar to the neck.

One observational study[414] reported no significant difference in mean nasal cavity volume measurements up to 10 minutes after application of cold compresses to the nasal dorsal skin. An observational study[415] with 10 healthy adults reported greater nasal airway volume after ice-water immersion of the feet compared with 1 hand and forearm immersion.

One SysRev[416] was identified evaluating the initial assessment and management of adults with epistaxis. Despite a lack of supporting evidence, the review concluded that the application of an intraoral ice pack is a simple first aid measure with the potential to decrease bleeding severity.

The gray literature review of cryotherapy in acute epistaxis identified 6 documents evaluating application of cryotherapy to the face or nose,[417,418] sucking on ice,[417,419] and application around[417] and to the back of the neck[420] or forehead (overview of these provided in Supplemental Appendix C3).[421,422,422a,422b] No evidence for these recommendations was provided in 3 records.[417,418,422] A narrative review[419] suggested that ice packs around the neck and intraorally significantly reduced nasal mucosa blood flow and could slow bleeding. However, they referenced investigators[410] who measured nasal mucosal blood flow in healthy adults. Two narrative reviews[420,421] suggested that the use of cryotherapy is inconclusive and controversial, citing work by other investigators.[411,413]

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A review of ILCOR member councils for guideline documentation identified 2 subcouncil guidelines statements addressing epistaxis, including a 2000 American Heart Association guideline[422a] and a 2017 Australian and New Zealand Committee on Resuscitation guideline.[422b] No reference to cryotherapy was addressed in either guideline.

Task Force Insights

The gray literature recommendations for cryotherapy in the first aid management of acute epistaxis are based on findings of reduced nasal blood flow and volume reported in 3 of 6 indirect studies performed on healthy adults without epistaxis.[410,412,413]

Cryotherapy application methods used in the studies were inconsistent and applied to the forehead, in the mouth, around the neck, on the feet, or on a single hand/forearm or a combination of locations. Cryotherapy application times also varied between studies. Gray literature recommendations for the use of cryotherapy in acute epistaxis are likely the result of opinion and the theory that cryotherapy induces vasoconstriction in the nasal mucosa. Current evidence does not support recommendations for use of cryotherapy as a first aid intervention for acute epistaxis. This ScopRev does not find sufficient evidence to support a SysRev but does highlight the need for clinical research studies.

Topics Reviewed by EvUps

The topics reviewed by EvUps are summarized in Table 19. Complete EvUps are included in Supplemental Appendix A1.

COVID-19 Working Group

COVID-19 Infection Risk to Rescuers From Patients in Cardiac Arrest (SysRev)

Rationale for Review

The COVID-19 pandemic has been associated with high mortality and morbidity throughout the world. In the context of cardiac arrest, there was concern that the transmissibility of COVID-19 may pose a risk to rescuers during delivery of chest compressions, defibrillation, and CPR. In view of this concern, ILCOR urgently commissioned a SysRev and developed treatment recommendations.[423,424] Subsequently, ILCOR has generated 4 EvUps to reflect the evolving COVID-19 literature and ongoing clinical interest. This summary describes evidence up to January 2021. The SysRev was registered on PROSPERO (registration CRD42017080475).

Full text of this CoSTR can be found on the ILCOR website.[425]

PICO, Study Design, and Time Frame

Our SysRev addressed 3 complementary research questions in relation to COVID-19 and risk to the rescuer delivering CPR. Specifically, we examined aerosol generation (research question 1), transmission of infection (research question 2), and PPE strategy (research question 3). Research questions 1 and 2 evaluate the effect of an exposure on the outcome and thus differ in structure somewhat from the PICO because there is no true intervention or comparator.

Research Question 1.

- Population: Individuals in any setting
- Exposure: Delivery of chest compressions, defibrillation, CPR (all CPR interventions that include chest compressions)
- Outcome: Generation of aerosols
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies, case reports/series, cadaver 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. Searches were updated in January 2021.

Research Question 2.

- Population: Individuals in any setting wearing any PPE or no PPE
- Exposure: Delivery of chest compressions, defibrillation, CPR (all CPR interventions that include chest compressions)
- Outcome: Transmission of infection
- Study designs: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies, case reports/series) 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. Searches were updated in January 2021.

Research Question 3.

- Population: Individuals delivering chest compressions, defibrillation, or CPR in any setting
- Intervention: Wearing of PPE
- Comparator: Wearing any alternative system of PPE or no PPE
- Outcome: Infection with the same organism as the patient, PPE effectiveness, quality of CPR
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies, cadaver studies, simulation 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. Searches were updated in January 2021.

Consensus on Science

We identified 3 studies for question 1,[426–428] 10 studies for question 2,[427–436] and 5 studies for question 3.[437–441] Results are summarized in Table 20.

Treatment Recommendations

We suggest that chest compressions and CPR have the potential to generate aerosols (weak recommendation, very low–certainty evidence).

We suggest that in the current COVID-19 pandemic, lay rescuers consider chest compressions and public-access defibrillation (good practice statement).

We suggest that in the current COVID-19 pandemic, lay rescuers who are willing, trained, and able to do so consider providing rescue breaths to children in addition to chest compressions (good practice statement).

We suggest that in the current COVID-19 pandemic, health care professionals use PPE for aerosol-generating procedures during resuscitation (weak recommendation, very low–certainty evidence).

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Table 19 – First Aid Topics Reviewed by EvUps

Topic/PICO	Year(s) last updated	Existing treatment recommendation	RCTs since last review, n	Observational studies since last review, n	Sufficient data to warrant SysRev?
Pressure immobilization bandaging for venomous snakebites (FA 1001)	2010CoSTR	Properly performed pressure immobilization of extremities should be considered in first aid after snake envenomation.	2	6	No
Second dose of epinephrine for anaphylaxis (FA 500)	2015CoSTR2020EvUp	We suggest that a second dose of epinephrine be administered by autoinjector to adults and children with severe anaphylaxis whose symptoms are not relieved by an initial dose (weak recommendation, very low–quality evidence).	0	0	No
Dietary sugars for treatment of hypoglycemia (FA 795)	2015CoSTR;2020EvUp	We recommend that first aid providers administer glucose tablets for the treatment of symptomatic hypoglycemia in conscious adults and children (strong recommendation, low–quality evidence). We suggest that if glucose tablets are not available, various forms of dietary sugars such as Skittles, Mentos, sugar cubes, jellybeans, or orange juice can be used to treat symptomatic hypoglycemia in conscious adults and children (weak recommendation, very low-quality evidence). There is insufficient evidence to make a recommendation on the use of whole milk, cornstarch hydrolysate, and glucose solution or glucose gels compared with glucose tablets for the treatment of symptomatic hypoglycemia.	0	0	No

EvUp indicates evidence update; FA, first aid; PICO, population, intervention, comparator, outcome; RCT, randomized controlled trial; and SysRev, systematic review.
CoSTR documents are available at https://costr.ilcor.org/.

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Table 20 – Summary of Study Findings

Research questions	Type of study/No. of participants	Certainty of evidence	Outcome importance	Summary of evidence
Research question 1				
Aerosol generation	2 case reports[427,428]1 cadaver study[426]	Very low (serious risk of bias, serious indirectness)	Critical	Studies reported generation of aerosols
Research question 2				
Transmission of infection	5 observational studies/2923 health care workers[429–433]5 case reports[427,428,434–436]	Very low (serious risk of bias, serious indirectness)	Critical	Inconsistent findings from observational studies Case reports reported transmission of infection after CPR
Research question 3				
Infection with the same organism as the patient	No evidence	. . .	Critical	. . .
PPE effectiveness	1 manikin RCT/30 health care workers[440]	Low (serious risk of bias, serious indirectness)	Critical	PPE effectiveness affected by CPR delivery
CPR quality	4 manikin RCTs/184 participants[437–440]1 manikin non-RCT/48 participants[441]	Very low (serious risk of bias, serious indirectness)	Important	Time to treatment increased with donning of PPE Inconsistent findings on quality of CPR delivery

CPR indicates cardiopulmonary resuscitation; PPE, personal protective equipment; and RCT, randomized controlled trial.

We suggest that it may be reasonable for health care providers to consider defibrillation before donning aerosol-generating PPE in situations in which the provider assesses that the benefits may exceed the risks (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplemental Appendix A6.

International organizations identify CPR (chest compressions and ventilation) as an aerosol-generating procedure such that transmission of COVID-19 is assumed to be possible if a rescuer delivers CPR to an individual with COVID-19 infection. CPR is a complex intervention with several components, including ventilation, defibrillation, chest compressions, and drug administration. The benefits of these interventions to the patient vary, as does the likely associated risk of infection transmission to the rescuer.

A key consideration in developing treatment recommendations is the importance of rescuer safety. During chest compressions, aerosol generation is plausible because chest compressions generate passive ventilation associated with small tidal volumes.[442] Furthermore, the person performing chest compressions is in physical contact with the patient and in close proximity to the airway. We did not identify evidence that defibrillation either does or does not generate aerosols. If it occurs, the duration of an aerosol-generating process would be brief.

In developing these treatment recommendations, the COVID-19 working group sought to carefully balance the benefit of early treatment with chest compressions and defibrillation (before donning PPE) with the potential harm to the rescuer, their colleagues, and the wider community if the rescuer were to be infected with COVID-19. We note that the vaccination status of the rescuer, patient, and the wider community may influence the potential for harm.

ILCOR recognizes that the impact of COVID-19 will vary across regions and countries. In applying these treatment recommendations to their local context, regional and national resuscitation councils should consider the values and preferences of their local communities, prevalence of disease, uptake of vaccination, availability of PPE, training needs of their workforce, and infrastructure and resources to provide ongoing care for patients resuscitated after cardiac arrest.

Task Force Knowledge Gaps

- The potential for aerosol generation through delivery of chest compressions or defibrillation without associated airway maneuvers
- The risks and benefits of resuscitation interventions in the context of the current COVID-19 pandemic
- The effects of strategies to mitigate the risk of viral transmission during chest compressions and defibrillation (eg, the use of a surgical mask, an oxygen mask, or a cloth applied to the patient's mouth and nose)

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Disclosures

Writing Group Disclosures

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Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Julie Considine	Deakin University (Australia)	NHMRC (chief investigator on a research grant testing an intervention to improve safety and quality of emergency nursing care)†; Eastern Health (chief investigator on a research grant to improve hospital discharge)†	None	None	None	None	None	None
Daniela T. Costa-obre	Universidade Federal de Sao Paulo (Brazil)	None	None	None	None	None	None	None
Keith Couper	University of Warwick, Warwick Medical School (United Kingdom)	None	None	None	None	None	None	None
Katie N. Dainty	North York General Hospital (Canada)	None	None	None	None	None	None	None
Peter G. Davis	Royal Women's Hospital (Australia)	Australian National Health and Medical Research Council (salary and project support)†; Australian National Health and Medical Research Council (practitioner fellow)†	None	None	Expert witness for plaintiff in a case of neonatal death*	None	None	None
Maria Fernanda de Almeida	Universidade Federal de Sao Paulo (Brazil)	None	None	None	None	None	None	None
Allan R. de Caen	University of Alberta (Canada)	None	None	None	None	None	None	None
Edison F. de Paiva	University of Sao Paulo–School of Medicine (Brazil)	None	None	None	None	None	None	None
Charles D. Deakin	NIHR Southampton Respiratory Biomedical Research Unit University Hospital Southampton (United Kingdom)	NIHR (PI, CRASH4 study)*; NIHR (PI, PRINCIPLE study)*; NIHR (PI, PARAMEDIC3 study)*	None	None	None	None	None	None
Therese Djärv	Karolinska Institutet (Sweden)	None	None	None	None	None	None	None
Matthew J. Douma	University of Alberta (Canada)	None	None	None	None	None	None	None
Ian R. Drennan	Sunnybrook Health Sciences Center Sunnybrook Research Institute (Canada)	None	None	None	None	None	None	None
Jonathan P. Duff	University of Alberta and Stollery Children's Hospital (Canada)	None	None	None	None	None	None	None

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Kathryn J. Eastwood	Monash University (Australia)	None	None	None	None	None	None	None
Jonathan L. Epstein	Ascend Learning	None	None	None	None	None	None	None
Raffo Escalante	Inter-American Heart Foundation (Peru)	None	None	None	None	None	None	None
Jorge G. Fabres	Pontificia Universidad Catolica de Chile (Chile)	None	None	None	None	None	None	None
Joe Fawke	University Hospitals Leicester NHS Trust (United Kingdom)	None	None	None	None	None	None	None
Judith C. Finn	Curtin University (Australia)	National Health and Medical Research Council (Australia)†; St. John Western Australia†	None	None	None	None	None	None
Elizabeth E. Foglia	Children's Hospital of Philadelphia	None	None	None	None	None	Concord Neonatal*	None
Fredrik Folke	Gentofte University Hospital, Hellerup (Denmark)	Novo Nordisk research grant (research grant in resuscitation)*; Laerdal Foundation Research Grant (unrestricted research grant for excellence in resuscitation science)*	None	None	None	None	None	None
Karoline Freeman	University of Warwick (United Kingdom)	None	None	None	None	None	None	None
Elaine Gilfoyle	Hospital for Sick Children (Canada)	None	None	None	None	None	None	None
Craig A. Goolsby	American Red Cross Scientific Advisory Council	None	None	None	None	None	None	None
Amy Grove	University of Warwick (United Kingdom)	None	None	None	None	None	None	None
Ruth Guinsburg	Federal University of Sao Paulo (Brazil)	None	None	None	None	None	None	None
Tetsuo Hatanaka	Emergency Life Saving zTechnique Academy (Japan)	None	None	None	None	None	Asahikasei Zoll Medical Japan*	None
Mary Fran Hazinski	Vanderbilt University	None	None	None	None	None	None	None
George S. Heriot	University of Melbourne (Australia)	None	None	None	None	None	None	None

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Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Karen G. Hirsch	Stanford University	NIH (PI on an NIH research grant to study post–cardiac arrest management)*	None	None	None	None	None	None
Mathias J. Holmberg	Aarhus University (Denmark)	None	None	None	None	None	None	None
Shigeharu Hosono	Jichi Medical University, Saitama Medical Center (Japan)	None	None	None	None	None	None	None
Ming-Ju Hsieh	National Taiwan University Hospital (Taiwan)	None	None	None	None	None	None	None
Kevin K.C. Hung	Chinese University of Hong Kong (Hong Kong)	None	None	None	None	None	None	None
Cindy H. Hsu	University of Michigan	AHA (Michigan Resuscitation Innovation and Science Enterprise [M-RISE])†; NHLBI/NINDS (1UG3HL145269-01A1: Influence of Cooling Duration on Efficacy in Cardiac Arrest Patients (ICECAP)†; NHLBI (5 R01 HL133129-04:ECPR After Prolonged Cardiac Arrest: Targeting Mechanisms of the No-Reflow)†	None	None	None	None	None	None
Takanari Ikeyama	Aichi Children's Health and Medical Center (Japan)	None	None	None	None	None	None	None
Tetsuya Isayama	National Center for Child Health and Development (Japan)	Japan Agency for Medical Research and Development (consultant for the development of respiratory function monitoring device of a company for low- to moderate-resource countries)†	None	None	None	None	None	None
Vishal S. Kapadia	UT Southwestern	NIH (principal investigator of K23 NIH grant investigating optimal oxygen saturation targets for preterm resuscitation at birth)†	None	None	None	None	None	None
Mandira Kawakami	Universidade Federal de São Paulo (Brazil)	None	None	None	None	None	None	None
Han-Suk Kim	Seoul National University College of Medicine (Republic of Korea)	None	None	None	None	None	None	None

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David A. Kloeck	Resuscitation Council of Southern Africa (South Africa)	None	None	None	None	None	None	None
Peter J. Kudenchuk	University of Washington Medical Center	NIH/NINDS (principal investigator for SIREN Network at University of Washington)†	None	None	None	None	None	None
Anthony T. Lagina	Wayne State University	NIH (coinvestigator title: Alleviating Reactive Carbonyl Species-Induced Progenitor Cell Dysfunction in Diabetic Would Healing; source: NIH/NIDDK)*; NIH/SIREN NIH/ NINDS (site principal investigator title: Hyperbaric Oxygen in Traumatic Brain Injury [HOBIT])*; Comprehensive Research Associates (site investigator for Treatment of Hyperkalemia Study)*	None	None	None	None	None	None
Kasper G. Lauridsen	Randers Regional Hospital Emergency Department (Denmark)	Laerdal Foundation (unrestricted research project grant)*	None	None	None	None	None	None
Eric J. Lavonas	Denver Health Emergency Medicine	None	None	None	None	None	AHA†	None
Andrew S. Lockey	European Resuscitation Council (United Kingdom)	None	None	None	None	None	First on Scene First Aid Co*	None
Carolina Malta Hansen	Copenhagen EMS (Denmark)	Duke Clinical Research Institute (Steering Committee Member, NIH funded trial)†; TrygFonden†; Capital Region of Denmark Strategic Research Fund†	None	None	None	None	None	None
David Markenson	American Red Cross	None	None	None	None	None	None	None
Tasuku Matsuyama	Kyoto Prefectural University of Medicine (Japan)	None	None	None	None	None	None	None
Christopher J.D. McKinlay	University of Auckland (New Zealand)	None	None	None	None	None	None	None
Amin Mehrabian	University of Warwick (United Kingdom)	None	None	None	None	None	None	None
Raina M. Merchant	Penn Medicine Emergency Medicine	None	None	None	None	None	None	None
Daniel Meyran	French Red Cross (France)	None	None	None	None	None	None	None

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Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Peter T. Morley	University of Melbourne (Australia)	None	None	None	None	None	None	None
Laurie J. Morrison	Rescu, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Division of Emergency Medicine, Department of Medicine, University of Toronto (Canada)	None	None	None	None	None	None	None
Kevin J. Nation	New Zealand Resuscitation Council (New Zealand)	None	None	None	None	None	None	None
Michael Nemeth	Sunnybrook Health Sciences Center (Canada)	None	None	None	None	None	None	None
Robert W. Neumar	University of Michigan	AHA (19SFRN34760762)†; NIH-NHLBI (R01 HL133129)†; NIH-NHLBI (K12HL133304)†	Stryker Physio-Control (equipment support for laboratory research)*	None	None	None	None	None
Tonia Nicholson	Waikato Hospital (New Zealand)	None	None	None	None	None	None	None
Susan Niermeyer	University of Colorado	None	None	None	None	None	None	None
Nikolaos Nikolaou	Konstantopouleio General Hospital (Greece)	Galactic HF-AMGEN (subinvestigator)*; SELECT EX9536-4388 NOVONORDISC GALACTIC-HF AMGEN 20110203 (subinvestigator)*	None	None	None	None	None	None
Chika Nishiyama	Kyoto University (Japan)	None	None	None	None	None	None	None
Jerry P. Nolan	Warwick Medical School, University of Warwick (United Kingdom)	UK NIHR (coinvestigator for PARAMEDIC3 Trial of IO vs IV drugs in out-of-hospital cardiac arrest)*	None	None	None	None	None	None
Brian J. O'Neil	Wayne State University	NIH (SIREN hub PI)*; Brainscope (site PI)*	None	Zoll Circulation*; Brainscope*	None	None	None	None
Aaron M. Orkin	University of Toronto (Canada)	Canadian Institutes of Health Research (coinvestigator on grant concerning a trial about opioid overdose and naloxone distribution)*	None	None	None	None	None	None
Osokogu Osemeke	University of Warwick (United Kingdom)	None	None	None	None	None	None	None
Michael J. Parr	Liverpool Hospital, University of New South Wales and Macquarie University Hospital, Macquarie University (Australia)	None	None	None	None	None	None	None

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Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Catherine Patocka	University of Calgary (Canada)	None	None	None	None	None	None	None
Jeffrey L. Pellegrino	University of Akron	None	None	None	None	None	None	None
Gavin D. Perkins	Warwick Clinical Trials Unit and University Hospitals Birmingham NHS Foundation Trust (United Kingdom)	National Institute for Health Research (funding to institution to conduct research in cardiac arrest)†; British Heart Foundation (funding to institution to support OHCAO registry)†; Resuscitation Council UK (funding to institution to support OHCAO registry)†	None	None	None	None	None	European Resuscitation Council (board member. travel and related expense)*; Resuscitation Council UK (chair, Community and Ambulance Committee)*
Jeffrey M. Perlman	Weill Cornell Medical College	None	None	None	None	None	None	None
Yacov Rabi	University of Calgary (Canada)	None	None	None	None	Masimo Corp†	None	None
Joshua C. Reynolds	Michigan State University	NIH (I am the site lead at my hospital for the ICECAP trial. Our site will receive per-subject reimbursement for enrolling in this trial.)†	None	None	None	None	None	None
Giuseppe Ristagno	Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan (Italy)	None	None	None	None	None	ZOLL Medical Corp*	None
Charles C. Roehr	University of Oxford (United Kingdom)	National Institute for Healthcare Research (NIHR, UK) (grant holder of a substantive grant (ended 2021)*	None	Chiesi Pharmaceuticals*	None	None	None	None
Tetsuya Sakamoto	Teikyo University (Japan)	None	None	None	None	None	None	None
Claudio Sandroni	Università Cattolica del Sacro Cuore (Italy)	None	None	None	None	None	None	None
Taylor Sawyer	Seattle Children's Hospital/ University of Washington	None	None	None	None	None	None	None

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Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Georg Schmölzer	University of Alberta (Canada)	Canadian Institute of Health Research (PI, to examine higher or lower starting oxygen concentration in premature infants at birth, the HiLo trial)*; Canadian Institute of Health Research (PI, to study 2 different chest compressions techniques in newborn infants at birth, the SURV1VE trial)*; NIH (co-PI, to study cord milking or early cord clamping in term infants, the MINVI trial)*	None	None	None	None	None	None
Sebastian Schnaubelt	Medical University of Vienna (Austria)	None	None	None	None	None	None	None
Federico Semeraro	Maggiore Hospital (Italy)	None	None	None	None	None	None	None
Markus B. Skrifvars	Helsinki University Hospital and University of Helsinki (Finland)	Numerous unrestricted academic research grants (funding for academic research)†	None	BARD Medical (Ireland)*	None	None	None	None
Christopher M. Smith	University of Warwick, Warwick Medical School (United Kingdom)	None	None	None	None	None	None	None
Michael A. Smyth	University of Warwick (United Kingdom)	None	None	None	None	None	None	None
Roger F. Soll	University of Vermont Medical Center	None	None	None	None	None	None	None
Takahiro Sugiura	Toyohashi Municipal Hospital (Japan)	None	None	None	None	None	None	None
Sian Taylor-Phillips	University of Warwick, Warwick Medical School (United Kingdom)	None	None	None	None	None	None	None
Daniele Trevisanuto	University of Padova (Italy)	None	None	None	None	None	None	None
Christian Vaillancourt	University of Ottawa, Ottawa Hospital Research Institute (Canada)	Heart and Stroke Foundation of Canada (co–principal investigator CanROC)†; Canadian Institutes of Health Research (co–principal investigator CanROC)†	None	None	None	None	None	University of Ottawa (senior scientist)†
Tzong-Luen Wang	Fu Jen Catholic University Hospital (Taiwan)	None	None	None	None	None	None	None

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Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Gary M. Weiner	University of Michigan	None	None	None	None	None	None	None
Michelle Welsford	McMaster University, Hamilton Health Sciences (Canada)	None	None	None	None	None	None	None
Jane Wigginton	UT Southwestern Medical Center, UT Dallas Emergency Medicine, and Texas Biomedical Device Center	None	None	None	None	None	None	None
Jonathan P. Wyllie	James Cook University Hospital (United Kingdom)	None	None	None	None	None	None	Resuscitation Council UK (president)[†]
Joyce Yeung	University of Warwick, Warwick Medical School (United Kingdom)	None	None	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

[*] Modest.

[†] Significant.

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Reviewer Disclosures

Reviewer	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Marieke T. Blom	Amsterdam University Medical Center (The Netherlands)	European Union (Horizon 2020 grant ESCAPE-NET [grant no. 733381])†; Netherlands CardioVascular Research Initiative (Dutch Heart Foundation, Dutch Federation of University Medical Centers, Netherlands Organization for Health Research and Development, and Royal Netherlands Academy of Sciences) (grant CVON-2018-30 Predict 2)†	None	None	None	None	Scientific Board of Dutch Resuscitation Council*	None
Patricia Conaghan	University of Manchester (United Kingdom)	None	None	None	None	None	None	None
Koert de Waal	John Hunter Children's Hospital (Australia)	None	None	None	None	None	None	None
Gustavo E. Flores	Emergency & Critical Care Trainings LLC (Puerto Rico)	None	None	None	None	None	None	None
Christian Hassager	Rigshospitalet (Denmark)	Lundbaek Foundation (A research grant that supports my professorship in critical care.)†; Novo Nordisk Foundation (A research grant for research on the effect of steroids on post cardiac arrest syndrome.)†; Abiomed (Local PI in the DanGershock trial)†	None	Abiomed*	None	None	None	None
Martin Kluckow	University of Sydney (Australia)	Australian NHMRC (APP1158494 for transitional research to improve delivery room CPR in an animal model)†	None	None	None	None	None	None
Caroline Leech	University Hospitals Coventry & Warwickshire NHS Trust (United Kingdom)	None	None	None	None	None	None	None
Matthew Levy	Johns Hopkins University School of Medicine	None	None	None	None	None	None	None
Andrew MacPherson	Canadian Red Cross (Canada)	None	None	None	None	None	None	None
Taylor McCormick	Denver Health	Society for Academic Emergency Medicine Foundation*	None	None	None	None	None	None

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Reviewer	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Mary Ann McNeil	University of Minnesota	None	None	None	None	None	None	None
Ari Moskowitz	Beth Israel Deaconess Medical Center	NIH (NIGMS K23 award for sepsis research)†	None	None	None	None	None	None
Sabine Nabecker	Bern University Hospital, University of Bern (Switzerland)	Burgergemeinde Bern (Research Grant for the project: Outcome after Out-of-Hospital Cardiac Arrest (OHCA) in the region of Bern, Switzerland before and after implementation of extracorporeal cardiopulmonary resuscitation (eCPR). Burgergemeinde Bern. Funding program of the Committee of the Natural Historic Museum of Bern. 2019-1077.SFR 3,000)*	None	None	None	None	European Resuscitation Council (education representative of the "young ERC" group of the European Resuscitation Council)*	None
Colm P.F. O'Donnell	National Maternity Hospital (Ireland)	Chieisi Farmaceutici (Manufacturers provided investigational medicinal product (Curosurf) free of charge for the POPART trial (EudraCT number: 2016-004198-41) of which I am the Chief Investigator)†	None	None	None	None	None	None
Peter Paal	Hospitallers Brothers Hospital, Paracelsus Medical University (Austria)	None	None	None	None	None	None	None
Sarah M. Perman	University of Colorado, School of Medicine	NIH (K23HL138164)†	None	None	None	None	None	None
Tom Quinn	Kingston University and St. George's University of London (United Kingdom)	NIHR*	None	None	None	None	ESC Association Acute Cardiovascular Care (board member)*	None
Thomas Rea	University of Washington	Philips (grant to evaluate community response strategies. We are not evaluating proprietary technology but rather general response strategies. The grant is to my employer, the University of Washington)*; AHA (grant evaluates whether brain oximetry during resuscitation changes during resuscitation and is predictive of outcome. The grant is to my employer, the University of Washington)*; federal government (pending grant to study components of CPR and outcome of cardiac arrest)*; Medtronic Foundation (HeartRescue Consortium.	None	None	None	None	None	None

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Reviewer	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
		Nonproprietary efforts to improve links in the chain of survival for large population-based regions)*; AHA (investigator in the Strategic Network to Investigate Sudden Cardiac Arrest)†						
Jon C. Rittenberger	Guthrie Medical Center	None	None	None	None	None	None	None
Sten Rubertsson	Uppsala University and Uppsala University Hospital (Sweden)	None	None	None	None	None	None	None
Mario Ruediger	TU Dresden, Medical Faculty Carl Gustav Carus Center for feto/neonatal Health (Germany)	None	None	None	None	None	None	None
Andrea Scapigliati	Catholic University of the Sacred Heart (Italy)	None	None	None	None	None	None	None
Stephen M. Schexnayder	University of Arkansas/ Arkansas Children's Hospital	None	None	None	None	None	None	None
Fred Severyn	University of Colorado	None	None	None	None	None	None	None
Anne Lee Solevåg	Oslo University Hospital (Norway)	None	None	None	None	None	None	None
Lynn Thomas	St. John Ambulance (United Kingdom)	None	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

* Modest.

† Significant.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resuscitation.2021.10.040.

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