Supplement to Circulation

2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

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2020 International Consensus on First Aid Science With Treatment Recommendations

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Circulation

Executive Summary

2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

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The International Liaison Committee on Resuscitation (ILCOR) was formed in 1992 as an international council of councils and currently includes representatives from the American Heart Association (AHA), the European Resuscitation Council, the Heart and Stroke Foundation of Canada, the Australian and New Zealand Committee on Resuscitation, the Resuscitation Council of Southern Africa, the InterAmerican Heart Foundation, and the Resuscitation Council of Asia.[1] The ILCOR mission is to promote, disseminate, and advocate international

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implementation of evidence-informed resuscitation and first aid by using transparent evaluation and consensus summary of scientific data. Resuscitation includes all responses necessary to treat sudden life-threatening events affecting the cardiovascular and respiratory systems, with a focus on sudden cardiac arrest. As in 2015, this 2020 consensus publication also includes first aid topics as part of the international review and consensus recommendations.

There are 6 ILCOR Task Forces: (adult) Basic Life Support (BLS); (adult) Advanced Life Support (ALS); Pediatric (basic and advanced) Life Support (PLS); Neonatal Life Support (NLS); Education, Implementation, and Teams (EIT); and First Aid. This *2020 International Consensus on Cardiopulmonary Resuscitation* (CPR) *and Emergency Cardiovascular Care* (ECC) *Science With Treatment Recommendations* (CoSTR) includes a separate publication from each of the 6 task forces as well as this Executive Summary and a publication detailing the evidence evaluation process and management of potential conflicts of interest.

In this publication, the separate sections for each task force highlights the "hot" topics and the new CoSTRs developed. Not all relevant references are cited here; refer to each task force publication in this supplement for details of each of the reviews and task force deliberations. In addition, each task force publication summarizes additional reviews that are not highlighted in this Executive Summary.

EVIDENCE EVALUATION PROCESS AND MANAGEMENT OF POTENTIAL CONFLICTS OF INTEREST

Evidence Evaluation Process

ILCOR is committed to a rigorous and continuous review of scientific literature focused on resuscitation, cardiac arrest, relevant conditions requiring first aid, related education and implementation strategies, and systems of care. After the publication of the *2015 International Consensus on CPR and ECC Science With Treatment Recommendations*, ILCOR also committed to sponsoring a continuous evidence-evaluation process, with topics prioritized for review by the task forces and with CoSTR updates published annually. For this 2020 CoSTR, the 6 ILCOR task forces performed structured reviews of 184 topics, completing the most ambitious evidence review that ILCOR has attempted to date.

The ILCOR systematic review process continues to be based on the methodological principles published by the National Academy of Health and Medicine (formerly the Institute of Medicine)[2]; Cochrane[3,4]; Grading of Recommendations Assessment, Development, and Evaluation (GRADE)[5]; and the reporting guidelines based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations.[6,7]

Three types of evidence evaluation provided the basis for this 2020 CoSTR: the systematic review, the scoping review, and the evidence update. Based on recommendations from the ILCOR Scientific Affairs Committee and agreement of the task forces, only systematic reviews could result in new or modified treatment recommendations.

Systematic Reviews

The systematic review (SysRev) represents the most structured and detailed of the reviews. It requires a rigorous process following strict methodology to answer a specific question, and each SysRev resulted in the generation of the task force CoSTR included in this publication. For this 2020 CoSTR process, ILCOR member councils agreed that treatment recommendations could be changed only as the result of a SysRev.

The SysRevs were performed by a knowledge synthesis unit (groups of well-respected researchers with methodological expertise in performing SysRevs), an expert systematic reviewer (an individual with methodological expertise and a track record of publications), or the task force. Many of the reviews resulted in separate published SysRevs.

To begin the SysRev, the task force and reviewers phrased the question to be answered in terms of the PICOST (population, intervention, comparator, outcome, study design, time) format. The literature searches were developed and conducted by information specialists who used, at a minimum, the MEDLINE, Embase, and the Cochrane Library databases. The clinical experts for the SysRev reviewed all identified studies and selected those that met inclusion criteria. The reviewers rated the risk of bias for each study, analyzed the data, and performed meta-analyses as appropriate. The reviewers used the GRADE framework to rate the certainty/confidence in the estimates of the effect of an intervention or assessment across a body of evidence for each of the predefined outcomes; certainty, or confidence, was rated as high, moderate, low, or very low. Evidence from randomized controlled trials (RCTs) generally began the analysis as high-certainty evidence, and evidence from observational studies generally began the analysis as low-certainty evidence; examination of the evidence using the GRADE approach could result in either downgrading or upgrading the certainty of evidence. For additional information, refer to "2020 Evidence Evaluation Process and Management of Potential Conflicts of Interest" in this supplement.[8,8a]

The data analysis was presented to the task force, and the task force drafted the summary consensus on science as well as the treatment recommendations. Each treatment recommendation indicates the strength of the recommendation (recommends=strong, suggests=weak)

and the certainty of the evidence. The structured deliberations that the task force completed are highlighted in an evidence-to-decision table, with a table for each new, completed CoSTR included in Appendix A of each task force publication in this supplement.

Draft 2020 CoSTRs were posted on the ILCOR website[9] for a 2-week comment period. The task forces reviewed the comments and modified the CoSTR content as needed. Each task force publication in this supplement contains the final wording of the CoSTR statements as approved by the ILCOR task forces and by the ILCOR member councils.

Scoping Reviews

Scoping reviews (ScopRevs) are designed to identify the extent, range, and nature of evidence on a topic or a question. They follow a rigorous process but use a broader search strategy and were performed by topic experts in consultation with the task forces. The ScopRev produces a narrative summary of evidence, with tables presenting key data from the studies identified but with no risk of bias analysis for each study. The task force analyzed the identified evidence and determined its value and implications for resuscitation practice or research. The rationale for each ScopRev, the summary of evidence, and task force insights are all highlighted in the body of each task force publication. If a ScopRev identified substantive evidence that may result in a future change in ILCOR treatment recommendations, the task force recommended that a new SysRev be performed. Draft ScopRevs were posted for a 2-week comment period on the ILCOR website, and the task forces revised text as needed in response to the public comments. All ScopRevs are included in their entirety in Appendix B of each task force publication in this supplement.

Evidence Updates

Evidence updates (EvUps) were performed to identify evidence published after the most recent ILCOR review of the topic. The EvUps were performed by volunteer members of the task forces or ILCOR member councils, who used the same search strategy that was used for the previous review. If the search strategy failed to identify new evidence, the search strategy was broadened to capture any relevant published studies. The task forces reviewed the EvUps to determine if sufficient evidence was identified to suggest the need for a new SysRev. All EvUps cited can be viewed in Appendix C of each task force publication in this supplement.

Potential Impact of Coronavirus Disease 2019 (COVID-19) on Resuscitation

The CoSTR reviews were all completed by early February 2020. As a result, this document does not address the topic of the potential influence of coronavirus disease 2019 (COVID-19) on resuscitation practice. An ILCOR writing group was assembled in the spring of 2020 to identify and evaluate the published evidence regarding risks of aerosol generation and infection transmission during attempted resuscitation of adults, children, and infants. This group developed a consensus on science with treatment recommendations and task force insights. This statement is published as a separate document.[10] As new evidence emerges, the ILCOR task forces will review and update this statement, so the reader is referred to the ILCOR website[9] for the most up-to-date recommendations.

Management of Potential Conflicts of Interest

ILCOR followed the rigorous conflict-of-interest (COI) policies that have been used successfully in previous years. Anyone involved in any part of the process was required to disclose all commercial relationships and other potential conflicts by using the standard AHA online COI disclosure process. Task force members as well as reviewers and collaborators all completed this online disclosure process before they were allowed to perform reviews and take part in discussions. Participants were asked to be sensitive to commercial conflicts as well as to any potential intellectual conflicts, such as having authored key studies related to a topic or being involved in ongoing studies related to a topic. AHA staff reviewed the disclosures before appointment to ensure that no disclosures were significant enough to preclude participation. Disclosure information for writing group members is listed in Appendix 1. Disclosure information for peer reviewers is listed in Appendix 2.

During in-person meetings, each participant was assigned a COI number, and a full list of disclosures was available to all participants throughout the meeting. Participants were required to state any relevant conflicts during in-person meetings as well as on webinars and conference calls and were required to abstain from voting on any wording of the consensus on science or treatment recommendations for any topics related to their potential conflicts. AHA staff members assisted the task force chairs in monitoring compliance. Any COI-related issues were brought to the attention of the task force chairs and the COI co-chairs. At each meeting, participants were notified of a toll-free telephone number to call to anonymously report any COI issues; no calls were received.

BASIC LIFE SUPPORT

Hot Topics

CPR During Transport

The question of whether to transport a cardiac arrest victim to the hospital or complete CPR on the scene continues to be controversial. This topic has not been reviewed

since 2005, and the BLS Task Force chose to undertake a ScopRev to determine if there was sufficient new evidence to warrant a SysRev. Eight nonrandomized studies reported that among patients with out-of-hospital cardiac arrest (OHCA) transported with CPR in progress, return of spontaneous circulation (ROSC) was achieved in the emergency department in approximately 9.5%, with 2.9% surviving to hospital discharge.

Manikin studies consistently document poorer CPR quality during transport while clinical studies evaluating the quality of CPR during transport report conflicting results. Three RCTs comparing manual CPR with mechanical CPR during transport showed no benefit from mechanical CPR with respect to ROSC or survival to discharge. Manikin studies indicate that mechanical CPR provided consistent CPR whereas the quality of manual CPR declined during transport. Nonrandomized studies showed that duration of transport with CPR and distance transported with CPR does not adversely impact patient outcomes. There are many facets to this question, and on the basis of the evidence identified, the task force concluded that there was a need for more than 1 SysRev.

Several questions remain unanswered, such as whether clinical outcomes are affected by the decision to transport with CPR in progress and when the decision to transport with ongoing CPR should be made. The use of feedback devices could improve the quality of CPR during transport. However, an important consideration is the risk of harm to personnel who perform manual CPR during transport—there is little evidence for this, but many anecdotal reports attest to the potential risk to unrestrained personnel in the back of a moving ambulance.

CPR Before Calling for Help for Adults With OHCA

The question of whether to first start CPR or call for help for adults with OHCA is likely to be influenced by the wide availability of mobile phones with a hands-free option, which makes it possible to call emergency medical services (EMS) and start CPR simultaneously. The SysRev identified just 1 cohort study including 17 461 adults with OHCA from a national registry of 925 288 cases.[11] Analysis was limited to cases in which lay rescuers witnessed the adult cardiac arrest and performed CPR without the need for dispatcher assistance. The groups differed in many respects, and despite adjustment, residual confounding was likely. The 3 groups (call and CPR first, call first, and CPR first) all had similar rates of survival with favorable outcome. The BLS Task Force chose to make a discordant recommendation (a strong recommendation despite very low-certainty evidence) that for an adult with OHCA, a lone bystander with a mobile phone should phone EMS, activate the speaker or other hands-free option on the mobile phone, and immediately begin CPR, with dispatcher assistance if required. If a lone rescuer must leave an adult victim to phone EMS, the priority should be prompt activation of EMS before returning to the victim to initiate CPR as soon as possible.

Resuscitation Care for Suspected Opioid-Associated Emergencies

Deaths from opioid overdose are increasing substantially, particularly in the United States. This topic was reviewed in 2015, but no treatment recommendation was made.[12,12a] An updated SysRev on this topic was considered essential to inform best-practice guidelines for bystander resuscitation for suspected opioid-induced emergencies. No studies were identified that compared bystander-administered naloxone (intramuscular or intranasal) plus conventional CPR with conventional CPR only. As a response to the growing opioid epidemic, naloxone has been widely distributed by healthcare authorities to laypeople in various opioid-overdose prevention schemes. A recent SysRev identified 22 observational studies evaluating the effect of overdose education and naloxone distribution and found an association between implementation of these programs and decreased mortality rates.[13] On the basis of expert opinion, the BLS Task Force suggested that CPR be started without delay on any unresponsive person who is not breathing normally and that naloxone be used by lay rescuers in suspected opioid-related respiratory or circulatory arrest.

Feedback for CPR Quality

CPR feedback or prompt devices are intended to improve CPR quality, the probability of ROSC, and survival from cardiac arrest. Real-time CPR guidance devices can be categorized as (1) digital audiovisual feedback, including corrective audio prompts; (2) analogue audio and tactile clicker feedback for chest compression depth and release; and (3) metronome guidance for chest compression rate. Several additional studies were identified in this updated SysRev. This topic proved particularly controversial. Most higher-certainty data did not demonstrate a clinically or statistically significant association between real-time feedback and improved patient outcomes; furthermore, these devices require resources to purchase and implement. On the other hand, several studies demonstrated clinically important improvements in outcomes associated with the use of feedback devices.

A permissive recommendation was considered appropriate because of the role that these devices play in CPR quality monitoring, benchmarking, and quality-improvement programs. The BLS Task Force agreed on a weak recommendation for healthcare systems to consider CPR feedback devices, given the evidence that they improve the quality of CPR and there was no signal of patient harm in the data reviewed. The task force highlighted that there was no consistent signal indicating that the real-time feedback function of these

devices has a significant effect on individual cardiac arrest patient outcomes, suggesting that the devices should not be implemented for this reason alone outside of a comprehensive quality-assurance program.

Analysis of Rhythm During Chest Compressions

Artifact-filtering algorithms for the analysis of electrocardiographic rhythms during CPR have been proposed as a method to reduce pauses in chest compressions and thereby increase the quality of CPR. Most of the 14 studies included in this SysRev used previously collected electrocardiograms, electric impedance, and/or accelerometer signals recorded during CPR to evaluate the ability of algorithms or machine learning to detect shockable rhythms during chest compressions. None of these studies evaluated the effect of the artifact-filtering algorithms on any critical or important outcomes, but they provide insights into the potential benefits of this technology. The BLS Task Force prioritized avoiding the costs of introducing a new technology when its effects on patient outcomes and the risk of harm remain to be determined; thus, the task force suggested against the routine use of artifact-filtering algorithms for analysis of ECG rhythms during CPR. The task force made a weak recommendation for further research because (a) there is currently insufficient evidence to support a decision for or against routine use, (b) further research may reduce uncertainty about the effects, and (c) further research is thought to be of good value for the anticipated costs.

New Systematic Reviews

Dispatch Diagnosis of Cardiac Arrest

It is not known if there are specific call characteristics that impact the ability of emergency medical dispatchers to recognize cardiac arrest. This SysRev identified a wide variety of algorithms and criteria used by dispatch centers to identify cardiac arrest and other medical emergencies. There was great variability in the accuracy of these algorithms and the criteria for recognizing OHCA in adults. The BLS Task Force recognized that minimizing the frequency of missed cardiac arrest events may increase the frequency of false-positive cases.

Effect on treatment recommendations: The task force recommended that dispatch centers implement a standardized algorithm and/or standardized criteria to immediately determine if a patient is in cardiac arrest at the time of an emergency call. It was also recommended that dispatch centers monitor and track diagnostic capability.

Firm Surface for CPR

This topic was last reviewed by the BLS Task Force in 2010.[14,14a] The evidence identified in this latest SysRev was grouped under the subheadings of mattress type, floor compared with bed, and backboard. The task force noted that effective manual compression depths can be achieved even on a soft surface if the CPR provider increases overall compression depth to compensate for mattress compression. Manikin studies indicate a marginal benefit to manual chest compression depth from the use of a backboard but use of these may cause significant interruption in chest compressions, and they have significant cost and training implications.

Effect on treatment recommendations: The treatment recommendations have been updated from 2010; they are all weak recommendations based on very low-certainty evidence. The BLS Task Force suggests performing manual chest compressions on a firm surface when possible; this includes activation of a bed's CPR mode if it has this feature. During in-hospital cardiac arrest, the task force suggests against moving a patient from a bed to the floor to improve chest compression depth. The task force was unable to make a recommendation about the use of backboards because the confidence in effect estimates was so low.

Starting CPR: Compressions-Airway-Breaths Versus Airway-Breaths-Compressions

Although most adult BLS guidelines recommend commencing chest compressions before giving rescue breaths, there is still considerable debate about this sequence. This SysRev did not identify any additional studies published after the 2015 ILCOR review.[12,12a]

Effect on treatment recommendations: The treatment recommendation is unchanged from 2015.[12,12a]

CPR Before Calling for Help for Adults With OHCA

This topic is discussed in more detail in the BLS Hot Topics section earlier in this publication. The SysRev identified just 1 cohort study on which to base the treatment recommendation.

Effect on treatment recommendations: Despite very low-certainty evidence, for adults with OHCA, the BLS Task Force made a strong recommendation 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.

Timing of CPR Cycles (2 Minutes Versus Other)

This topic had not been updated since 2015.[12,12a] The current SysRev identified 2 older studies that included comparisons of groups with different CPR durations between rhythm checks, but both studies were designed to address the question of CPR first compared with defibrillation first. Consequently, the certainty of evidence supporting the optimal duration of CPR is low.

Effect on treatment recommendations: The treatment recommendation is unchanged from 2015.[12,12a]

Hand Position During Compressions

This topic was last reviewed in 2015.[12,12a] This latest SysRev did not identify any studies that evaluated the

effect of any specific hand position on short-term or long-term survival after cardiac arrest. Physiological surrogate outcomes were reported in 3 very low-certainty studies.

Effect on treatment recommendations: The treatment recommendation is unchanged from 2015.[12,12a]

Rhythm Check Timing

During CPR, rhythm checks cause pauses in chest compressions, and frequent pauses are associated with worse outcomes from cardiac arrest. This SysRev was undertaken to assess the evidence for optimal timing for rhythm checks. Although only very low-certainty evidence addressing this question was identified, worse short-term and long-term outcomes have been reported with immediate rhythm check after shock delivery.

Effect on treatment recommendations: The treatment recommendation is unchanged from 2015.[12,12a]

Feedback for CPR Quality

Feedback for CPR quality is discussed in more detail in the BLS Hot Topics section earlier in this publication. This topic was last reviewed in 2015, and several additional studies were identified in this updated SysRev.

Effect on treatment recommendations: The treatment recommendation is unchanged from 2015.[12,12a]

Alternative Techniques (Cough CPR, Precordial Thump, Fist Pacing)

This topic was last reviewed in 2010.[14,14a] Reports on social media continue to advocate cough CPR, and it may be perceived by the public as an effective way of preventing cardiac arrest. There is no evidence that cough CPR is effective in OHCA. Precordial thumping and fist pacing are techniques previously recommended to healthcare professionals.

Effect on treatment recommendations: Although the treatment recommendations remain essentially unchanged from 2010, the BLS Task Force has updated them to clarify the special circumstances when these alternative techniques might be appropriate. The strong recommendation against cough CPR, precordial thump, and fist pacing for cardiac arrest remains unchanged. The Task Force suggests that fist pacing may be considered only as a temporizing measure in the exceptional circumstance of a witnessed, monitored, in-hospital arrest (such as in a cardiac catheterization laboratory) with bradyasystole, if recognized promptly, before loss of consciousness.

Public-Access Automated External Defibrillator Programs

The impact on outcomes from cardiac arrest after implementation of a public-access automated external defibrillator (AED) program was last reviewed by ILCOR in 2015,[12,12a] and SysRevs on the effects of public-access defibrillation on OHCA survival were published after 2015.[15,16] This updated ILCOR SysRev focused on comparing outcomes in systems with public-access AED programs with outcomes in systems with a traditional EMS response, and the review included 1 RCT and 30 observational studies.

Effect on treatment recommendations: The strong recommendation to implement public-access defibrillation programs for patients with OHCA is unchanged from 2015.[12,12a]

Analysis of Rhythm During Chest Compressions

This topic is discussed in more detail in the BLS Hot Topics section earlier in this publication. Artifact-filtering algorithms for the analysis of electrocardiographic rhythm during CPR have been proposed as a method to reduce pauses in chest compressions and thereby increase the quality of CPR.

Effect on treatment recommendations: The weak recommendation against the routine use of artifact-filtering algorithms for the analysis of electrocardiographic rhythm during CPR is unchanged from 2015.[12,12a] However, the previous weak suggestion that it would be reasonable for EMS systems that use integrated artifact-filtering algorithms in clinical practice to continue with their use has been changed to a weak recommendation that the usefulness of artifact-filtering algorithms for the analysis of electrocardiographic rhythm during CPR be assessed in clinical trials or research initiatives.

CPR Before Defibrillation

This topic was last reviewed by ILCOR in 2015.[12,12a] Although previous treatment recommendations for CPR before defibrillation have been based on RCTs, the results from these trials are inconsistent, and the optimal timing of defibrillation remains uncertain. No new RCTs were identified.

Effect on treatment recommendations: The treatment recommendation is unchanged from 2015.[12,12a]

Removal of Foreign Body Airway Obstruction

The topic of foreign body airway obstruction (FBAO) was last reviewed by ILCOR in 2010, and at that time, the principal treatment recommendation was that "chest thrusts, back blows, or abdominal thrusts are effective for relieving FBAO in conscious adults and children older than 1 year."[12,12a] Recently, manual suction devices (airway clearance devices) that use a vacuum to remove foreign bodies have become commercially available. These devices have not previously been reviewed by ILCOR and were included in this SysRev. The data in the peer-reviewed literature assessing the efficacy of suction-based airway clearance devices comprised just 1 case series of 9 adults, which the task force deemed insufficient to support the implementation of a new technology with an associated financial and training cost.

Effect on treatment recommendations: The treatment recommendation has been substantially updated from 2010.[12,12a] The BLS Task Force suggested that back slaps are used initially in adults and children with an FBAO and an ineffective cough and that abdominal thrusts are used where back slaps are ineffective (weak recommendation, very low-certainty evidence). Chest thrusts are suggested in unconscious adults and children with an FBAO. The task force suggested that rescuers consider the manual extraction of visible items in the mouth but should not perform blind finger sweeps in patients with an FBAO and that appropriately skilled healthcare providers use Magill forceps to remove an FBAO in patients with OHCA caused by FBAO. The task force suggested that suction-based airway clearance devices should not be used routinely.

Resuscitation Care for Suspected Opioid-Associated Emergencies

This topic is discussed in more detail in the BLS Hot Topics section earlier in this publication. In this updated SysRev, no studies were identified that compared bystander-administered naloxone (intramuscular or intranasal) plus conventional CPR with conventional CPR only.

Effect on treatment recommendations: No treatment recommendation was made in 2015, but given the scale of the opioid problem, on this occasion, on the basis of expert opinion, the BLS Task Force suggested that CPR be started without delay in any unresponsive person who is not breathing normally, and that naloxone be used by lay rescuers in suspected opioid-related respiratory or circulatory arrest.

Drowning

Prognostic factors that predict outcome after a drowning incident were last reviewed in 2015.[12,12a] Attempting to rescue a submerged victim has substantial resource implications and may place rescuers at risk; thus, it was deemed important to update this SysRev for 2020. The findings from the 6 new papers identified in this update are consistent with the 2015 treatment recommendation.

Effect on treatment recommendations: The treatment recommendation is unchanged from 2015.[12,12a]

Harm From CPR to Victims Not in Cardiac Arrest

Lay rescuers may not begin CPR even when a victim is in cardiac arrest because of concern that delivering chest compressions to a person who is not in cardiac arrest could cause serious harm. Evidence that chest compressions are unlikely to cause harm in these circumstances may encourage more bystanders to commence CPR for cardiac arrest victims. This topic was last reviewed in 2015, and this updated SysRev did not find any studies.

Effect on treatment recommendations: The treatment recommendation is unchanged from 2015.[12,12a]

Additional Reviews

The BLS Task Force also evaluated 3 other ScopRevs and 1 EvUp. These reviews, per ILCOR agreement, did not change treatment recommendations, but several resulted in the suggestion for new SysRevs.

ADVANCED LIFE SUPPORT

Hot Topics

Vasopressors During Cardiac Arrest

In 2019, the ILCOR ALS Task Force published a SysRev and meta-analysis[17] and a CoSTR[18,19] on this topic. The meta-analysis of 2 placebo-controlled trials showed that after OHCA, epinephrine increases ROSC, survival to discharge, and survival at 3 months but did not show an increase in survival to discharge with favorable neurological outcome.[17,20,21] The much larger and more recent trial (8000 patients)[20] found no difference in survival with favorable or unfavorable neurological outcome at 3 months; thus, the impact of epinephrine administration on neurological outcome for patients with OHCA remains uncertain.

Another meta-analysis of these 2 RCTs has shown that relative to placebo, the effects of adrenaline on ROSC are greater for patients with an initially nonshockable rhythm than for those with shockable rhythms.[22] Similar patterns are observed for longer-term survival outcomes, but the differences in effects are less pronounced.

The ALS Task Force recommends giving epinephrine as soon as feasible in cardiac arrest with nonshockable rhythms unless there is a clearly reversible cause that can be addressed rapidly. The optimal timing for epinephrine in patients with shockable rhythms is unknown. The task force suggests administering epinephrine after initial defibrillation attempts have been unsuccessful; however, the optimal timing or number of shocks after which epinephrine should be administered remains unclear.

There are few data to guide the specific dose and dose interval of epinephrine during cardiopulmonary resuscitation; however, the 2 OHCA RCTs comparing epinephrine with placebo used standard dose epinephrine (1 mg intravenous [IV] or intraosseous [IO] every 3–5 minutes).

There is limited RCT evidence on the use of epinephrine for in-hospital cardiac arrest; therefore, on the basis of the evidence for OHCA, in 2019 the ILCOR ALS Task Force made the same recommendations for epinephrine administration for in-hospital and OHCA.

The use of vasopressin alone or in combination with epinephrine does not improve outcomes in comparison with epinephrine alone; thus, to reduce complexity, epinephrine alone is suggested.

Targeted Temperature Management

Targeted temperature management (TTM) has been the subject of considerable controversy for many years. A SysRev of TTM and treatment recommendations was included in the 2015 CoSTR.[23–26]

Several studies have been published after 2015, but the most important is HYPERION (Therapeutic Hypothermia After Cardiac Arrest in Non Shockable Rhythm), a French trial in which 581 adult, comatose patients with OHCA and in-hospital cardiac arrest (IHCA) and an initial nonshockable rhythm were randomized to either TTM with a target temperature of 33°C or TTM with a temperature of 37°C, both for 24 hours.[27] At 90 days, 10.2% in the 33°C group were alive with a Cerebral Performance Category score of 1 or 2 (the primary outcome) compared with 5.7% in the normothermia group (risk difference, 4.5%; 95% CI, 0.1–8.9; *P*=0.04). There was no difference in mortality at 90 days (81.3% versus 83.2%; risk difference, –1.9%; 95% CI, –8.0 to 4.3).

This trial reinforces the 2015 ILCOR treatment recommendations to consider TTM, targeting a constant temperature between 32°C and 36°C in patients who remain comatose after resuscitation from either IHCA or OHCA with an initial nonshockable rhythm.[25,26] This may be considered by some as controversial because, despite the result of the HYPERION trial, it remains a weak recommendation. However, the ALS Task Force chose to delay updating this SysRev until the completion and publication of the TTM-2 (Targeted Hypothermia Versus Targeted Normothermia After Out-of-Hospital Cardiac Arrest) RCT (NCT02908308). Instead, EvUps on this topic have been undertaken to assist in formulating regional guidelines.

Double Sequential Defibrillation

Patients in refractory ventricular fibrillation, comprising about 20% of patients with ventricular fibrillation/pulseless ventricular tachycardia, have significantly lower rates of survival than patients who respond to standard resuscitative treatments. Increasingly, these patients are being treated with double (dual) sequential defibrillation—the use of 2 defibrillators to deliver 2 overlapping shocks or 2 rapid sequential shocks—as a possible means of increasing ventricular fibrillation termination rates. The ALS Task Force's SysRev identified only observational studies that were at critical or serious risk of bias because of confounding, and the task force discussed the results of a small RCT comparing standard defibrillation with changing pad position or double sequential defibrillation.[28] Given this very low-certainty evidence, the task force suggested against the routine use of a double sequential defibrillation strategy to treat cardiac arrest with a shockable rhythm.

IV Versus IO Drug Delivery

The IO route is being used more frequently to deliver drugs during resuscitation. Although some EMS personnel are using the IO route in preference to the IV route for drug delivery in cardiac arrest, most commonly, the IO route is used only after failed attempts at IV cannulation or when IV cannulation is likely to be very difficult. Several observational studies have documented an association between IO drug delivery during resuscitation and a worse outcome in comparison with IV drug delivery. However, such studies are likely to include considerable bias. Subgroup analyses from 2 recent RCTs showed no significant interaction between the IO and IV routes for the delivery of epinephrine or placebo[29] or amiodarone, lidocaine, or placebo,[30] although the point estimates generally favored IV access. The ALS Task Force decided to suggest the IV route for the first attempt for drug delivery during adult cardiac arrest, but if IV attempts fail or IV access is not feasible, IO access is suggested. Prospective studies will be important to determine whether drug delivery first by IV or IO route impacts long-term outcomes in cardiac arrest.

Point of Care Echocardiography for Prognostication During CPR

In 2015, the ALS Task Force addressed the question of whether the use of cardiac ultrasound during CPR changed outcomes and suggested its use as an additional diagnostic tool to identify potentially reversible causes of arrest.[25,26] For 2020, the task force undertook a different SysRev that looked at the intra-arrest prognostic capabilities of point-of-care echocardiography. No RCTs were identified, and the 15 relevant observational studies included in the review were rated as very low-certainty evidence because of a high risk of bias. The bias related to inconsistent prognostic factor measurement, outcome measurement, lack of adjustment for other prognostic factors, and confounding from self-fulfilling prophecy. There was wide variation in classification of anatomy, type of cardiac motion, and timing of the intervention. The task force cautioned against the overinterpretation of right ventricular dilatation as a diagnostic indicator of massive pulmonary embolism because this finding is seen commonly in cardiac arrest from any cause. After careful consideration of the evidence, the task force suggested against the use of point-of-care echocardiography for prognostication during CPR. In the future, identifying a standardized definition of cardiac motion as seen during point-of-care echocardiography and minimizing other sources of bias will be essential to obtaining high-certainty evidence.

New Systematic Reviews

Double Sequential Defibrillation

This topic is discussed in more detail in the ALS Hot Topics section earlier in this publication. The task force's SysRev identified only observational studies that were at critical or serious risk of bias because of confounding and 1 recently published small pilot RCT.[31]

Effect on treatment recommendations: In this new recommendation, the ALS Task Force suggests against

the routine use of a double sequential defibrillation strategy to treat cardiac arrest with a shockable rhythm.

IV Versus IO Drug Delivery

This topic is discussed in more detail in the ALS Hot Topics section earlier in this publication. A SysRev[32] provided the data supporting a new treatment recommendation.

Effect on treatment recommendations: This is a new treatment recommendation: the ALS Task Force suggests the IV route for the first attempt for drug delivery during adult cardiac arrest, but if IV attempts fail or IV access is not feasible, IO access is suggested.

Point of Care Echocardiography for Prognostication During CPR

The ALS Task Force undertook this new SysRev of the intra-arrest prognostic capabilities of point-of-care echocardiography. This topic is discussed in more detail in the ALS Hot Topics section earlier in this publication.

Effect on treatment recommendations: The task force suggested against the use of point-of-care echocardiography for prognostication during CPR.

Cardiac Arrest Associated With Pulmonary Embolism

The ALS Task Force updated a SysRev previously undertaken in 2015[25,26] that sought to identify whether any specific alteration in the ALS treatment algorithm compared with standard ALS care would result in better outcomes when treating an adult in cardiac arrest caused by pulmonary embolism or suspected pulmonary embolism. One additional observational study was identified that found no difference in outcome with or without fibrinolysis.[33]

Effect on treatment recommendations: The treatment recommendation is unchanged from 2015.[25,26]

Oxygen Dose After ROSC

Observational studies have shown that after ROSC, there is an association between both hypoxemia and hyperoxemia and worse outcome. A SysRev conducted to inform the 2020 CoSTR identified 6 RCTs that generally failed to show a benefit of a titrated (lower concentration of inspired oxygen) approach compared with standard care (higher concentration of inspired oxygen).[34] A subgroup analysis of patients with suspected hypoxic-ischemic encephalopathy in 1 larger RCT documented better survival in patients for whom hyperoxemia was aggressively avoided.[35]

Effect on treatment recommendations: The treatment recommendation is unchanged from 2015.[25,26]

Ventilation Strategy After ROSC in Adults

Whether targeting a specific $Paco_2$ after ROSC in adults impacts outcomes was previously reviewed in 2015.[25,26] The ALS Task Force identified 2 small RCTs and 3 additional observational studies published since 2015. Unfortunately, differences in the $Paco_2$ targets used in the arms of the 2 RCTs precluded meta-analysis.

Effect on treatment recommendations: The treatment recommendation was modified from 2015 and now states that there is insufficient evidence for or against targeting mild hypercapnia compared with normocapnia in adults with ROSC after cardiac arrest. The task force also suggests not routinely targeting hypocapnia in adults with ROSC after cardiac arrest.

Prophylactic Antibiotics After Cardiac Arrest

This new topic was prioritized by the ALS Task Force on the basis of the recent publication of a SysRev on the topic.[36] Pneumonia affects approximately 50% of intensive care unit patients after cardiac arrest. Meta-analyses of both randomized trials and observational studies showed no overall benefit in the use of prophylactic antibiotics during post–cardiac arrest care. One RCT documented a reduced incidence of early pneumonia in patients treated with prophylactic antibiotics but no effect on mortality.[37]

Effect on treatment recommendations: A new recommendation was provided that suggested not using prophylactic antibiotics in patients after ROSC.

Post–Cardiac Arrest Seizure Prophylaxis and Treatment

Clinical convulsions and epileptiform activity in the electroencephalogram (EEG) occur in 20% to 30% of comatose cardiac arrest survivors. Whether seizure prophylaxis and treatment in cardiac arrest survivors reduces the incidence of seizures and improves outcomes is unclear. This SysRev updated a review undertaken in 2015.[25,26]

Effect on treatment recommendations: This treatment recommendation has been updated from 2015. The ALS Task Force suggested that seizures be treated but suggested against post–cardiac arrest seizure prophylaxis in adults with ROSC. In 2015, there was a strong recommendation to treat seizures, and the weakening of this treatment recommendation takes into consideration the absence of direct evidence that seizure treatment improves critical outcomes in these patients.

Prognostication in Comatose Patients After Resuscitation From Cardiac Arrest

In many healthcare systems, life-sustaining treatment may be limited or withdrawn when unfavorable neurological outcomes are expected. Thus, timely and reliable prognostication is an important component of the treatment of patients who remain comatose after cardiac arrest. The 2015 ILCOR treatment recommendations on this topic distinguished between studies of prognostication among patients treated with or without hypothermia. The updated SysRevs and treatment recommendations

for 2020 apply regardless of the temperature management strategy used. Many observational studies on this topic have been published since 2013, when the previous SysRev on neuroprognostication was undertaken. For 2020, separate SysRevs were undertaken for the 4 prognostication domains of clinical examination, neurophysiological tests, biomarkers, and imaging.

Effect on treatment recommendations: The treatment recommendations have been updated since 2015, the most important being a strong recommendation (albeit based on very low-certainty evidence) that neuroprognostication always be undertaken with the use of a multimodal approach because no single test has sufficient specificity to eliminate false positives.

Clinical Examination for Prognostication

The ALS Task Force suggests using the following components of clinical examination as part of a multimodal approach to predicting the neurological outcome of adults who are comatose after cardiac arrest (all based on very low-certainty evidence): pupillary light reflex, quantitative pupillometry, and bilateral absence of corneal reflex (all at 72 hours or more after ROSC) and the presence of myoclonus or status myoclonus within 7 days after ROSC. The task force also suggests recording EEG in the presence of myoclonic jerks to detect any associated epileptiform activity.

Neurophysiological Tests for Prognostication

The ALS Task Force suggests using the following neurophysiological tests as part of a multimodal approach to predicting the neurological outcome of adults who are comatose after cardiac arrest (all based on very low-certainty evidence): bilaterally absent N20 wave of somatosensory evoked potential, the presence of seizure activity on EEG, and burst suppression on EEG. The task force suggests not using the absence of EEG background reactivity alone to predict poor outcome in these patients.

Biomarkers for Prognostication

The ALS Task Force suggests using neuron-specific enolase within 72 hours as part of a multimodal approach to predicting neurological outcome of adults who are comatose after cardiac arrest. The task force suggests not using S-100B protein, glial fibrillary acidic protein, serum tau protein, or neurofilament light chain for predicting poor neurological outcome of adults who are comatose after cardiac arrest.

Imaging for Prognostication

The ALS Task Force suggests using the following imaging as part of a multimodal approach to predicting neurological outcome of adults who are comatose after cardiac arrest (all based on very low-certainty evidence): gray matter to white matter ratio on brain computed tomography, diffusion-weighted brain MRI, and apparent diffusion coefficient on brain MRI.

Additional Reviews

The ALS Task Force also evaluated 2 ScopRevs and 15 EvUps. These reviews, per ILCOR agreement, did not change treatment recommendations, but several resulted in the suggestion for new SysRevs.

PEDIATRIC LIFE SUPPORT (BASIC AND ADVANCED)

Hot Topics

Fluid Administration Rate for Septic Shock and Management of Septic Shock

Although substantial progress has been made in reducing mortality and morbidity from septic shock in infants and children, recommendations for management are often based on a consensus of experts because available evidence is limited. A very detailed 2020 EvUp identified several relevant studies, and the PLS Task Force agreed that a SysRev is needed in the near future.

In early February 2020, as the PLS Task Force was finalizing the CoSTR publication, the Society of Critical Care Medicine published their "Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children."[38] The task force cited recommendations from these guidelines in several of the septic shock topics in the PLS publication in this supplement and also agreed to request a SysRev about the general management of septic shock in infants and children.

Adrenaline/Epinephrine Initial Dose and Dose Intervals for Cardiac Arrest

Although epinephrine has been part of pediatric resuscitation for more than 50 years, there is little pediatric data about its effectiveness or the optimal initial dose or dose interval during resuscitation. The epinephrine SysRev identified evidence associating benefit with shorter time to initial epinephrine administration and improved outcomes in children with nonshockable rhythms and OHCA,[39–41] and a new treatment recommendation reflected this evidence. However, there remains insufficient evidence about the effect of time to initial epinephrine dose for OHCA with shockable rhythms. The 2 observational studies evaluating epinephrine dose intervals during IHCA yielded contradictory results, so evidence remains insufficient about the optimal dose interval for pediatric IHCA.[42,43] More data, ideally in the form of RCTs, is needed on this important topic.

Management of Traumatic Shock in Infants and Children

The 2020 CoSTR for PLS addresses the topic of graded volume resuscitation for infants and children with traumatic hemorrhagic shock as well as management of the child with cardiac arrest after trauma. The ScopRev on

graded volume resuscitation identified a single observational study in the prehospital setting assessing the volume of fluid given to children with traumatic injuries,[44] with an additional 4 studies comparing total crystalloid volume given over 24 hours[45–48] and 1 study evaluating the volume of crystalloids given to children who needed transfusion.[49] The task force agreed that the evidence was sufficient to consider a SysRev in the near future.

The task force discussions included the issue of the scope of the ILCOR PLS Task Force mandate and whether trauma should be included among topics that this task force evaluates, given that other organizations are addressing the topic. However, because trauma remains a leading cause of infant and child deaths worldwide, the task force agreed to continue to evaluate evidence addressing the management of seriously injured infants and children but agreed that traumatic cardiopulmonary arrest will, after 2020, remain in the purview of organizations such as the American College of Surgeons (eg, via the Advanced Trauma Life Support Course[50]).

Ventilation Rate With Advanced Airway During CPR

In 2010, the PLS Task Force identified insufficient pediatric evidence to identify any optimal minute ventilation during CPR with an advanced airway, and the treatment recommendations noted that it would be reasonable to provide a minute ventilation less-than-normal for age because cardiac output and pulmonary blood flow are much lower than normal during CPR.[51,52] This left the decision about ventilation rate up to individual council guidelines. For simplicity, some councils recommended the same ventilation rate used for adults. The 2020 EvUp search identified 1 small multicenter study in children with advanced airways during CPR, reporting an association between a ventilation rate of 30/min or greater for infants and 25/min or greater for children and improved outcomes.[53] These results raised the question of the need for a faster ventilation rate during CPR in children compared with adults. The task force agreed that more data are needed (eg, larger observational studies, RCTs) and agreed to request a SysRev when additional studies are published.

Use of Hemodynamic Monitoring When Available During CPR

CPR quality is essential to good resuscitation outcomes. Monitoring devices and systems available in critical care may provide valuable feedback and data about CPR quality. The task force requested a ScopRev to determine the evidence available to support the use of intra-arterial pressure monitoring if it is already in place during CPR. A single observational study reported an association between a mean diastolic (relaxation) blood pressure of 25 mm Hg or higher in infants and 30 mm Hg or higher in children and survival.[54] Although the task force agreed that identification of a threshold diastolic blood pressure associated with survival in children could be very helpful to guide resuscitation efforts, at this time, there is insufficient evidence to identify any such threshold.

New Systematic Reviews

Sequence of Compression and Ventilation

In 2015, there was inadequate evidence to support a PLS Task Force recommendation about the sequence of compressions and ventilation in infants and children.[55,55a] In 2020, the PLS Task Force combined efforts with the BLS Task Force to perform a SysRev to identify evidence supporting a CPR sequence beginning with either compressions first or ventilation first. The search identified no studies in children. As a result, there is no change in the 2015 PLS treatment recommendation. To review the BLS summary, see "Starting CPR: Compressions-Airway-Breaths Versus Airway-Breaths-Compressions" (BLS 661: SysRev) in the 2020 CoSTR for BLS in this supplement.

Effect on treatment recommendation: no change from 2015; we are unable to make a recommendation.[55,55a]

IO Versus IV Route of Drug Administration

The PLS Task Force joined with the NLS and ALS Task Forces in a SysRev to identify the evidence of superiority of either IO or IV routes of drug administration during CPR.[32] The search strategy included newborns, infants, children, and adults. Although evidence was identified in newborns and adults, the search yielded no studies that included infants (beyond newborns) or children. To review the neonatal evidence identified by the SysRev, see "Intraosseous Versus Umbilical Vein for Emergency Access" (NLS 616: SysRev) in the 2020 CoSTR for NLS in this supplement.

Effect on treatment recommendation: No change from 2010.[51,52]

Adrenaline/Epinephrine Time of Initial Dose and Dose Interval During CPR

The SysRev identified only observational (registry) data (including 1 large study reporting data from 26 755 children,[39] suggesting benefit associated with earlier rather than later initial epinephrine administration, especially for children with OHCA and nonshockable rhythms.[39–41] Because the 2 registry studies of epinephrine dose intervals in children with IHCA provided directly contradictory evidence,[42,43] the task force concluded that there was insufficient evidence to make a new recommendation about epinephrine dose interval.

Effect on treatment recommendations: New recommendations were provided suggesting that the initial dose of epinephrine be given as soon as possible for children with OHCA and nonshockable rhythm, but there was insufficient evidence to make

a recommendation for initial epinephrine dose timing for OHCA with shockable rhythms and insufficient evidence to identify an optimal epinephrine dose interval.

Oxygen and Carbon Dioxide Targets in Pediatric Patients With ROSC

The PLS Task Force joined with the ALS Task Force to request a SysRev to identify evidence about optimal targets for Pa_{O_2} and Pa_{CO_2} after ROSC.[56] The PLS Task Force agreed to evaluate only the pediatric evidence. The search identified only observational studies about oxygen targets.[57–59] The SysRev also identified 2 observational studies that suggested potential harm (increased mortality) associated with both hypercapnia and hypocapnia (compared with normocapnia) after ROSC.[59,60]

Effect on treatment recommendations: The recommendations were modified from those published in 2015[55,55a] targeting a Pa_{O_2} appropriate for the child's condition or normoxemia, adding that it might be reasonable to target an oxygen saturation of 94% to 99%. The treatment recommendations for targeting Pa_{CO_2} continue to suggest targeting normocapnia but now include examples of clinical problems where normocapnia would not be desirable.

Additional Reviews

In addition to the SysRevs, the PLS Task Force evaluated 10 ScopRevs and 37 EvUps. These reviews, per ILCOR agreement, did not change treatment recommendations, but several resulted in the suggestion for new SysRevs. All are available in Appendixes B and C of the PLS CoSTR.

NEONATAL LIFE SUPPORT

Hot Topics

Tracheal Intubation and Suction of Nonvigorous Meconium-Stained Newborns

The 2015 recommendation about tracheal intubation and suctioning was based on 1 RCT and observational studies and GRADE reassessment of previously quoted evidence. In 2020, the NLS Task Force requested a SysRev to include studies published after 2015 to determine if any modification of the 2015 treatment recommendation was needed. None of the studies identified by the new SysRev[61] showed any benefit associated with the use of immediate laryngoscopy with or without suctioning for nonvigorous newborns delivered through meconium-stained amniotic fluid. As a result, the task force agreed to increase the certainty of the treatment recommendations against routine immediate direct laryngoscopy after delivery with or without suctioning for nonvigorous newborns delivered through meconium-stained amniotic fluid.

Adrenaline/Epinephrine for Neonatal Resuscitation

Before 2020, the NLS Task Force never performed a SysRev on the use, dose, and dose interval of epinephrine in newborn resuscitation. The 2020 SysRev identified only 2 small studies[62,63] including 97 infants from the same newborn intensive care unit (although in different epochs). The task force agreed that the 2010 treatment recommendations remain valid, with minor editorial revisions.

Initial Oxygen Concentration for Preterm Infants at Birth

During stabilization of the preterm newborn in the delivery room, medical practitioners must prevent or rapidly treat hypoxia while limiting exposure to excess oxygen that may cause complications. In 2019, the NLS Task Force requested a new SysRev after the publication of several relevant studies about the initial oxygen concentration to use in preterm newborn resuscitation.[64] In that review, pooled data from 2 observational studies of 1225 newborns showed an association between initiating resuscitation with lower oxygen concentration and significant benefit in reduction of long-term mortality for all preterm newborns 28 weeks of gestational age or less.[65,66] Although these results and associated treatment recommendations were published in the 2019 CoSTR[18,19] and not reevaluated in this 2020 CoSTR, the NLS Task Force agreed that initial oxygen concentration to use for resuscitation of the preterm newborn remains an important topic.

Impact of Duration of Intensive Resuscitation

Neonatal clinicians face a critical decision when intensive resuscitative efforts fail to result in ROSC. They must decide when to redirect care of the infant from resuscitation to providing comfort and contact with the parents. The timing of this decision is crucial—if made too early, it could deny the opportunity for the infant to survive with good neurodevelopmental outcome, but if made too late, it could result in very limited chance for survival without severe neurodevelopmental impairment. The NLS Task Force sought a SysRev to identify published evidence of any resuscitation exposure or duration that is associated with outcomes. The task force carefully weighed the very limited data and acknowledged that quality of resuscitative efforts will affect any study of resuscitation duration and outcomes. The new treatment recommendations suggest that discussion of discontinuing resuscitative efforts with the clinical team and the family might be appropriate after approximately 20 minutes after birth (see more information below).

New Systematic Reviews

Tracheal Intubation and Suction of Nonvigorous, Meconium-Stained Newborns

As previously noted, the evidence identified by the 2020 SysRev[61] added additional evidence of lack of benefit to immediate tracheal suctioning of nonvigorous newborns born through meconium-stained amniotic fluid.

Effect on treatment recommendations: The NLS Task Force strengthened the wording of the certainty of the evidence for the treatment recommendation, suggesting against routine immediate direct laryngoscopy after delivery of nonvigorous infants delivered through meconium-stained amniotic fluid. The recommendations acknowledged that meconium-stained amniotic fluid remains a risk factor for advanced resuscitation in the delivery room and noted that rarely an infant may require intubation and tracheal suctioning to relieve airway obstruction.

Sustained Inflation

If the newborn does not breathe spontaneously, providers must establish a functional residual capacity to replace lung fluid with air. However, published evidence has not identified the optimum method to accomplish this. In 2015, the NLS Task Force suggested against the routine use of sustained inflation[67–69]; in 2020, the task force sought a new SysRev to identify and analyze the results of several clinical trials published after 2015. The new SysRev[70] identified 10 RCTs enrolling 1502 preterm newborns.[71–80] Although the studies demonstrated no benefit or harm from initiating positive pressure ventilation with sustained inflation(s) in preterm infants, in the subset of very preterm infants (less than 28+0 weeks), 5 RCTs found potential harm from the use of sustained inflation(s).[71,72,75,76,79]

Effect on treatment recommendations: The task force strengthened the recommendation suggesting against the routine use of sustained inflation(s) of more than 5 seconds for preterm newborns. There is no evidence to support a recommendation about the use of any specific duration for initial inflations for term or late-preterm infants.

Adrenaline/Epinephrine for Neonatal Resuscitation

The 2019 SysRev about the effects of epinephrine dose and dose intervals[81] represents the first attempt to identify and analyze the evidence on this topic. Given the very limited evidence identified, the task force agreed that the 2010 treatment recommendations remained valid, suggesting epinephrine administration for a persistent heart rate of less than 60/min despite optimal ventilation and chest compressions.[67,68,82,83]

Effect on treatment recommendations: Only minor editorial changes were made to the 2010 recommendations.

IO Versus Umbilical Vein for Emergency Access

Although small case series and case reports suggest that fluids and medications can be delivered by the IO route during newborn resuscitation,[84,85] complications have also been reported.[84,86–90] In 2019, the NLS Task Force joined the ALS Task Force and the PLS Task Force to complete a joint SysRev with meta-analysis.[32] The SysRev identified no published evidence addressing any of the preidentified outcomes in newborns.

Effect on treatment recommendations: The task force strengthened the recommendation for use of the umbilical venous route for fluid and drug administration during resuscitation in the delivery room but did allow use of the IO route if umbilical venous access is not feasible.

Impact of Duration of Intensive Resuscitation

During resuscitation of the newborn, clinicians and parents often ask how long resuscitative efforts can continue and still result in potential survival of the infant with good neurological outcome. In 2019, the NLS Task Force requested a SysRev to identify any evidence of an incremental time of resuscitation exposure from birth that was associated with very poor likelihood of survival. This SysRev identified 15 outcome studies of only 470 newborns.[91] The task force agreed that the limited number of infants in the studies and the heterogeneity of the studies provided very low-certainty evidence on which to base new 2020 treatment recommendations.

Effect on treatment recommendations: The task force noted that although there is no evidence that a specific duration of resuscitation consistently predicts mortality or moderate-to-severe neurodevelopmental impairment, the failure to achieve ROSC despite 10 to 20 minutes of intensive resuscitation is associated with high risk of mortality as well as severe neurodevelopmental impairment among survivors. The task force agreed that a reasonable time frame to suggest discussion of discontinuing resuscitative efforts is around 20 minutes after birth.

Additional Reviews

In addition to the SysRevs, the NLS Task Force performed 3 ScopRevs and 12 EvUps. All reviews are highlighted in the NLS publication, including appendixes in this supplement.

EDUCATION, IMPLEMENTATION, AND TEAMS

Hot Topics

EMS Experience and Exposure

Resuscitation knowledge and skills are likely to degrade with time if not refreshed with regular use or training;

however, a SysRev published in 2016[92] found very little evidence to support this concept. The EIT Task Force undertook a SysRev that identified 6 observational studies of very low-certainty evidence.[92a] Comparisons were divided into exposure to resuscitation by the team or individual, and years of career experience of individuals within the team. A critical risk of bias and a high degree of heterogeneity precluded meta-analyses. The task force made a weak recommendation that EMS systems should monitor exposure to resuscitation by clinical personnel and, where possible, implement strategies to address low exposure. This could include the rotation of EMS personnel through higher OHCA volume areas and the use of team simulation.

Community Initiatives to Promote BLS Implementation

This topic was last reviewed for the 2010 CoSTR,[93,94] although the role of communities in providing and promoting bystander CPR, a related topic, was reviewed for the 2015 CoSTR.[95,96] The EIT Task Force decided to search for evidence supporting the benefit of community initiatives (interventions aimed at increasing the engagement of the community in providing BLS with early defibrillation) in promoting BLS implementation. Studies evaluating the role of healthcare professionals or first responders with any duty to respond were excluded as were several specific interventions that are reviewed elsewhere in the 2020 CoSTR. Given the high heterogeneity among studies, a ScopRev was undertaken. Although only 40% of the 17 identified studies reported an increase in survival to hospital discharge, almost all showed a benefit with implementation of community initiatives, and this was greater in those evaluating bundled interventions. The task force suggests that a SysRev be undertaken, but in the meantime, the treatment recommendation from 2015 remains unchanged: "We recommend implementation of resuscitation guidelines within organizations that provide care for patients in cardiac arrest in any setting (strong recommendation, very low-quality evidence)."[95,96]

Opioid Overdose First Aid Education

The opioid overdose crisis is recognized as a major challenge, particularly in the United States. In 2015, the ALS Task Force made a strong recommendation for the use of naloxone for individuals in cardiac arrest caused by opioid toxicity.[25,26] At that time, the BLS Task Force made a weak recommendation to offer opioid overdose response education, with or without naloxone distribution, to persons at risk for opioid overdose.[12,12a] The EIT Taskforce undertook a ScopRev of current opioid overdose response education programs to determine whether a new SysRev is required. Of 59 studies identified, only 8 used a comparator group and only 1 was a randomized controlled trial. Inconsistent reporting of educational interventions made it difficult to compare studies, and the EIT Task Force suggests that the use of the Guideline for Reporting Evidence-Based Practice Educational Interventions and Teaching checklist would improve standardization.[97] Another limitation in the evidence identified is that first aid and survival outcomes were generally self-reported by individuals refilling naloxone prescriptions and, therefore, are of questionable validity. The EIT Task Force found no evidence to change the current weak recommendation: "We suggest offering opioid overdose response education, with or without naloxone distribution, to persons at risk for opioid overdose in any setting."[12,12a]

Willingness to Perform Bystander CPR

This topic was last reviewed by ILCOR in 2010.[93,94] Given the low incidence of bystander provision of CPR and use of AEDs, the EIT Task Force chose to undertake a ScopRev comparing factors that increase or decrease the willingness of bystanders to perform CPR for OHCA. The facilitators and barriers to performing CPR were categorized into personal factors, CPR knowledge, and procedural issues.[98] The 18 observational studies that were identified had significant heterogeneity among study populations and methodologies, definitions of factors associated with willingness to provide CPR, and outcomes reported. The task force agreed that there were insufficient data to warrant a SysRev. Although the treatment recommendation remains unchanged from 2010,[93,94] the EIT Task Force proposed that BLS training should include information to overcome potential barriers to CPR faced by lay rescuers. When providing CPR instructions, EMS dispatchers should recognize the emotional barriers and physical factors that may make lay rescuers reluctant to perform CPR, and it will be important for dispatchers to support bystanders in starting and continuing CPR.

Out-of-Hospital CPR Training in Low-Resource Settings

To date, treatment recommendations with respect to CPR training have generally been made from the perspective of a well-resourced environment; these recommendations may not be applicable to lower-resource settings (per the World Bank definition by gross national income per capita). The EIT Task Force undertook a ScopRev to raise awareness of gaps in emergency care services around the world, to identify gaps in the literature, and to suggest future research priorities. Clinical outcomes were sought from studies of prehospital resuscitation among adults and children in low-resource settings. Of the 24 studies identified, none came from low-income countries, 4 came from lower-middle-income countries, and all others were from upper-middle-income economies. Longer-term outcomes, reported in 15 of the studies, were generally worse in the lower-middle-income countries.

The EIT Task Force encourages organizations responsible for emergency care in low-resource environments to collect data and document outcomes, ideally in the form of registries that comply with the Utstein-style reporting template.[99] In the future, experts and clinicians from low-resource environments should be involved in global initiatives such as ILCOR so that its recommendations can be made acceptable and applicable locally. Whether prehospital resuscitation is feasible, cost-effective, or even ethically justifiable in these regions has been questioned recently. Given the limited resources in low-income countries, the feasibility of full ALS and postresuscitation care is debatable. The priorities for healthcare systems should be determined locally. In the meantime, the weak recommendation made in 2015 stands: "We suggest that alternative instructional strategies would be reasonable for BLS or ALS teaching in low-income countries."[95,96]

New Systematic Reviews

EMS Experience and Exposure

This topic is discussed in more detail in the EIT Hot Topics section earlier in this publication. The EIT Task Force's SysRev identified only 6 observational studies, and because of the critical risk of bias and a high degree of heterogeneity, meta-analyses were not performed.[92a]

Effect on treatment recommendations: With this new treatment recommendation, the task force suggests that EMS systems monitor their clinical personnel's exposure to resuscitation and, where possible, implement strategies to address low exposure.

Patient Outcomes as a Result of a Member of the Resuscitation Team Attending an ALS Course

Whether resuscitation team member completion of an advanced cardiac life support course improves patient outcomes after cardiac arrest has long been debatable, not least because of the costs of these courses to participants and healthcare organizations. This EIT Task Force review is an adolopment of an existing SysRev and meta-analysis of 8 observational studies.[100] Although this was deemed very low-certainty evidence, it consistently favors advanced cardiac life support training.

Effect on treatment recommendations: The EIT Task Force made a weak recommendation for the provision of accredited adult advanced cardiac life support training for healthcare professionals.

Spaced Learning

A recent AHA scientific statement on education science describes spaced or distributed practice as the separation of training into several discrete sessions over a prolonged period with measurable intervals between training sessions (typically weeks to months).[101] The EIT Task Force undertook a SysRev of learners taking resuscitation courses and compared educational and clinical outcomes among those undergoing spaced learning with those undergoing massed learning (ie, training provided at a single time point). In all 17 of the studies identified, practical skills were assessed using manikins, so this was deemed only very low-certainty evidence to support spaced learning in resuscitation education.

Effect on treatment recommendations: In 2010, there was insufficient evidence to recommend any specific training intervention, compared with traditional lecture/practice sessions, to learning, retention, and use of ALS skills.[93,94] However, for 2020, the EIT Task Force suggests that spaced learning may be used instead of massed learning.

Opioid Overdose First Aid Education

This topic is discussed in more detail in the EIT Hot Topics section above. The EIT Task Force undertook a ScopRev of studies that compared education about response or care of an individual by first aid providers in an opioid overdose emergency with response by those with any other or no specialized education. Among the 8 identified studies with a comparator group, the task force found no evidence to change the current treatment recommendation.

Effect on treatment recommendations: The treatment recommendation is unchanged from 2015.[12,12a]

Prehospital Termination of Resuscitation Rules

A recent SysRev identified 32 studies that addressed the use of termination of resuscitation rules that predict in-hospital outcomes among adults and children who do not achieve ROSC out-of-hospital.[102] The majority of these describe either the derivation and internal validation of individual termination of resuscitation rules or the external validation of previously published termination of resuscitation rules. Although the termination of resuscitation is commonly undertaken in many EMS systems, the identification of futile cases is challenging. The EIT Task Force advocates the adoption of termination of resuscitation guidelines that take into account the patient's prior wishes and/or expectations, consideration of patient preexisting comorbidities, and quality of life both before and after the cardiac arrest. However, a termination of resuscitation rule should not be the sole determinant of when to discontinue resuscitation. Global variation in cultural and legal issues must also be considered.

Effect on treatment recommendations: The 2010 CoSTR recommended the use of validated termination of resuscitation rules in adults.[93,94] For 2020, the EIT Task Force softened this to a conditional recommendation, taking into consideration the social acceptability of excluding potential survivors from

in-hospital treatment and the very limited clinical validation of such rules.

In-Hospital Termination of Resuscitation

Knowing when to stop a resuscitation attempt in-hospital is challenging. The EIT Task Force undertook a SysRev to determine whether the use of any clinical decision rule would predict a poor outcome with sufficient certainty to enable termination of the resuscitation attempt. Three studies used unwitnessed arrest, nonshockable rhythm, and 10 minutes of CPR without ROSC (the 3 variables of the so-called UN10 rule) to predict death before hospital discharge. These studies were based on historical cohorts and carry substantial risk of self-fulfilling prophecy bias. No single clinical factor or decision rule has been identified as sufficient to terminate resuscitation.

Effect on treatment recommendations: The EIT Task Force made a strong recommendation (based on very low-certainty evidence) against the use of the UN10 rule as a sole strategy to terminate in-hospital resuscitation. Clinicians should rely on clinical examination, their experience, and the patient's condition and wishes to inform their decision to terminate resuscitative efforts.

Additional Reviews

The EIT Task Force also evaluated 7 EvUps. The ScopRevs and EvUps, per ILCOR agreement, did not change treatment recommendations, but several resulted in the suggestion for new SysRevs.

FIRST AID

Hot Topics

Control of Life-Threatening External Bleeding

Trauma remains the leading cause of mortality and morbidity worldwide, and uncontrolled bleeding is the primary cause of death in up to 35% of patients who die from trauma.[103–105] The "Stop the Bleed" White House initiative[106] aims to bring battleground experience to the civilian world, with dissemination of education and equipment to recognize and control life-threatening bleeding. The combined SysRev for control of life-threatening bleeding used a common search strategy to evaluate evidence about direct manual pressure, tourniquets, hemostatic dressings, and hemostatic techniques.[107] The First Aid Task Force developed new recommendations about the use of tourniquets for life-threatening external extremity bleeding amenable to the use of a tourniquet. Additional recommendations include the use of direct manual pressure, with or without a hemostatic dressing, for life-threatening external bleeding not amenable to the use of a tourniquet.

Cooling of Heatstroke and Exertional Hyperthermia

Cooling for heatstroke and exertional hyperthermia was prioritized in light of the rising global risk of heat waves coupled with athletic events staged under these challenging conditions. The First Aid Task Force developed new treatment recommendations based on evidence suggesting that water immersion (between 1°C and 26°C, or between 33.8°F and 78.8°F) of the torso or whole body lowered the core body temperature faster than other active and passive cooling modalities.

Stroke Recognition

A new SysRev evaluated the available tools to assist the first aid provider in identifying potential stroke.[108] All tools were applied by trained EMS providers or nurses in the prehospital setting, so the evidence was only indirect when applied to the first aid setting; the ability of first aid providers to use the tools correctly remains an important question to be answered. The task force simplified previous recommendations[109,110] and continued to suggest that first aid providers use stroke assessment tools, noting an increased specificity (without loss of sensitivity) in tools that include measurement of blood glucose.

Dental Avulsion

When an injury causes tooth avulsion (ie, the tooth is pulled out with the root), the tooth must be stored in an appropriate medium to preserve viability until the tooth can be reimplanted. The First Aid Task Force sought a 2020 SysRev[111] to identify optimal media for temporary tooth storage, comparing the effects of many different media on periodontal ligament cell viability (surrogate for viability of the tooth for reimplantation). Although milk remains an effective medium, the task force concluded that other media as well as the use of clear cling film (ie, plastic wrap) were more effective in preserving viability.

New Systematic Reviews

Methods of Glucose Administration

The 2020 SysRev focused on methods and forms of glucose administration.[112] The review identified very limited evidence, and 2 of the 4 studies identified enrolled healthy volunteers (very indirect evidence).

Effect on treatment recommendations: The task force suggested oral swallowed sugar in preference to buccal administration of sugar. In a select group of children, sublingual administration of a wet paste of sugar improved resolution of hypoglycemia compared with oral swallowed glucose.

Heatstroke Cooling

The 2020 SysRev[113] focused on the potential for increased survival and reduced morbidity associated

with heatstroke with the use of rapid core cooling. The task force evaluated limited evidence of 12 different active or passive cooling techniques in healthy adults with exertional hyperthermia (ie, indirect evidence about cooling for heatstroke). Evidence about cooling during heatstroke was based on observational studies and case series. Whole-body (neck-down) immersion in water with temperatures of 1°C to 26°C, or 33.8°F to 78.8°F (eg, in a small tub) produced the most rapid rate of cooling and was faster than other active-cooling techniques.

Effect on treatment recommendations: The new First Aid Task Force recommendation for adults with exertional hyperthermia or exertional heatstroke is immediate active cooling using whole-body (ie, neck-down) water immersion (1°C–26°C, or 33.8°F–78.8°F) until the core body temperature is less than 39°C (102.2°F). If water immersion is not possible, the task force recommends any other active-cooling methods.

Stroke Recognition

Because the prompt recognition of stroke is critical for effective treatment,[114] the First Aid Task Force requested a SysRev of stroke recognition tools appropriate for use in the first aid setting.[108] As noted previously, in all identified studies, the stroke scales or scoring tools were applied by trained EMS providers or nurses. As in the 2015 CoSTR, the 2020 First Aid Task Force recommended the use of stroke assessment scales or tools, based on the ability to perform point-of-care glucose measurement.

Effect on treatment recommendations: The treatment recommendations are essentially unchanged from 2015, although the specific stroke assessment tools cited vary slightly from those listed in 2015.[109,110]

Supplementary Oxygen in Acute Stroke

The 2020 SysRev focused exclusively on oxygen use for those with suspected stroke, rather than on general first aid oxygen use.[115] With few exceptions,[116] the studies reviewed reported no benefit associated with oxygen use (compared with room air) in those with suspected stroke, and 1 study[117] reported a higher rate of respiratory complications associated with oxygen use.

Effect on treatment recommendations: In a new recommendation focusing on the use of oxygen for those with suspected stroke, the task force suggested against the routine use of oxygen for those with suspected stroke.

First Aid Administration of Aspirin for Chest Pain: Early Compared With Late

The 2020 SysRev[118] evaluated the evidence about effects of early (prehospital or within 2 hours of symptom onset) compared with later, often in-hospital aspirin administration to anyone with nontraumatic chest pain. Two observational studies found an association of increased survival at 7 and 30 days[119,120] and 1 year[119] with early aspirin administration to those later diagnosed with acute myocardial infarction. However, increased survival at 35 days was not noted in a study administering enteric-coated aspirin.[121]

Effect on treatment recommendations: Early administration of aspirin is again suggested. However, the recommendation is no longer restricted to those with chest pain and suspected myocardial infarction but applies to all adults with nontraumatic chest pain.

Control of Life-Threatening Bleeding

A 2020 combined SysRev enabled the First Aid Task Force to evaluate the evidence for several methods to control life-threatening external bleeding, including direct pressure, pressure dressings, pressure points, tourniquets, hemostatic dressings, and hemostatic devices.[107] As noted previously, evidence from both military and civilian environments was identified. Key outcomes included mortality as well as time to cessation of bleeding. Direct manual pressure was demonstrated to be beneficial compared with compression devices, pressure dressings or bandages, or pressure points for severe life-threatening external bleeding. Tourniquet use was associated with a higher rate of bleeding cessation compared with direct pressure in military cohort studies[122,123] and lower all-cause mortality in 1 large prehospital cohort study.[124]

In-hospital RCTs performed in patients after endovascular procedures[125–137] demonstrated more rapid bleeding cessation with the use of hemostatic dressings plus direct manual pressure compared with direct manual pressure alone. Many patients in these studies also received anticoagulant medications.

Effect on treatment recommendations: The 2020 treatment recommendations now suggest the use of tourniquets for life-threatening external extremity bleeding that is amenable to the use of a tourniquet; direct pressure, with or without a hemostatic dressing is recommended for life-threatening external bleeding that is not amenable to tourniquet use.

Compression Wrap for Closed Extremity Joint Injury

First aid providers are often called to assist in the treatment of closed extremity joint injuries. The task force requested a SysRev to identify and analyze the evidence about treatment of these injuries.[138] The evidence, consisting of only in-hospital RCTs, found that compression wraps did not reduce pain[139,140] or swelling[139,141,142] or improve range of motion.[139–141,143,144] One small randomized trial found that a compression wrap did reduce recovery time and shorten time to return to sports.[141] The included studies may suffer from confounding related to the use of other standard therapy for acute joint injuries.

Effect on treatment recommendations: The recommendation is unchanged from 2010, when there was insufficient evidence to recommend for or against the

application of a pressure bandage for an acute closed extremity joint injury.[145]

Dental Avulsion

The First Aid Task Force requested a 2020 SysRev of media used to store an avulsed tooth until it can be reimplanted.[111] Many RCTs found benefit from immersion of the tooth in Hanks' Balanced Salt Solution[146–157] as well as in oral rehydration salt solutions[154,155] or from wrapping the tooth in cling film (ie, plastic wrap)[158] as compared with immersion in milk. However, milk was better than many other media for storing a tooth until reimplantation.

Effect on treatment recommendations: The task force-recommended list of media and methods for storing an avulsed tooth is expanded and includes cling film (ie, plastic wrap); 2 solutions (coconut water and egg white) that were previously recommended are no longer included in the recommendations.

Additional Reviews

The First Aid Task Force also evaluated 8 ScopRevs and 2 EvUps.

NEXT STEPS

The ILCOR councils, task forces, and members are committed to the process of continuous evidence evaluation. Through the ScopRevs and EvUps identified in this 2020 document, the task forces have identified many topics that require new SysRevs. The task forces will prioritize the next set of reviews, adding topics that result from the emerging evidence. The ILCOR leadership and task forces have set ambitious goals designed to analyze published studies and develop evidence-based treatment recommendations in a continuous, annual fashion to assist resuscitation councils in the creation and revision of their guidelines for CPR, ECC, education, and first aid.

ARTICLE INFORMATION

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Disclosures

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*Modest.

†Significant.

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*Significant.

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Circulation

Evidence Evaluation Process and Management of Potential Conflicts of Interest

2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

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> *"Measurement is the first step that leads to control and eventually to improvement. If you can't measure something, you can't understand it. If you can't understand it, you can't control it. If you can't control it, you can't improve it."*
>
> — H. James Harrington

The *2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations* (CoSTR) is the result of a long period of collaboration of international experts under the umbrella of the International Liaison Committee on Resuscitation (ILCOR). The ILCOR organization comprises the world's leading resuscitation councils: the American Heart Association (AHA), the European Resuscitation Council, the Heart and Stroke Foundation of Canada, the Australian and New Zealand Committee on Resuscitation, the Resuscitation Council of Southern Africa, the InterAmerican Heart Foundation, and the Resuscitation Council of Asia. The vision of ILCOR is "saving more lives globally through resuscitation," and its mission is "to promote, disseminate, and advocate international implementation of evidence-informed resuscitation and first aid, using transparent evaluation and consensus summary of scientific data." These goals are outlined in more detail in the 2016 to 2020 ILCOR Strategic Plan (as electronic supplement).[1]

There are 6 ILCOR task forces: Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; Education, Implementation, and Teams; and First Aid.[2] Task force members represent diverse countries and bring expertise in all aspects of prearrest, arrest, postarrest care, and first aid. ILCOR appoints task force members by using a request for application and a rigorous selection process, with the goal of balancing scientific and clinical expertise, representation across ILCOR member councils, representation across gender, and diversity across career levels (early, mid, senior). Each task force also has an elected chair and deputy chair, and all positions have a required (time-based) turnover of positions. The Acute Coronary Syndromes Task Force was not continued after 2015, but relevant questions continue to be addressed within existing task forces.

Key Words: AHA Scientific Statements ■ cardiopulmonary resuscitation ■ evidence evaluation ■ measurement ■ systems of care

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ILCOR maintains its commitment to a rigorous and continuous review of scientific literature focused on resuscitation, cardiac arrest, relevant conditions requiring first aid, related education, implementation strategies, and systems of care.

ILCOR is also committed to publishing regular and ongoing CoSTRs. The science evaluation performed by ILCOR underpins the development of international resuscitation council guidelines (including the AHA and the European Resuscitation Council).

EVIDENCE EVALUATION PROCESS

The most important product of the ILCOR evidence evaluation process is the summary of the evidence identified (consensus on science) and the accompanying treatment recommendations. ILCOR is committed to transparency in presenting consensus descriptions and summaries of the evidence, and the creation of treatment recommendations whenever consensus can be achieved. The processes to evaluate the information available has evolved substantially over the past 2 decades, as has ILCOR's approach to reviewing the science related to its mission.

2015 Evidence Evaluation Process

In 2015, ILCOR published its detailed *2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations.*[3,4] It was a very detailed process in which 250 evidence reviewers from 39 countries completed 165 systematic reviews (SysRevs) on resuscitation-related questions. These reviews were completed according to a detailed process, including the use of the Grading of Recommendations Assessment, Development, and Evaluation (GRADE).[5,6] These reviews were published in summary format as the 2015 CoSTR.[3,4] The supporting documentation for these SysRevs was published in electronic format with the key components of the review (including PICO [population, intervention, comparator, outcome] question, search strategies, bias assessment tools, GRADE evidence profile tables, and CoSTRs) housed in a repository. This process was also underpinned by a rigorous conflict of interest (COI) process, and each SysRev was peer reviewed.[5,6]

The detailed methodology for the SysRevs completed for the 2015 CoSTR is outlined in the evidence evaluation chapter.[5,6] Very few of these SysRevs went on to publication.

2016 to 2020 Evolution of the Evidence Evaluation Process

Beginning in 2016, ILCOR reviewed and restructured the evidence evaluation process to better meet its commitment to facilitate a rigorous, continuous evidence review. ILCOR committed to change the CoSTR evidence review and publication from every 5 years to an annual update. The organization then began creating the infrastructure to support these reviews and facilitate ILCOR's vision and mission.[1]

Continuous Evidence Evaluation Working Group

ILCOR created a governance process to support ongoing evidence evaluation. The Continuous Evidence Evaluation Working Group (CEE WG) was created, and it commissioned high-quality SysRevs to be performed by knowledge synthesis units (KSUs) and expert systematic reviewers (ESRs). More details of the role and components of these KSUs and ESRs are described in the subsequent sections. The publication of peer-reviewed SysRevs in addition to the peer-reviewed ILCOR CoSTRs maximizes dissemination of the evidence. The first of these commissioned SysRevs was published in 2017,[7] and, on the basis of this review, the basic life support and pediatric life support CoSTR Updates were published in 2017.[8,9] Additional SysRevs provided the foundation for CoSTR Updates in 2018[10,11] and 2019.[12,13] In all, 4 KSU pilots and 24 expert SysRev pilots were commissioned. The CoSTRs and evidence-to-decision frameworks and links to the International Prospective Register of Systematic Reviews (PROSPERO) registration and published SysRev manuscripts are posted on ILCOR.org.[14]

The CEE WG provided additional expertise and resources to support the task forces. Domain leads are researchers and clinicians with specialized knowledge in topics such as defibrillation or cardiopulmonary resuscitation adjuncts. They were appointed to assist the task forces in identifying and analyzing relevant evidence. CEE WG members, domain leads, task force chairs and other experts subscribed to publication alerts to keep them aware of studies published relevant to their review topics and areas of expertise.

ILCOR also facilitated the creation of a more permanent document and template repository on its website.[14] This repository houses the instructional and process documents that support the continuous evidence evaluation process,[15] an explanatory video about the continuous evidence evaluation process,[16] the draft CoSTRs,[17] and final versions of the CoSTRs. This site has a public interface where draft material is posted for public review and comments during the creation of the SysRevs and CoSTRs.

The ILCOR SysRev process continues to be based on the methodological principles published by the National Academy of Health and Medicine (formerly the Institute of Medicine) in 2011,[18] the Cochrane Library,[19–21] GRADE,[22] and the reporting guidelines based on the recommendations from Preferred Reporting Items for a Systematic Review and Meta-Analysis (PRISMA[23]).[24] The details of this evidence evaluation process established by the CEE WG for the KSUs and ESRs can be found in the workflow document[25] and are outlined in a descriptive video.[16]

Scientific Advisory Committee

The CEE WG was created as the interim methodological governance process in 2016, and it continued to function until the ILCOR Scientific Advisory Committee (SAC) was convened. The SAC first met in August 2019, with elected members and some ex-officio representation. Committee appointments required methodological expertise, a track record of involvement with review of resuscitation science, and appropriate content knowledge. Members met regularly (every 1–2 weeks) by webinar and continued the governance of the CEE process. The new and updated process documents and reporting templates were posted on the ILCOR website.[15] Specific SAC members were assigned to work with specific ILCOR task forces, to provide a conduit for methodological expertise and advice, and to facilitate completion of and the methodological rigor of the task force–based evidence reviews.

Prioritization of Questions Asked

The ILCOR task forces prioritized topics for review in several ways. Topics related to the large existing list of ILCOR PICO questions from 2010 and 2015 were initially prioritized by the relevant ILCOR task forces. The task forces continually reevaluated their priorities using several tools, including areas identified as gaps by the 2015 reviews,[26,27] ongoing literature searches performed by the domain leads, information gleaned from recently completed studies, "hot" topics, and areas of controversy or confusion raised by task force members or ILCOR member councils. All prioritized questions were revised and written into a PICOST (population, intervention, comparator, outcome, study design, time frame) format to facilitate the planned review. Diagnostic and prognostic questions required a modification of the standard PICOST format. All PICOSTs for ILCOR reviews were required to be reviewed and approved by members of the CEE WG/SAC.

Public Comment

ILCOR is committed to obtaining input from the broadest community possible to help it establish the most relevant topics, the best way to describe its processes for maximum transparency, and the most useful treatment recommendations. Beginning in 2016, ILCOR has communicated with lay and professional organizations to direct the public to the ILCOR website and sends email communications to those previously engaged to notify them of any additional postings for comment. The individual draft 2020 CoSTRs were accessed and viewed more than 200 000 times.

Each submitted CoSTR is accompanied by a completed GRADE evidence-to-decision framework,[28,29] which is used by the task force to guide its members through a list of key questions. The ILCOR task forces are given guidance on how to provide background information outlining their discussions in sections of the reviews titled "Justification and Evidence-to-Decision Framework Highlights" and "Task Force Insights." The task forces are also requested to provide a list of key gaps in knowledge that had been identified. The product of these deliberations is published as a draft CoSTR online,[17] in the yearly CoSTR summary documents,[8–13] and in the more complete summary documents (such as this publication series).[30] The integrity of these products and a transparent description of the processes that underly them is crucial because these products are used by the international guideline-writing bodies to write the resuscitation guidelines.

Types of Evidence Evaluation

The 2020 CoSTR includes many SysRevs (performed by the relevant task forces, with or without additional appointed experts), but for the first time it also includes other evidence evaluation processes: task force–based scoping reviews (ScopRevs) and international collaborator-based evidence updates (EvUps). Table 1 lists some of the key components of each of these reviews.

Systematic Reviews

Ideally, every ILCOR topic reviewed would have the benefit of a meticulously performed SysRev as the basis for critical appraisal. The Academy of Medicine defines a SysRev as a "scientific investigation that focuses on a specific question and uses explicit, prespecified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies. It may include a quantitative synthesis (meta-analysis), depending on the availability of data."[18] Although the ILCOR membership values SysRevs, many resuscitation topics and questions are still not addressed by adequately powered, randomized clinical trials or high-quality observational studies to evaluate outcomes that the task forces agree are critical.[31,32]

The list of processes common to all ILCOR SysRevs is outlined in Table 2. Some of these steps are outlined in more detail in the sections that follow. The information from these SysRevs has been incorporated into the respective task force chapters. The CoSTR and evidence-to-decision frameworks for these reviews were posted in draft form on the ILCOR website,[17] and the approved CoSTRs are included in the respective task force publication, with an evidence-to-decision table for each new CoSTR in Supplement Appendix A in the Data Supplement.

Pathways to Completion of SysRevs

In the evidence evaluation process that resulted in the 2015 CoSTR, all SysRevs were performed by the task forces. Since 2016, the process has involved several options for completing SysRevs; these options are outlined below.

Knowledge Synthesis Units. ILCOR began a pilot program that commissioned internationally renowned groups of systematic-review methodologists who had completed a request for proposals to perform SysRevs. These groups had experience publishing high-quality

Table 1. Overview of the Evidence Evaluation Processes for the 2020 CoSTR

	KSU SysRev	ESR SysRev	Task Force SysRev	Task Force ScopRev	EvUp
Question based on task force priorities	✓	✓	✓	✓	±
Guidance for review	PRISMA	PRISMA	PRISMA	PRISMA-ScR	ILCOR and member councils
Search strategy created by information specialist*	✓	✓	✓	✓	±
Lead for review	KSU	ESR	ILCOR Task Force	ILCOR Task Force	ILCOR member council collaborators
Content experts from task force	✓	✓	✓	✓	±
Review of published data	✓	✓	✓	✓	✓
Combination of data (eg meta-analysis)	✓	✓	✓	-	-
Bias assessment	✓	✓	✓	-	-
GRADE evidence profile tables	✓	✓	✓	-	-
GRADE EtD	✓	✓	✓	-	-
Task force review and insights incorporated	✓	✓	✓	✓	-
Consensus on science	✓	✓	✓	-	-
Revision/creation of treatment recommendation†	✓	✓	✓	-	-
Opportunity for public comment	✓	✓	✓	✓	-
Peer-reviewed publication†	✓	✓	±	±	-
Included in 2020 CoSTR manuscript	Summary, including PICOST, CoSTR	Summary, including PICOST, CoSTR	Summary, including PICOST, CoSTR	Summary, including PICOST	Summary, including PICOST
Included in 2020 CoSTR appendixes in the Data Supplement	EtD: Supplement Appendix A	EtD: Supplement Appendix A	EtD: Supplement Appendix A	Supplement Appendix B	Supplement Appendix C

*Peer-reviewed search strategies were created by information specialists for all ESR and KSU SysRevs.

†Independent peer review was required for all KSU and ESR SysRevs before posting of CoSTRs and journal submission of SysRevs.

✓ indicates required; ±, not required but preferred; -, not consistent with methodology; CoSTR, Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations; ESR, expert systematic reviewer; EtD, evidence-to-decision framework; EvUp, evidence update; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; ILCOR, International Liaison Committee on Resuscitation; KSU, knowledge synthesis unit; PICOST, population, intervention, comparator, outcome, study design, time frame; PRISMA, Preferred Reporting Items for a Systematic Review and Meta-Analysis[23]; PRISMA-ScR, Preferred Reporting Items for a Systematic Review and Meta-Analysis–extension for Scoping Reviews[32]; ScopRev, scoping review; and SysRev, systematic review.

SysRevs, and some adopted the name *knowledge synthesis unit*. The KSUs were commissioned to research evidence addressing particularly complex questions and multiple PICOSTs that usually involved more than 1 task force and to capture and analyze data to address multiple subgroup issues. The KSU staff worked in conjunction with content experts (as well as members of the CEE WG/SAC) who ensured that all relevant task forces were involved when questions were common to 2 or more of the task forces.

The KSUs performed a commissioned review, based on contracts created with strict timelines for delivery. The KSU process included clear instructions about engagement of task force(s) and expectations for the final product, which included a peer-reviewed publication. Details are included in an online instructional document[35] (see Table 1 summary for more details).

Expert Systematic Reviewer. ILCOR invited expressions of interest for the ESR roles. These individuals or small collaborative groups were required to have methodological expertise and a track record of publications within the relevant domains. The appointed ESRs were then commissioned to perform SysRevs (see Table 1 for more details). The PICOSTs assigned to ESRs were less complex, with limited subgroup analyses, and usually involved a single task force. The first SysRev conducted by an ESR was published in 2018.[36]

Task Force SysRev. The detailed KSU and ESR process for completion of SysRevs was commissioned by ILCOR with a contractual requirement to publish a SysRev in a peer-reviewed journal. The task forces, however, identified many topics that did not address complex questions or require extensive subgroup analyses. As in the ILCOR evidence evaluation processes through 2015, the ILCOR

Table 2. Summary Outline of the Process Steps for the 2020 CoSTR SysRevs

Task forces select, prioritize, and refine questions (using PICOST format)
Task forces allocate level of importance to individual outcomes
Task forces allocate PICOST question to SysRev team*
SysRev registered with PROSPERO
SysRev team works with information specialists to develop and fine-tune database-specific search strategies
Revised search strategies used to search databases
Articles identified by the search are screened by allocated members of the SysRev team using inclusion and exclusion criteria
SysRev team agrees on final list of studies to include
SysRev team agrees on assessment of bias for individual studies
GRADE Evidence Profile table created
Draft CoSTRs created by SysRev team
Evidence-to-decision framework completed by task force
Public invited to comment on draft CoSTRs
Detailed iterative review of CoSTRs to create final version
Peer review of final CoSTR document

CoSTR indicates Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; PICOST, population, intervention, comparison, outcome, study design, time frame; PROSPERO, International Prospective Register of Systematic Reviews; and SysRev, systematic review.

*Systematic review team could be knowledge synthesis unit, expert systematic reviewer, or task-force–led team involving content experts from the International Liaison Committee on Resuscitation task force(s), and delegated member of the Continuous Evidence Evaluation Working Group and Scientific Advisory Committee.

task forces were empowered to complete such reviews. If a topic was considered appropriate for a task force SysRev, the task force created a SysRev team and followed a formal process[37] (see Table 2). The CoSTRs for these SysRevs are incorporated into the task force chapters. The supporting evidence-to-decision framework for each of the task force SysRevs is published in Supplement Appendix A. The first task force–based SysRev was published in 2020.[38]

Adolopment. For some prioritized questions, the task force identified an existing, relevant, recently published SysRev (with or without a meta-analysis). The SAC recognized that duplication of effort to complete a new SysRev would be a waste of resources. For these situations, the CEE WG/SAC recommended use of the GRADE-Adolopment methodology[39] to assess whether the identified review could be adopted and adapted as needed. This methodology includes a rigorous process with strict steps to allow the incorporation of the information into an ILCOR SysRev. The result of this process could be the construction of a CoSTR. This process was first used by the Advanced Life Support Task Force to review prophylactic antibiotic use after cardiac arrest.[40,40a,41]

Components of a SysRev

Formulating the Question. Existing and new questions for any SysRevs were formulated to comply with the population, intervention, comparison, outcome, study design[42] and time frame. The CEE WG/SAC developed a generic template to facilitate the development of a sensitive and specific search strategy.[43]

Search Strategy. The search strategies were created by information specialists on the basis of the PICOST question. Most of the searches were conducted by an information specialist contracted by ILCOR, while some were conducted by information specialists working with topic experts. Many of the search strategies themselves were independently peer reviewed. The CEE WG/SAC requested that the searches be performed, at a minimum, using MEDLINE, Embase, and the Cochrane Library. The CEE WG/SAC also requested a search of relevant databases of submitted protocols, to identify any incomplete or unpublished trials, and for the search to be registered with PROSPERO.

Questions Related to Prognosis and Diagnostic Test Accuracy. Most topics reviewed by the task forces related to interventions, but some by necessity were focused on prognosis or diagnostic test accuracy. GRADE has formulated processes to support these,[44,45] and the CEE WG/SAC provided guidance on outcome selection, tools for bias assessment, evidence profile tables, and variation in the evidence-to-decision framework. For some of the prognostic questions, the outcome measures used for diagnostic methodology (eg, specificity) were considered to have especially significant clinical relevance.[46]

Combination of Data (Meta-Analysis). One reason to complete a SysRev is to facilitate the performance of meta-analyses. It is not always appropriate to combine data from identified studies, and reviewers were encouraged to consider the methodological rigor of the identified studies, and how similar they were with regard to components of the PICOST. If there were limitations to performing the meta-analysis (including heterogeneity), task forces were asked to describe these and to consider sensitivity analyses by including or excluding specific types of studies.[19] The task forces were asked to state explicitly situations where the heterogeneity of studies precluded meta-analysis (eg, the nature of the results, the extent to which the results addressed the PICOST question, the methodology).

GRADE Process

GRADE was adopted by ILCOR for the 2015 evidence evaluation process.[5,6] The GRADE process and ILCOR evidence evaluation have both continued to evolve, and a number of changes were made to the ILCOR evidence evaluation process to ensure consistency with the GRADE process. The GRADE risk-of-bias tools for randomized controlled trials and nonrandomized studies have changed, and the online guideline development tool has been updated. The GRADE developers

continue to refine their processes, including improving ways to explain the published evidence.[47] These updates were introduced through use of the online GRADE handbook[22] and via specific publications.

Key components of the GRADE process that were incorporated into the SysRevs completed for the 2020 ILCOR CoSTRs are listed below.

Bias Assessment for Randomized Controlled Trials. The recommended risk of bias tool for randomized controlled trials is now the revised Cochrane Risk of Bias tool.[48] This tool assesses the risk of bias using signaling questions to explore 5 domains for individually randomized trials, including bias arising from the randomization process, due to deviations from intended interventions, due to missing outcome data, in measurement of the outcome, and in selection of the reported result.

Bias Assessment for Nonrandomized Trials. When using GRADE to evaluate certainty of evidence, the original certainty of evidence started at high for randomized controlled trials for interventions and started at low for observational (nonrandomized studies).[49] As the types of evidence reviewed using the GRADE methodology expanded, some concern was expressed that the GRADE approach was unnecessarily harsh in its assessment of the certainty of the evidence.[50] The GRADE group revisited this automatic allocation of evidence. The new recommended tool to assess risk of bias for nonrandomized studies was Risk of Bias In Non-randomised Studies - of Interventions (ROBINS-I).[51] This tool enables all nonrandomized studies to start at low risk of bias, but it is expected that they will be adjusted to moderate, serious, or critical risk on the basis of methodological concerns.[50]

Evidence Profile Tables. The GRADE evidence profile tables have been created to present a summary of the evidence that addresses the particular outcome. The ILCOR task forces continue to use the guidance from instructional documents on the ILCOR website, and the online GRADE guideline development tool[52] to complete these tables. These tables include the following information: the specific outcome; the number of studies and their study design(s); judgments about risk of bias, inconsistency, indirectness, imprecision, and other considerations (including publication bias and factors that increase the certainty of evidence); relative and absolute effects for that outcome; a rating of the overall certainty of evidence for each outcome (which may vary by outcome); classification of the importance of each outcome; and explanatory footnotes, if needed. The use of these tables facilitates the translation of a body of science into a summary of science. The ILCOR task forces use the content of the evidence profile tables as a way to create the consensus on science statements. Wording may be: "For the critical outcome of survival to hospital discharge, we identified low-certainty evidence (downgraded for risk of bias and indirectness) from 3 randomized studies that enrolled 873 patients." The evidence profile tables are not included in the task force chapter or appendices but are included in the SysRevs published in the peer-reviewed literature.

Table 3. Certainty (Quality) of Evidence for a Specific Outcome (or Across Outcomes)[22]

Grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Certainty (Quality) of Evidence. The GRADE process requires an allocation of the overall quality of the evidence identified to support each important or critical outcome. ILCOR adopted the phrase "certainty of evidence" as recently recommended by the GRADE working group.[53] The ratings of the certainty of evidence reflect the extent of our confidence that the estimates of the effect are correct. This certainty of evidence, which is based on our confidence in the estimate of the relative importance of the outcomes (and their variability) is adequate to support a particular recommendation.[54] The allocated certainty can be high, moderate, low, or very low (see Table 3).[22]

The GRADE approach to the certainty of evidence states that information from randomized trials without important limitations provides high-certainty evidence, and expects that information from observational (nonrandomized) studies without special strengths or important limitations provides low-certainty evidence.[49,50] The final allocation of certainty of evidence for an outcome is derived from the information provided in the fields of the evidence profile tables: limitations in study design or execution (risk of bias), inconsistency of results, indirectness of evidence, imprecision, publication bias, large magnitude of effect, plausible confounding, and dose-response gradient (see Table 4).[22]

For the ILCOR treatment recommendations, the GRADE process requires an assessment of the overall certainty of evidence across all critical outcomes for that question. The recommended approach is that the lowest certainty of evidence for any of the critical outcomes determines the overall certainty of evidence.[50]

Evidence-to-Decision Framework. The 2015 CoSTR adhered to GRADE methodology by including statements about values and preferences. ILCOR

Table 4. Factors That Can Alter the Certainty (Quality) of Evidence[22]

Factor	Consequence
Limitations in study design or execution (risk of bias)	↓ 1 or 2 levels
Inconsistency of results	↓ 1 or 2 levels
Indirectness of evidence	↓ 1 or 2 levels
Imprecision	↓ 1 or 2 levels
Publication bias	↓ 1 or 2 levels
Large magnitude of effect	↑ 1 or 2 levels
All plausible confounding would reduce the demonstrated effect or increase the effect if no effect was observed	↑ 1 level
Dose-response gradient	↑ 1 level

has continued with this process and, for SysRevs, has incorporated an evidence-to-decision framework. This process required the task force to consider additional factors while developing their CoSTRs.[28,29] The questions to be considered relate to 6 main areas: the problem being addressed, the benefits and harms of the options, the anticipated resource use, equity, acceptability, and feasibility (see Table 5). The task force discussions during this process are captured by the task forces for each question in a subsection entitled "Justification and Evidence-to-Decision Framework Highlights."

Treatment Recommendations

Strength of Recommendation. The strength of a recommendation reflects the extent to which the task force is confident that the desirable effects of an action or intervention outweigh the undesirable effects. As noted above, the strength of a recommendation usually relies on evidence regarding those outcomes that the task force considered critical, and the certainty of evidence for each of these outcomes. GRADE suggests using 2 strengths of recommendations: strong and weak. A strong recommendation suggests that the task force is confident that desirable effects outweigh the undesirable effects; the recommendation could be adopted as a policy, and adherence to this recommendation could be used as quality measure. In such cases, the words "we recommend" reflect this certainty. In contrast, a weak recommendation suggests that the task force is not confident that desirable effects outweigh the undesirable effects. The recommendation may need further qualification or decision tools, and as a result, policies may vary among different regions. The task force's wording usually reflects this lack of certainty, with the words "we suggest," or the recommendations can be "conditional," "discretionary," or "qualified."[55]

Table 5. Components of Evidence-to-Decision Framework for Questions Related to Interventions[28,52]

Component	Questions
Problem	Is there a problem priority?
Benefits and harms of the options	What is the overall certainty of this evidence?
	Is there important uncertainty about how much people value the main outcomes?
	Are the desirable anticipated effects large?
	Are the undesirable anticipated effects small?
	Are the desirable effects large relative to undesirable effects?
Resource use	Are the required resources small?
	Is the incremental cost small relative to the net benefits?
Equity	What would be the impact on health inequities?
Acceptability	Is the option acceptable to key stakeholders?
Feasibility	Is the option feasible to implement?

Discordant Recommendations. In general, the expectation was that the strength of the recommendation (strong or weak) is consistent with the certainty (quality) of the evidence.[55] There are some situations where the task force wished to make a strong recommendation despite having low- or very low-certainty (quality) evidence. In this situation, the task forces were requested to justify their "discordant" recommendation. Such justification could result from scenarios where a very high value is placed on an uncertain but potentially life-preserving benefit, a much higher value or confidence is placed on adverse events than on an uncertain benefit, a high value is placed on the reduction in harm, or a high value is placed on avoiding harm.[56]

No Recommendations. In many situations, the task forces deliberated at length about whether to make a recommendation for or against a particular treatment or diagnostic study. The body of evidence supporting outcomes that the task force rated critical or important may be either large but without significant benefit (or harm) observed (with a degree of certainty); small (or nonexistent) with no significant benefit (or harm) observed (with a very low degree of certainty); or the analysis made using the evidence-to-decision framework suggested that there are trade-offs related to a change in practice (eg, educational requirements, cost benefits, additional equipment, inequities).

The task forces, given the geographical diversity and broad and deep expertise of their members, are in a unique position to provide guidance for the international community. They were encouraged to make recommendations for each question asked, when consensus allowed.[57]

Good Practice Statements. In situations where there is no relevant evidence, the task forces could consider making a good practice statement.[58] In general, the message in a good practice statement should adhere to the following principles: the message should be clear, specific and actionable; the message should be necessary (without the guidance, clinicians might fail to take the appropriate action); the message should be

associated with a net benefit that is considered large and unequivocal; and the values and preferences are clear, or it would be a poor use of a guideline panel's time and resources to collect evidence (eg, limited opportunity or high cost). The task force should provide the rationale, including an explicit statement of the chain of evidence that supports the recommendation.[58]

Scoping Reviews

ScopRevs are useful to examine and map the extent, range, and nature of research activity (for example, when examining areas that are emerging, to clarify key concepts, to identify gaps or to identify topics for future SysRevs).[59,60] These reviews tend to start with a broad question, search widely, iteratively focus in on key issues and outcomes, and produce a narrative (descriptive) summary of the studies identified but not an estimate of the magnitude of effect.

The task forces often completed a preliminary search relating to a specific topic or wished to perform a broader search to help define the next steps. In such cases, they performed a ScopRev. The SAC developed a process to incorporate ScopRevs into the ILCOR evidence evaluation process.[61]

ScopRevs can result in a publishable manuscript, but they do not assess the bias of included studies or the magnitude and direction of outcomes in a quantitative way; therefore, they cannot support the construction of a CoSTR without an additional SysRev. The methodology for reporting ScopRevs is based on the PRISMA Extension for ScopRevs.[32]

The ILCOR task forces were empowered to appoint a task force–based ScopRev team to coordinate the development of a ScopRev. Components of the ScopRev that were included in the review template included a COI declaration; a methodological preamble; the PICOST; the search strategies; the inclusion and exclusion criteria; data tables; task force insights, including the rationale for the search, a narrative summary of evidence identified; a narrative reporting of the task force discussions; and knowledge gaps and references.[62]

The task forces performed a detailed review of the contents of the ScopRev, including a recommendation for next steps, specifically whether the task force agreed that the evidence identified was sufficient to consider requesting a SysRev. The Basic Life Support Task Force published an extensive ScopRev.[63] ScopRevs were each posted for 2 weeks on the ILCOR website for public comment and are published in their entirety in Supplement Appendix B in each of the task force manuscripts (see Table 1 for more details).

Evidence Updates

The ILCOR task forces and the member councils identified a number of topics that had not been formally reviewed in several years. Volunteer members from the councils agreed to perform an update of these topics to identify any relevant evidence published after the last formal review. The volunteers reran or revised the original search strategy in consultation with the task forces, documented results of the search, and tabulated the data identified within the included studies. Similar to ScopRev methodology, there was no requirement for bias assessment of the individual studies or GRADE review of evidence across outcomes. The authors were then asked to indicate whether they thought that a formal SysRev should be considered. The task forces were able to review these updates to a variable degree, but given that ILCOR agreed that any new treatment recommendation requires completion of a SysRev, these EvUps did not result in development of new treatment recommendations or revision of current recommendations. The topics reviewed as EvUps are listed in each task force manuscript, with a note as to whether the EvUp identified sufficient published evidence to suggest the need for a future SysRev. The methodology and draft summary of these updates as submitted by the reviewers is included in Supplement Appendix C in each of the task force manuscripts (see Table 1 for more details).

MANAGEMENT OF POTENTIAL CONFLICTS OF INTEREST THROUGHOUT THE PROCESS

To ensure the integrity of the evidence evaluation and the process of consensus on science development, ILCOR followed its rigorous COI management policies at all times. A full description of these policies and their implementation can be found in Part 4 of the 2010 CoSTR.[64,64a] Any person involved in any part of the process disclosed all commercial relationships and other potential conflicts by using the standard AHA online COI disclosure process. Disclosure information for writing group members is listed in Appendix 1. Disclosure information for peer reviewers is listed in Appendix 2.

In total, the AHA, on behalf of ILCOR processed more than 200 COI declarations. In addition to disclosing commercial relationships, volunteers were asked to be sensitive to any potential intellectual conflicts, such as having authored key studies related to a topic, or involvement in ongoing studies related to a topic. All disclosures were reviewed by AHA staff and considered in the assignment of task force chairs, vice chairs, members, and other leadership roles. Relationships were screened for conflicts in assigning individual PICOST questions to task force members, ESRs, or KSUs. Evidence reviewer roles were reassigned when potential conflicts surfaced.

Participants, 2 COI co-chairs, task force chairs, task force members, and staff raised COI questions and issues throughout the process and referred them to the COI co-chairs if they could not be resolved within the task force. The COI co-chairs kept a log of each COI-related

issue and its resolution. None of the COI issues required serious intervention, such as replacement of anyone in a leadership role. When a commercial relationship or intellectual conflict was discovered for a specific PICOST question, that question was reassigned to an evidence reviewer without a potential conflict. This happened several times during the continuous evidence evaluation process. During conferences, each participant was assigned a COI number, and a full list of disclosures was available to all participants throughout the meeting. Participants were asked to state any potential conflict when they participated in discussions, and they abstained from voting on any issue for which they had a conflict. COI co-chairs were available during conferences for anonymous reporting; no such reports were received.

NEXT STEPS

The resuscitation community continues to conduct research to improve the effectiveness of resuscitation. As these manuscripts are published, ILCOR will incorporate them into the continuous evidence evaluation processes. ILCOR plans to continually review all topics related to resuscitation through a comprehensive evidence evaluation strategy that includes publication alerts, current peer-reviewed search strategies, the various systematic review pathways outlined in this chapter, and the use of ScopRevs where appropriate. ILCOR is also expanding online options to assist with the enormous task of evaluating published evidence and timely dissemination of treatment recommendations by using various digital platforms and further engaging the resuscitation and general communities through opportunities for input and feedback. Consistent with the Utstein Formula for Survival,[65] where science and education and implementation result in improved survival, ILCOR will strive to shorten the time from evidence evaluation to translation to clinical practice.

ARTICLE INFORMATION

The American Heart Association requests that this document be cited as follows: Morley PT, Atkins DL, Finn JC, Maconochie I, Nolan JP, Rabi Y, Singletary EM, Wang T-L, Welsford M, Olasveengen TM, Aickin R, Billi JE, Greif R, Lang E, Mancini ME, Montgomery WH, Neumar RW, Perkins GD, Soar J, Wyckoff MH, Morrison LJ. Evidence evaluation process and management of potential conflicts of interest: 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation*. 2020;142(suppl 1):S28–S40. doi: 10.1161/CIR.0000000000000891

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Disclosures

Appendix 1. Writing Group Disclosures

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, Royal Melbourne Hospital (Australia)	None	None	None	None	None	None	None
Richard Aickin	Starship Children's Hospital (New Zealand)	None	None	None	None	None	None	None
Dianne L. Atkins	University of Iowa	None	None	None	None	None	None	None
John E. Billi	University of Michigan	None	None	None	None	None	None	None
Judith C. Finn	Curtin University	National Health and Medical Research Council (Australia)(project funds and salary support)†	None	None	None	None		Salary: National Health and Medical Research Council (Australia)†; St John Western Australia†
Robert Greif	Bern University Hospital, University of Bern (Switzerland)	None	None	None	None	None	None	None
Eddy Lang	University of Calgary (Canada)	None	None	None	None	None	None	None

(*Continued*)

Appendix 1. Continued

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Ian Maconochie	Imperial College Healthcare Trust(United Kingdom)	None	None	None	None	None	None	None
Mary E. Mancini	University of Texas at Arlington	None	None	Stryker*	None	None	None	None
William H. Montgomery	Straub Clinic and Hospital	None	None	None	None	None	None	None
Laurie J. Morrison	St Michael's Hospital, University of Toronto	None	None	None	None	None	None	None
Robert W. Neumar	University of Michigan	NIH (R01 HL133129, K12 HL133304)†; AHA (19SFRN34760762)†	Stryker/ PhysioControl (Equipment support for laboratory and clinical research)*	None	None	None	None	None
Jerry P. Nolan	Warwick Medical School (United Kingdom)	None	None	None	None	None	None	None
Theresa M. Olasveengen	Oslo University Hospital (Norway)	Zoll Foundation*; Laerdal Foundation*	None	None	None	None	None	None
Gavin D. Perkins	Warwick Medical School and University Hospitals NHS Foundation Trust (United Kingdom)	None	None	None	None	None	None	None
Yacov Rabi	University of Calgary (Canada)	None	None	None	None	None	None	None
Eunice M. Singletary	University of Virginia	None	None	None	None	None	American Red Cross Scientific Advisory Council (Volunteer Chairperson)*	None
Jasmeet Soar	Southmead Hospital North Bristol NHS Trust Bristol (United Kingdom)	None	None	None	None	None	None	None
Tzong-Luen Wang	Chang Bing Show Chwang Memorial Hospital (Taiwan)	None	None	None	None	None	None	None
Michelle Welsford	Center for Paramedic Education and Research, Hamilton Health Sciences Center	None	None	None	None	None	None	None
Myra H. Wyckoff	UT Southwestern	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.

Appendix 2. Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Enrico Baldi	University of Pavia (Italy)	None	None	None	None	None	None	None
David G. Buckler	University of Pennsylvania	None	None	None	None	None	None	None
Athanasios Chalkias	University of Thessaly (Greece)	None	None	None	None	None	None	None
Aparna Hoskote	CVICU Specialist Great Ormond Street Hospital (United Kingdom)	None	None	None	None	None	None	None
Mary Ann McNeil	University of Minnesota	None	None	None	None	None	None	None
Vincent P. Reyes	Tuality Hospital	None	None	None	None	None	None	None
Taylor Sawyer	Seattle Children's Hospital/University of Washington	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.

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Circulation

Adult Basic Life Support

2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

ABSTRACT: This *2020 International Consensus on Cardiopulmonary Resuscitation* (CPR) *and Emergency Cardiovascular Care Science With Treatment Recommendations* on basic life support summarizes evidence evaluations performed for 22 topics that were prioritized by the Basic Life Support Task Force of the International Liaison Committee on Resuscitation. The evidence reviews include 16 systematic reviews, 5 scoping reviews, and 1 evidence update. Per agreement within the International Liaison Committee on Resuscitation, new or revised treatment recommendations were only made after a systematic review.

Systematic reviews were performed for the following topics: dispatch diagnosis of cardiac arrest, use of a firm surface for CPR, sequence for starting CPR (compressions-airway-breaths versus airway-breaths-compressions), CPR before calling for help, duration of CPR cycles, hand position during compressions, rhythm check timing, feedback for CPR quality, alternative techniques, public access automated external defibrillator programs, analysis of rhythm during chest compressions, CPR before defibrillation, removal of foreign-body airway obstruction, resuscitation care for suspected opioid-associated emergencies, drowning, and harm from CPR to victims not in cardiac arrest.

The topics that resulted in the most extensive task force discussions included CPR during transport, CPR before calling for help, resuscitation care for suspected opioid-associated emergencies, feedback for CPR quality, and analysis of rhythm during chest compressions. After discussion of the scoping reviews and the evidence update, the task force prioritized several topics for new systematic reviews.

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Key Words: AHA Scientific Statements ■ cardiopulmonary resuscitation ■ defibrillators ■ drowning ■ emergency medical services communication systems ■ heart arrest ■ heart massage ■ respiration, artificial

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This 2020 document is the fourth in a series of annual International Liaison Committee on Resuscitation (ILCOR) *International Consensus on Cardiopulmonary Resuscitation* (CPR) *and Emergency Cardiovascular Care* (ECC) *Science With Treatment Recommendations* (CoSTR) summary publications. This 2020 CoSTR for basic life support (BLS) includes new topics addressed by systematic reviews (SysRevs) performed within the past 12 months and prioritized by the BLS Task Force. It also includes updates of the BLS treatment recommendations published from 2010 through 2019,[1–8] as needed, based on additional evidence evaluations. As a result, this 2020 CoSTR for BLS is the most comprehensive update since 2010.

The 3 major types of evidence evaluation supporting this 2020 document are the SysRev, the scoping review (ScopRev), and the evidence update (EvUp).

The SysRev is a rigorous process, following strict methodology to answer a specific question; each of these ultimately resulted in generation of the task force consensus on science with treatment recommendations included in this document. The SysRevs were performed by a knowledge synthesis unit, an expert systematic reviewer, or the BLS Task Force, and many resulted in separate published SysRevs.

To begin the SysRev, the question to be answered was phrased in terms of the PICOST (population, intervention, comparator, outcome, study design, time frame) format. The methodology used to *identify* the evidence was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[9] The approach used to *evaluate* the evidence was based on that proposed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) working group.[10] Using this approach, the task force rated as high, moderate, low, or very low the certainty/confidence in the estimates of effect of an intervention or assessment across a body of evidence (excluding animal studies) for each of the predefined outcomes. Randomized controlled trials (RCTs)

generally began the analysis as high-certainty evidence, and observational studies generally began the analysis as low-certainty evidence; examination of the evidence using the GRADE approach could result in downgrading or upgrading of the certainty of evidence. For additional information, refer to this supplement's "Evidence Evaluation Process and Management of Potential Conflicts of Interest."[11] Disclosure information for writing group members is listed in Appendix 1. Disclosure information for peer reviewers is listed in Appendix 2.

When a pre-2015 treatment recommendation was not updated, the language used differs from that used in the GRADE approach because GRADE was not used before 2015.[12,13]

Draft 2020 CoSTRs for BLS were posted on the ILCOR website[14] public comment between December 31, 2019, and February 16, 2020, with comments accepted through February 29, 2020. These new draft 2020 CoSTR statements for BLS received 45 694 views and 27 comments.

This summary statement contains the final wording of the CoSTR statements as approved by the ILCOR task forces and by the ILCOR member councils after review and consideration of comments posted online in response to the draft CoSTRs. Within this publication, each topic includes the PICOST as well as the CoSTR, an expanded "Justification and Evidence-to-Decision Framework Highlights" section, and a list of knowledge gaps requiring future research studies. An evidence-to-decision table is included for each CoSTR in Appendix A in the Supplemental Materials of this document.

The second major type of evidence evaluation performed to support this 2020 CoSTR for BLS is a ScopRev. ScopRevs are designed to identify the extent, range, and nature of evidence on a topic or a question, and they were performed by topic experts in consultation with the BLS Task Force. The task force analyzed the identified evidence and determined its value and implications for resuscitation practice or research. The rationale for the ScopRev, the summary of evidence, and the task force insights are all highlighted in the body of this publication. The most recent treatment recommendation is included. The task force notes whether the ScopRev identified substantive evidence that may result in a change in ILCOR treatment recommendations. If sufficient evidence was identified, the task force suggested consideration of a (future) SysRev to supply sufficient detail to support the development of an updated CoSTR. All ScopRevs are included in their entirety in Appendix B in the Supplemental Materials of this publication.

The third type of evidence evaluation supporting this 2020 CoSTR for BLS is an EvUp. EvUps are generally performed for topics previously reviewed by ILCOR to identify new studies published after the most recent ILCOR evidence evaluation, typically through use of search terms and methodologies from previous reviews. These EvUps were performed by task force members, collaborating experts, or members of council writing groups. The EvUps are cited in the body of this document with a note about whether the evidence suggested the need to consider a SysRev; the existing ILCOR treatment recommendation was reiterated. In this document, no change in ILCOR treatment recommendations resulted from an EvUp; if substantial new evidence was identified, the task force recommended consideration of a SysRev. All EvUps are included in Appendix C in the Supplemental Materials of this publication.

The BLS Task Force considered the availability of new evidence as well as the evidence needed to create, confirm, or revise treatment recommendations. The chapter topics are organized in sections that approximate the order of the steps of resuscitation. For each reviewed topic, the method of review (SysRev, ScopRev, EvUp) is clearly labeled, with links to the relevant review documents in the Appendixes in the Supplemental Materials.

TOPICS REVIEWED IN THIS 2020 BLS CoSTR

Note: As indicated above, the new BLS CoSTR evidence reviews were all completed in February 2020. As a result, this document does not address the topic of potential influence of coronavirus disease 2019 (COVID-19) on resuscitation practice. In the spring of 2020, an ILCOR writing group was assembled to identify and evaluate the published evidence regarding risks of aerosol generation and infection transmission during attempted resuscitation of adults, children, and infants. This group developed a consensus on science with treatment recommendations and task force insights. This statement is published as a separate document.[15] As new evidence emerges, the ILCOR task forces will review and update this statement, so the reader is referred to the ILCOR website[14] for the most up-to-date recommendations.

Early Access and Cardiac Arrest Prevention, Including Emergency Medical Dispatch and Dispatcher-Assisted CPR (DA-CPR)

- Dispatch diagnosis of cardiac arrest (BLS 740: SysRev)
- Dispatcher instructions in CPR (2019 CoSTR BLS 359: SysRev)
- Dispatcher-assisted compression-only CPR versus conventional CPR (2017 CoSTR BLS 359: SysRev)

Compression-Only CPR

- Lay rescuer chest compression–only versus standard CPR (2017 CoSTR BLS 547: SysRev)
- Emergency medical services (EMS) chest compression–only compared with conventional CPR (2017 CoSTR BLS 360: SysRev)
- In-hospital chest compression–only CPR versus conventional CPR (2017 CoSTR BLS 372: SysRev)

- Rescuer fatigue in chest compression–only CPR (BLS 349: ScopRev)

CPR Sequence

- Firm surface for CPR (BLS 370: SysRev)
- Starting CPR (compressions-airway-breaths [C-A-B] versus airway-breaths-compressions [A-B-C]) (BLS 661: SysRev)
- CPR before call for help (BLS 1527: SysRev)
- Duration of CPR cycles (2 minutes versus other) (BLS 346: SysRev)
- Check for circulation during BLS (BLS 348: EvUp)

Components of High-Quality CPR

- Hand position during compressions (BLS 357: SysRev)
- Chest compression rate, chest compression depth, and chest wall recoil (BLS 366, BLS 367, BLS 343: ScopRev)
- Compression-to-ventilation ratio (2017 CoSTR BLS 362: SysRev)
- Timing of rhythm check (BLS 345: SysRev)
- Feedback for CPR quality (BLS 361: SysRev)

Alternative Techniques

- Alternative techniques (cough CPR, precordial thump, fist pacing) (BLS 374: SysRev)

Defibrillation

- Public access automated external defibrillator (AED) programs (BLS 347: SysRev)
- Analysis of rhythm during chest compressions (BLS 373: SysRev)
- CPR before defibrillation (BLS 363: SysRev)
- Paddle size and placement for defibrillation (ALS-E-030A: ScopRev)

Special Circumstances

- CPR during transport (BLS 1509: ScopRev)
- Removal of foreign-body airway obstruction (BLS 368: SysRev)
- Resuscitation care for suspected opioid-associated emergencies (BLS 811: SysRev)
- Drowning (BLS 856: SysRev)

Potential Harm From CPR

- Harm from CPR to victims not in cardiac arrest (BLS 353: SysRev)
- Harm to rescuers from CPR (BLS 354: ScopRev)

EARLY ACCESS AND CARDIAC ARREST PREVENTION, INCLUDING EMERGENCY MEDICAL DISPATCH AND DA-CPR

A variety of terms have been used to identify the person(s) at an emergency telephone call center who are charged with answering the call, interacting with the caller, and assigning the needed care providers to the incident scene (traditionally called dispatchers). Terminology is similarly varied for the process the dispatcher uses to provide real-time CPR instructions to bystanders at the scene of an out-of-hospital cardiac arrest (OHCA). To remain consistent with the ILCOR evidence review, the term DA-CPR will be used to describe such coaching in this update, recognizing that other terms (eg, telecommunicator CPR and telephone CPR) could be substituted.

Dispatch Diagnosis of Cardiac Arrest (BLS 740: SysRev)

Rationale for Review

Accurate recognition of cardiac arrest by emergency medical dispatchers at the time of the emergency call is an important early step in cardiac arrest management, enabling initiation of DA-CPR and appropriate and timely emergency response. The overall accuracy of dispatchers in recognizing cardiac arrest is not well known. Furthermore, it is not known if there are specific call characteristics that affect the ability to recognize cardiac arrest.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with OHCA
- Intervention: Characteristics of the call process (these might include the specific words by the caller, language or idioms spoken by the caller and understood by the call taker, perceptions of the call receiver, emotional state of the caller, other caller characteristics, type of personnel receiving the call, background noises, etc)
- Comparator: Absence of identified characteristics of the call process
- Outcome: Any diagnostic test outcomes
- 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, provided there was an English abstract. The literature search was updated November 28, 2019.
- International Prospective Register of Systematic Reviews (PROSPERO) registration: CRD42019140265

Consensus on Science

A variety of algorithms and criteria (both commercial and locally developed) are used by dispatch centers to identify potential life-threatening events, such as cardiac arrest and triage emergency responders, to the scene appropriately. The dispatch centers reported great variability of overall accuracy of these algorithms and criteria for recognizing an OHCA in adults (Table 1).

Table 1. Overall Diagnostic Performance of Dispatch Centers for Recognizing OHCA

Outcome	Certainty	Studies	No. of Patients	Median (IQR)
Sensitivity	Very low (risk of bias, imprecision, inconsistency)	46*	84 534†	0.79 (0.69–0.83)
False-negative rate (undertriage)	Very low (risk of bias, imprecision, inconsistency)	46*	84 534†	0.21 (0.17–0.32)
Specificity	Very low (risk of bias, inconsistency)	12‡	789 004§	0.99 (0.93–1.00)
False-positive rate (overtriage)	Very low (risk of bias, inconsistency)	12‡	789 004§	0.01 (0.01–0.07)
Negative predictive value	Low (risk of bias, inconsistency)	12‡	789 004§	1.00 (0.92–1.00)
Positive predictive value	Low (risk of bias, inconsistency)	12‡	789 004§	0.76 (0.50–0.85)
Positive likelihood ratio	Low (risk of bias, inconsistency)	12‡	789 004§	54.72 (11.28–152.22)
Negative likelihood ratio	Low (risk of bias, inconsistency)	12‡	789 004§	0.22 (0.19–0.24)

IQR indicates interquartile range; and OHCA, out-of-hospital cardiac arrest.

Sensitivity = proportion of confirmed cardiac arrest patients labeled as cardiac arrest by the dispatcher. False-negative rate = proportion of confirmed cardiac arrest patients who are not labeled as cardiac arrest by the dispatcher. Specificity = proportion of patients without confirmed cardiac arrest identified who are not labeled as cardiac arrest by dispatchers. False-positive rate = proportion of patients without cardiac arrest who are incorrectly labeled as cardiac arrest by the dispatcher. Negative predictive value = the proportion of patients labeled as not cardiac arrest by the dispatcher who are found not to have confirmed cardiac arrest. Positive predictive value = the proportion of patients labeled as cardiac arrest by dispatchers who are found to have confirmed cardiac arrest. Positive likelihood ratio = the likelihood of a patient with confirmed cardiac arrest to be labeled positive compared with a person without cardiac arrest (the higher the likelihood ratio, the better the test to rule in cardiac arrest). Negative likelihood ratio = the likelihood of a patient with confirmed cardiac arrest to be labeled negative compared with a person without cardiac arrest (the smaller the likelihood ratio, the better the test to rule out cardiac arrest).

*References 16–61.

†Patients strictly with confirmed OHCA.

‡References 16,21,22,27,34,39,41,42,47,48,60,61.

§All patients inclusive of those without and with confirmed OHCA.

We compared subgroups of studies that used predetermined or proprietary dispatching algorithms with those that used less structured criteria for diagnosis of cardiac arrest (dispatch algorithms versus criteria-based dispatch) and studies that reported different credential or training requirements for emergency dispatchers. No identifiable differences were noted in these subgroup analyses. Heterogeneity in studies and lack of adjusted analyses precluded meta-analysis for any subgroup.

Treatment Recommendations

We recommend that dispatch centers implement a standardized algorithm and/or standardized criteria to immediately determine 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.

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-1. In making these new recommendations, we prioritized the desirable benefits (increase in potential lifesaving treatment) that would result from the immediate accurate identification of cardiac arrest by dispatchers. These benefits include the provision of DA-CPR and dispatching of appropriate EMS resources compared with the undesirable consequences of lack of early recognition of the event, such as delays to CPR and AED use. We realize that efforts to minimize the frequency of undertriage (false-negative) may increase the frequency of overtriage (false-positive cases). Importantly, whether in cardiac arrest or not, the potential acuity of such patients still demands the need for immediate EMS assistance at the scene. In tiered response systems, if first-arriving EMS responders find a less emergent situation on arrival, the secondary advanced life support (ALS) response could be cancelled. In either event, the consequences of failing to recognize a genuine cardiac arrest in a timely manner is significant enough to justify some false-positive events. By comparison, the default position of most trauma systems is to have a high overtriage rate and a low undertriage rate because of similar concerns.

We were unable to make any recommendations on specific algorithms or criteria for identification of cardiac arrest because the variability across studies did not allow for direct comparisons or pooling of data. Furthermore, as the result of unexplained variability across studies, even among those using similar dispatch criteria, there was considerable variation in their diagnostic accuracy, which prevented pooling of data to find overall diagnostic accuracy measures for each of the algorithms. One factor that significantly influences the diagnostic accuracy is the prevalence of cardiac arrest in the reported population. In multiple studies, the denominator of total evaluated calls was different—some studies reporting cardiac arrests as a proportion of all emergency calls, others reporting cardiac arrests as a proportion of calls strictly among patients who were described as being unresponsive, and still other studies that (retrospectively) only included patients who were actually in cardiac arrest at the time of the call. Reporting the accuracy of identifying

a cardiac arrest as a proportion of all emergency calls can produce misleadingly favorable diagnostic statistics because, for the majority of such calls, it is obvious at the time that the patient is not in cardiac arrest.

Last, although studies that examined barriers to cardiac arrest identification were identified, these studies were not done in a manner that enabled calculation of the effect of these characteristics on OHCA diagnosis or on dispatcher performance.

Knowledge Gaps

Current knowledge gaps include but are not limited to the following:

- Are there other potentially important criteria or ancillary tools in addition to standard dispatch algorithms that might improve dispatcher recognition of cardiac arrest? These might include use of a remote video link or pulse detection technologies via a caller's mobile telephone.
- What are the potential obstacles to dispatcher recognition of cardiac arrest (eg, language barriers, caller characteristics, patient characteristics)?
- Could the use of artificial intelligence improve recognition of cardiac arrest compared with emergency medical dispatcher recognition?
- What are the operational costs required for implementing and monitoring dispatcher recognition programs?
- What is the most accurate dispatch algorithm, and what are the optimal criteria for rapidly recognizing cardiac arrest?
- What is the relationship between dispatch algorithms and time to cardiac arrest recognition and time to initiation of DA-CPR?

Dispatcher Instructions in CPR (2019 CoSTR BLS 359: SysRev)

DA-CPR has been reported in individual studies to significantly increase the rate of bystander CPR and survival from cardiac arrest. In 2019, we undertook a SysRev and meta-analysis to evaluate the impact of DA-CPR programs on key clinical outcomes after OHCA.[62] Consensus on science, values, preferences, and task force insights and knowledge gaps can be found in the *2019 International Consensus on CPR and ECC Science With Treatment Recommendations*.[7,8]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults with presumed OHCA
- Intervention: Patients/cases or EMS systems for which DA-CPR is offered
- Comparator: Studies with comparators in which either systems or specific cardiac arrest patients/cases were not offered DA-CPR were included
- Outcome: Critical—survival with favorable neurological function (at hospital discharge, 1 month, or 6 months), survival (to hospital discharge, 1 month, or 1 year), short-term survival (return of spontaneous circulation [ROSC], hospital admission), provision of bystander CPR; important—initial shockable rhythm, time to CPR
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and all languages included with the last search, performed July 1, 2018; ongoing or unpublished studies identified through a search of ClinicalTrials.gov online registry
- PROSPERO registration: CRD42018091427

Treatment Recommendations

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 dispatchers provide CPR instructions (when deemed necessary) for adult patients in cardiac arrest (strong recommendation, very-low-certainty evidence).[7,8]

DA-Assisted Compression-Only CPR Versus Conventional CPR (2017 CoSTR BLS 359: SysRev)

Emergency medical dispatchers typically are trained to provide telephone instructions for both compression-only CPR and conventional CPR with mouth-to-mouth ventilation. There is still some degree of controversy about whether it is sufficient for dispatchers to instruct callers to do only compression-only CPR for adult cardiac arrests or whether it is feasible to teach untrained lay rescuers over the phone how to perform mouth-to-mouth ventilation. This topic has been included in a SysRev and meta-analysis.[63] The task force CoSTR as well as values and preferences can be found in the *2017 International Consensus on CPR and ECC Science With Treatment Recommendations Summary*.[5,6] These note that the treatment recommendations prioritized the effective treatment for the most common causes of cardiac arrest (ie, cardiac causes). There remains uncertainty about the optimal approach when the cardiac arrest is caused by noncardiac causes, especially hypoxia.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with OHCA
- Intervention: Dispatcher-assisted compression-only CPR
- Comparator: Dispatcher-assisted standard CPR

- Outcome: The primary outcome was favorable neurological outcomes, measured by cerebral performance or a modified Rankin scale. Secondary outcomes were survival, ROSC, and quality of life.
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Study designs without a comparator group (ie, case series, cross-sectional studies), reviews, and pooled analyses were excluded.
- Time frame: Published studies in English were searched on January 15, 2016.
- PROSPERO registration: CRD42016047811

Treatment Recommendation

We recommend that dispatchers provide chest compression–only CPR instructions to callers for adults with suspected OHCA (strong recommendation, low-certainty evidence).[5,6]

COMPRESSION-ONLY CPR

One of the primary measures taken to improve survival after cardiac arrest is a focused effort to improve the quality of CPR. Although the impact of high-quality chest compressions has been studied extensively,[64–69] the role of ventilation and oxygenation in the initial management of cardiac arrest is less clear. Shortly after the publication of the *2015 International Consensus on CPR and ECC Science With Treatment Recommendations*,[3,4] a 23 711-patient RCT was published evaluating the effectiveness of continuous chest compressions (during which breaths were given without pausing chest compressions) in the EMS setting.[70] In parallel, developments of large national and regional registries are continually providing new insights into the epidemiology of cardiac arrest and effects of bystander CPR on outcomes.[71] These emerging publications generated an urgent need to review all available evidence on continuous compression strategies to provide an updated evidence evaluation that includes the latest science available. This topic has been included in a 2017 SysRev and meta-analysis.[63] The BLS Task Force CoSTR and its values and preferences can be found in the 2017 CoSTR summary.[5,6]

Lay Rescuer Chest Compression–Only Versus Standard CPR (2017 CoSTR BLS 547: SysRev)

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with OHCA
- Intervention: Lay rescuer compression-only CPR
- Comparator: Lay rescuer standard CPR
- Outcome: The primary outcome was favorable neurological outcomes, measured by cerebral performance or a modified Rankin scale. Secondary outcomes were survival, ROSC, and quality of life.
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Study designs without a comparator group (ie, case series, cross-sectional studies), reviews, and pooled analyses were excluded.
- Time frame: Published studies in English were searched on January 15, 2016.
- PROSPERO registration: CRD42016047811

Treatment Recommendations

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 adult patients in cardiac arrest (weak recommendation, very-low-certainty evidence).[5,6]

EMS Chest Compression–Only Compared With Conventional CPR (2017 CoSTR BLS 360: SysRev)

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with OHCA treated by EMS
- Intervention: Compression-only CPR or minimally interrupted CPR (protocol for resuscitation based on commencing an initial 200 uninterrupted chest compressions and passive oxygen insufflation).
- Comparator: Standard CPR
- Outcome: The primary outcome was favorable neurological outcomes, measured by cerebral performance or a modified Rankin scale. Secondary outcomes were survival, ROSC, and quality of life.
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Study designs without a comparator group (ie, case series, cross-sectional studies), reviews, and pooled analyses were excluded.
- Time frame: Published studies in English were searched on January 15, 2016.
- PROSPERO registration: CRD42016047811

Treatment Recommendations

We recommend that EMS providers perform CPR with 30 compressions to 2 breaths (30:2 ratio) or continuous chest compressions with positive pressure ventilation delivered without pausing chest compressions until a tracheal tube or supraglottic device has been placed (strong recommendation, high-certainty evidence).

We suggest that, when EMS systems have adopted minimally interrupted cardiac resuscitation, this strategy

is a reasonable alternative to conventional CPR for witnessed shockable OHCA (weak recommendation, very-low-certainty evidence).[5,6]

In-Hospital Chest Compression–Only CPR Versus Conventional CPR (2017 CoSTR BLS 372: SysRev)

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with in-hospital cardiac arrest (IHCA)
- Intervention: Compression-only CPR
- Comparator: Standard CPR
- Outcome: The primary outcome was favorable neurological outcomes, measured by cerebral performance or a modified Rankin scale. Secondary outcomes were survival, ROSC, and quality of life.
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Study designs without a comparator group (ie, case series, cross-sectional studies), reviews, and pooled analyses were excluded.
- Time frame: Published studies in English were searched on January 15, 2016.
- PROSPERO registration: CRD42016047811

Treatment Recommendation

Whenever tracheal intubation or a supraglottic airway is achieved during in-hospital CPR, we suggest that providers perform continuous compressions with positive pressure ventilation delivered without pausing chest compressions (weak recommendation, very-low-certainty evidence).[5,6]

Rescuer Fatigue in Chest Compression–Only CPR (BLS 349: ScopRev)

Rationale for Review

This topic was not a part of the 2017 SysRev[63] and CoSTR summary on continuous compressions versus standard CPR.[5,6] It was prioritized by the BLS Task Force for an updated evidence review, because this topic had not been reviewed by ILCOR since 2005.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Rescuers performing CPR
- Intervention: Compression-only CPR
- Comparator: Standard CPR
- Outcome: Rescuer fatigue, CPR quality parameters (compression rate, compression depth, compression pauses, leaning or incomplete release, etc)
- Study design: RCTs, interrupted time series, controlled before-and-after studies, cohort studies, and manikin studies were eligible for inclusion.
- Time frame: All years and all languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to October 29, 2019.

Summary of Evidence

This ScopRev is included in Supplement Appendix B-1. Fifteen manikin studies evaluating fatigue at various compression-to-ventilation ratios were identified. These studies compared fatigue and its effects on CPR quality in volunteers performing continuous compressions and 30:2 or 15:2 CPR.[72–86] Evidence from these manikin studies comparing fatigue and effects on CPR quality suggest that continuous compressions are effective in the first 2 minutes with regard to depth and frequency, and there are indications that short periods of rest (pauses in compression) reduce rescuer fatigue and increase CPR quality.

Task Force Insights

Continuous compression strategies increasingly have been advocated in an effort to increase overall bystander CPR rates. Evidence reviews evaluating the effect of continuous chest compressions versus standard CPR on critical outcomes, such as long-term survival, have been performed by the BLS Task Force in a separate published CoSTR.[5,6]

Although the BLS Task Force regards rescuer fatigue as an important barrier to high-quality bystander CPR, a higher value is placed on patient-centered outcomes.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[3,4]

We suggest pausing chest compressions every 2 minutes to assess the cardiac rhythm (weak recommendation, low-certainty evidence).

In making this recommendation, we placed a high priority on consistency with previous recommendations and the absence of contradictory evidence to prompt a change. We placed value on simplifying resuscitation logistics by coordinating rhythm and pulse checks with standard recommendations for rotating the provider performing chest compressions every 2 minutes.

CPR SEQUENCE

Firm Surface for CPR (BLS 370: SysRev)

Rationale for Review

This topic was prioritized for review by the BLS Task Force because it had not been updated since 2010.[1,2] Members of the task force reported variation in backboard use and the practice of moving a patient from

Table 2. Firm Surface for CPR

Group	Certainty	Studies	No. of Participants	Results
Mattress type	Low (serious indirectnesss)	Four manikin RCTs*[87–90]	33	No study identified a difference in chest compression depth between mattress types
Floor compared with bed	Low (serious indirectness)	Two manikin RCTs (meta-analyzed)[88,91]	64	No effect on chest compression depth: mean difference 4.29 mm (95% CI, –0.70 to 9.27)
		Two manikin RCTs*[89,92]	34	Neither study identified a difference in chest compression depth between groups
Backboard use	Low (serious indirectness)	Six manikin RCTs (meta-analyzed)[90,93–97]	221	Improved chest compression depth: mean difference 2.74 mm (95% CI, 1.19 to 4.28)
		One manikin RCT*[98]	24	No difference in chest compression depth between groups

*Heterogeneity precluded meta-analysis
CPR indicates cardiopulmonary resuscitation; and RCT, randomized controlled trial.

the bed to the floor to improve the quality of CPR, so it was considered timely to review the published evidence.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults or children in cardiac arrest (OHCA and IHCA) on a bed
- Intervention: CPR on a hard surface (eg, backboard, floor, deflatable or specialist mattress)
- Comparator: CPR on a regular mattress
- Outcome: Survival, survival with a favorable neurologic outcome, ROSC, CPR quality
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Randomized manikin/simulation/cadaver studies were only included if insufficient human studies were identified. Unpublished studies (eg, conference abstracts, trial protocols), nonrandomized manikin/simulation/cadaver studies, animal studies, experimental/laboratory models, mathematical models, narrative reviews, and editorials and opinions with no primary data were excluded.
- Time frame: January 1, 2009, to September 16, 2019
- PROSPERO registration: CRD42019154791

Consensus on Science

The identified science has been grouped under the following subheadings: mattress type, floor compared with bed, and backboard in Table 2.

Treatment Recommendations

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.

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-2.

The context for this question was that, when manual chest compressions are performed on a mattress, the compression force is dissipated through both chest compression and compression of the mattress under the patient. Manikin models indicate that the amount of mattress compression ranges from 12% to 57% of total compression depth, with softer mattresses compressed the most.[87,90,99,100] This mattress compression can lead to reduced spinal-sternal displacement and a reduction in effective chest compression depth.

Effective compression depths can be achieved even on a soft surface, providing the CPR provider increases overall compression depth to compensate for mattress compression.[90,97,101–105] CPR feedback devices that account for mattress compression (eg, the use of dual accelerometers or increasing compression depth targets) can help CPR providers ensure adequate compression depth when CPR is performed on a mattress.[95,99,101,103,105,106]

In making these recommendations, the task force highlights the importance of high-quality chest compressions for optimizing outcomes from cardiac arrest.

The task force noted that there were no clinical studies reporting on the critical outcomes of survival and favorable neurological outcome or important outcome of chest compression quality.

The weak recommendations are based on extrapolation from manikin studies, typically undertaken on a mattress placed on a hospital bed, for which manual CPR was performed by a trained healthcare professional. The hospital beds involved in the studies typically had rigid bases. The task force noted that, although this configuration is common in hospitals in many developed countries, it may not be applicable to all hospitals

or the out-of-hospital setting. The absence of studies simulating out-of-hospital settings (where beds may be softer) and in which the CPR provider may be a single untrained rescuer led the task force to focus recommendations on the in-hospital setting.

The task force supported performing manual chest compressions on a firm surface when possible because this reduces the risks of shallow compressions attributable to performing CPR on a soft surface. On the other hand, moving a patient onto a hard surface can be a major barrier to CPR, and the importance of performing CPR on a firm surface needs to be weighed against the likelihood of significant delay in providing CPR. In the setting of DA-CPR, in particular, logistical aspects of moving patients from bed to floor can impede if not thwart the performance of CPR.

The task force considered that, when a mattress with CPR function was available, activating a CPR function on a mattress, although unlikely to substantially improve compression depth, posed a low risk of harm to rescuers and patients, leading to a weak recommendation of support.

In considering whether to transfer a patient from a hospital bed to the floor to improve compression depth, the task force considered that the risks of harm (eg, interruption in CPR, risk of losing vascular access for intravenous drug delivery, and more confined space) to the patient and resuscitation team outweighed any small improvement in chest compression depth, leading to a weak recommendation against routine use of this practice.

The task force was unable to make a recommendation for the use of a CPR backboard during IHCA. Within the limitations of manikin studies, the available evidence indicates a marginal benefit to chest compression depth from use of a backboard. For example, placing a firm surface (eg, a backboard) between the patient and a soft surface may merely transfer the same force from CPR to the underlying softness and not obviate potential concern over chest compression depth. No studies specifically evaluated backboard deployment or any impact this has on interruptions to chest compressions and/or displacement of tubes and catheters during insertion. For healthcare systems that have already incorporated backboards into routine use during IHCA, the evidence was considered insufficient to suggest against their continued use. For healthcare systems that have not introduced backboards, the limited improvement in compression depth and uncertainty about harms seemed insufficient to justify the costs of purchasing backboards and training staff in their use. When backboards are deployed, users should be aware that mattress stiffness, backboard size (larger is better), and orientation (longitudinal is better) influence their effectiveness.[107–111]

Knowledge Gaps

Current knowledge gaps include but are not limited to the following:

- Studies reporting clinical outcomes
- Studies examining the logistical aspects of backboard deployment or moving a patient from a bed to the floor
- Studies relevant to OHCA
- Studies in both high- and low-resource settings, in which hospital bed or prehospital stretcher configurations may vary

Starting CPR (C-A-B Compared With A-B-C) (BLS 661: SysRev)

Although, internationally, most adult BLS guidelines recommend commencing chest compressions before rescue breaths, debate about this sequence continues. In addition, there is variability in the sequences used for pediatric resuscitation and for aquatic rescue, with different approaches in various jurisdictions.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with OHCA
- Intervention: Commencing CPR beginning with compressions first (30:2)
- Comparator: CPR beginning with ventilation first (2:30)
- Outcome: Survival with favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; and ROSC
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion.
- Exclusion criteria: Unpublished studies (eg, conference abstracts, trial protocols) and animal studies were excluded. Studies of dispatcher- or telephone-assisted CPR were excluded.
- Time frame: All languages were included as long as there was an English abstract. The literature search was updated in September 2019.

Consensus on Science

This current SysRev did not identify any additional human or manikin studies published since the 2015 CoSTR SysRev.[3,4] The published evidence remains limited to 4 manikin studies: 1 randomized study[112] focused on adult resuscitation, 1 randomized study focused on pediatric resuscitation,[113] and 2 observational studies focused on adult resuscitation.[114,115] The results from these studies are summarized in Table 3.

The overall certainty of evidence was rated as very low for all outcomes primarily because of a very serious risk of bias and indirectness. The individual observational studies were all at a critical risk of bias because of confounding, and the RCTs were all at critical risk of bias

Table 3. Starting CPR

Outcome	Certainty	Studies	No. of Patients	Results
Time to commencement of chest compressions	Very low	1 RCT (manikin): Lubrano 2012[113]	155 two-person teams	Statistically significant 24-s difference (P<0.05) in favor of C-A-B
		2 observational (manikin): Kobayashi 2008,[114] Sekiguchi 2013[115]	40 individual rescuers[115] and 33 six-person teams[114]	The observational studies found statistically significant decreases of 20 s (P<0.001)[115] and 26 s (P<0.001)[114] in favor of C-A-B.
Time to commencement of rescue breaths	Very low	2 RCTs (manikin): Marsch 2013,[112] Lubrano 2012[113]	210 two-person teams	In a respiratory arrest scenario, there was a 4-second difference (P<0.05) in favor of C-A-B[113]; in a cardiac arrest scenario, A-B-C decreased the time to commencement of rescue breaths by 6 s (P<0.05), and C-A-B decreased time to commencement of rescue breaths by 5 s (P<0.05).[112]
Time to completion of first CPR cycle (30 chest compressions and 2 rescue breaths)	Very low	1 RCT (manikin): Marsch 2013[112]	55 two-person teams	C-A-B decreased time to completion of first CPR cycle by 15 s (P<0.001).

A-B-C indicates airway-breathing-compression; C-A-B, compression-airway-breathing; CPR, cardiopulmonary resuscitation; and RCT, randomized controlled trial.

because of lack of blinding. Because of this and a high degree of heterogeneity, no meta-analyses could be performed. Individual studies are difficult to interpret.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[3,4]

We suggest commencing CPR with compressions rather than ventilation in adults with cardiac arrest (weak recommendation, very-low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-3. No change was made to this adult treatment recommendation. For all outcomes, starting CPR with compressions resulted in faster times to key elements of resuscitation (rescue breaths, chest compressions, completion of first CPR cycle) across the 4 papers reviewed, with the exception of simulated pediatric resuscitation, for which starting with compressions delayed time to commencement of rescue breaths in cardiac arrest by 6 seconds. This difference was statistically significant but reflects a delay that is not considered clinically significant.[113] This delay in commencing rescue breaths may be acceptable given the decreased time to other elements of resuscitation; however, the certainty of the evidence is very low, and all studies reviewed were manikin studies. There is no clinical evidence to guide whether to initiate compressions before ventilation in adult cardiac arrest. There should also be consideration given to the impact of simplification of training requirements by using a single approach compared with separate approaches for adults and children.

Knowledge Gaps

- No human studies evaluating this question in any setting were identified.
- Important uncertainties regarding timing and delays in initiation of the CPR components (chest compressions, opening airway, and rescue breaths) remain and may not be readily extrapolated from manikin studies.

CPR Before Call for Help (BLS 1527: SysRev)

This question was suggested by the resuscitation community during the public commentary process. The question of the optimal sequence for calling for help and starting CPR frequently arises during CPR training courses, and a SysRev of the literature to guide recommendations was therefore prioritized by the BLS Task Force. Searching for new science from the era of increased availability of communication devices and hands-free alternatives for lone rescuers was also considered important in this evidence review.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with OHCA
- Intervention: CPR before call for help; immediate CPR by a lone bystander performed for a short time interval (ie, 1 minute) before alerting EMS dispatch center with a mobile phone
- Comparator: An immediate call for help to the EMS dispatch center by a lone bystander with a mobile phone
- Outcome: Survival with favorable neurological outcome until and beyond hospital discharge or 30 days; survival until and beyond hospital discharge or 30 days; ROSC
- Study design: We included RCTs, nonrandomized studies, and case series with at least 5 cases. We considered papers in all languages provided there was an English language abstract available for review. We excluded unpublished studies, conference abstracts, manikin or simulation studies, narrative reviews, editorials or opinions with no primary data, animal studies and experimental/laboratory models.
- Time frame: All years and all languages were included as long as there was an English abstract;

unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to October 2019.

Consensus on Science

For the critical outcome of survival with favorable neurological outcome, we identified only a single observational study.[116] The overall certainty of evidence was rated as very low because of a very serious risk of bias. With the identification of only 1 study, no meta-analyses were performed.

For the critical outcome of survival with favorable neurological outcome, we identified very-low-certainty evidence (downgraded for very serious risk of bias) from 1 cohort study including 17 461 OHCA occurrences from Japan (2005–2012), which showed no benefit from a "CPR-first" strategy (cohort of 5 446 OHCA patients) compared with a "call-first" strategy (cohort of 1 820 OHCA patients).[116]

Adjusted analyses were performed on various subgroups and suggested significant improvements in survival with a favorable neurological outcome with a "CPR-first" strategy compared with a "call-first" strategy for noncardiac etiology OHCA (adjusted odds ratio [AOR], 2.01; 95% CI, 1.39–2.98); under 65 years of age (AOR, 1.38; 95% CI, 1.09–1.76); under 20 years of age (AOR, 3.74; 95% CI, 1.46–9.61); and both under 65 years of age and noncardiac etiology together (AOR, 4.31; 95% CI, 2.38–8.48).[116]

Treatment Recommendation

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).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-4. This SysRev was based on a new PICOST question suggested during public commenting and, therefore, includes a new treatment recommendation. The included paper analyzed only 17 461 OHCA occurrences from 925 288 recorded in the Japan national registry in the period from 2005 to 2012. Analysis was limited to cases in which lay rescuers witnessed the OHCA and spontaneously performed CPR (without the need for dispatcher assistance), and the groups compared were different with respect to age, gender, initial rhythm, bystander CPR characteristics, and EMS intervals. Although some factors were adjusted for in subgroup analyses, there is significant risk of confounding. Despite very-low-certainty evidence, there was consensus among the BLS Task Force to make a strong recommendation.

There were many exclusion criteria: unwitnessed, prehospital involvement of physician or unknown, EMS-witnessed OHCA, bystander-witnessed cases with missing data on time to intervention, no bystander CPR, DA-CPR, no intervention in 0 to 1 minutes, no CPR at all within 4 minutes, and etiology (cardiac or noncardiac) unknown.

There were some benefits noted in subgroup analyses, but these groups were not specified a priori. We cannot expect a bystander to reliably determine whether a cardiac arrest is of cardiac or noncardiac etiology. The results are not generalizable to all OHCAs because they refer specifically to bystander-witnessed cases in which the bystander spontaneously initiates CPR after only a short delay.

The timings of interventions were determined after the event by EMS personnel who interviewed the bystanders. These timings may be imprecise or inaccurate in an undetermined number of cases.

The wide availability of mobile phones may reduce the likelihood that a lone bystander would have to leave a victim to phone EMS. Pragmatically, it is now often possible to perform both actions simultaneously, and the focus should be on empowering people to recognize OHCA and initiate both an EMS call and CPR as soon as possible. In the absence of any evidence to the contrary, this would apply to both witnessed and unwitnessed OHCA, except in circumstances when there are appropriate reasons not to start CPR. When more than 1 bystander is at the scene, calling EMS and initiating CPR can be performed simultaneously. For the single rescuer, a call-first strategy ensures that EMS providers are dispatched as soon as possible, bringing additional assets (including a defibrillator) that might otherwise be delayed by a later call. Telecommunicator prompting may promote the initiation of bystander CPR that might not otherwise occur or may support better quality CPR (eg, instructing the caller to press hard and count aloud, helping to pace the compression rate).

In the situation when a lone rescuer would have to leave a victim alone to dial EMS, the priority is prompt activation of EMS before subsequently returning to the victim to initiate CPR as soon as possible.

Knowledge Gaps

There is no evidence comparing an immediate call to EMS for help with a call after 1 minute of CPR in the specific circumstance of a lone bystander with a mobile phone. There is also no evidence about how long it takes to call EMS after a witnessed cardiac arrest. The delay between a witnessed arrest and a call to EMS may be substantial.

Duration of CPR Cycles (2 Minutes Versus Other) (BLS 346: SysRev)

Rationale for Review

The recommendations for CPR cycle duration have changed with time, but these changes have never

Table 4. 1-Minute CPR Duration Compared With 3-Minute Duration for Postshock VF/pVT

Outcome	Certainty	Studies	No. of Patients	Results
Hospital discharge with favorable neurological outcome	Low (risk of bias, imprecision)	RCT: Wik 2003[117]	200	No difference: Relative risk 1.68 (95% CI, 0.85–3.32), 78 more patients/1000 (–17 to 266)
Survival to hospital discharge	Low (risk of bias, imprecision)	RCT: Wik 2003[117]	200	No difference: Relative risk 1.52 (95% CI, 0.83–2.77), 76 more patients/1000 (–25 to 258)
ROSC	Low (risk of bias, imprecision)	RCT: Wik 2003[117]	200	No difference: Relative risk 1.22 (95% CI, 0.92–1.50), 101 more patients/1000 (–37 to 229)

CPR indicates cardiopulmonary resuscitation; RCT, randomized controlled trial; ROSC, return of spontaneous circulation; pVT, pulseless ventricular tachycardia; and VF, ventricular fibrillation.

Both relative and absolute risks are written as mean values (95% CIs).

been based on high-certainty evidence that any specific interval or CPR cycle duration was superior in terms of patient survival. Because the topic has not been reviewed since 2015,[3,4] when no direct evidence was identified, the following PICOST question was prioritized for evidence review.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with cardiac arrest
- Intervention: Pausing chest compressions at another interval
- Comparator: Pausing chest compressions every 2 minutes to assess the cardiac rhythm
- 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.
- Time frame: All years and all languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to September 2019.

Consensus on Science

Data were derived from 2 RCTs[117,118] for which the principal focus was on the period of time allotted for CPR *before* the first rhythm analysis. Assessment of the duration (in minutes) of uninterrupted CPR between subsequent rhythm checks and outcome were not formally reported analyses in either study. The published data in these 2 studies enabled an ad hoc analysis by ILCOR evidence evaluation experts that indirectly addressed this question. Outcomes were not adjusted for possible confounders.

1-Minute CPR Duration Compared With 3-Minute Duration for Postshock Ventricular Fibrillation (VF)/Pulseless Ventricular Tachycardia (pVT)

In the 2003 study including 1-minute and 3-minute durations of uninterrupted CPR between rhythm checks,[117] the control group included patients who received immediate defibrillation (up to 3 stacked shocks) for VF/VT followed by 1 minute of CPR for patients in refractory VF/VT at the next rhythm check and 3 minutes of CPR for those patients who exhibited nonshockable rhythms after 1 to 3 shocks. The intervention group included patients who received 3 minutes of CPR before the first defibrillation attempt (up to 3 stacked shocks) for VF/VT followed by CPR for 3 minutes regardless of postshock rhythm. Of note, none of the patients received 2-minute periods of CPR. This RCT showed no benefit from the intervention compared with the control CPR duration between rhythms checks for all of the outcomes listed (Table 4).

1-Minute CPR Duration Compared With 2-Minute CPR Duration

In the 1 study that included 1-minute and 2-minute durations of uninterrupted CPR between rhythm checks,[118] the 2-minute group included patients who were enrolled in the RCT after implementation of new guidelines introducing single shocks, 30:2 CPR, and

Table 5. 1-Minute CPR Duration Compared With 2-Minute CPR Duration

Outcome	Certainty	Studies	No. of Patients	Results
Survival to hospital discharge	Very low (serious risk of bias, indirectness, imprecision)	RCT: Baker 2008[118]	202	No difference: Relative risk 0.49 (95% CI, 0.23–1.06), 92 fewer patients/1000 (–139 to 11)
ROSC	Very low (serious risk of bias, indirectness, imprecision)	RCT: Baker 2008[118]	202	No difference: Relative risk 0.95 (95% CI, 0.73–1.24), 27 fewer patients/1000 (–144 to 128)

CPR indicates cardiopulmonary resuscitation; RCT, randomized controlled trial; and ROSC, return of spontaneous circulation.

Both relative and absolute risks are written as mean values (95% CIs).

2-minute CPR cycles between rhythm checks. The 1-minute group included patients who were enrolled in the RCT before implementation of new guidelines and were therefore treated with stacked shocks (up to 3 in refractory VF/VT), 15:2 CPR, and 1-minute CPR cycles between rhythm checks. No clear benefit from either the 1- or 2-minute duration between rhythm checks was observed (Table 5).

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[3,4]

We suggest pausing chest compressions every 2 minutes to assess the cardiac rhythm (weak recommendation, low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-5. No change was made to this treatment recommendation. This topic was prioritized for review by the BLS Task Force because it had not been updated since the 2015 CoSTR. Although the current review identified 2 older studies that included comparisons of groups with different CPR durations between rhythm checks, each had significant limitations. Both studies were designed to address the question of CPR first compared with defibrillation first. As a result, the certainty of evidence derived from these studies is low, and recommendations regarding optimal duration of CPR before a scheduled rhythm analysis are seriously confounded.

In making the suggestion to pause chest compressions every 2 minutes to assess cardiac rhythm, we placed a high value on being consistent with previous recommendations, and noting the only limited indirect evidence identified in this review. The BLS Task Force acknowledges that every change in guidelines comes with a significant risk and cost as CPR educators and providers are asked to change current practice and implement new treatment strategies for complex and high-stress medical emergencies.

Knowledge Gaps

- Does the optimal CPR duration (ie, interval between rhythm analyses) differ for patients with different initial or postshock cardiac rhythms?
- Does the duration between collapse and EMS arrival affect the optimal CPR duration/interval between rhythm checks?
- Do different intervals between rhythm checks interfere with the overriding goal of minimizing interruptions in chest compressions?
- What is the relationship between rescuer fatigue, chest compression quality, and the optimal CPR duration/interval between rhythm checks?

Check for Circulation During BLS (BLS 348: EvUp)

An EvUp (see Supplement Appendix C-1) identified no evidence to justify a SysRev or a change in the 2015 treatment recommendation.[3,4]

Future reviews could focus on combination/alternative techniques used to confirm presence of circulation: plethysmography, arterial pressure monitoring, end-tidal carbon dioxide ($ETCO_2$), near infrared spectroscopy, ultrasound, and more.

Treatment Recommendation

Outside of the ALS environment, where invasive monitoring is available, there are insufficient data about the value of a pulse check while performing CPR. We therefore do not make a treatment recommendation regarding the value of a pulse check.[3,4]

COMPONENTS OF HIGH-QUALITY CPR

Hand Position During Compressions (BLS 357: SysRev)

Rationale for Review

The recommendations for hand position during compressions have changed with time, but these changes have been based on only low- or very-low-certainty evidence, with no data demonstrating that a specific hand position was optimal in terms of patient survival. The topic has not been reviewed since 2015,[3,4] when no direct evidence was identified, so the following PICOST question was prioritized for evidence review.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with cardiac arrest
- Intervention: Delivery of chest compressions on the lower half of the sternum
- Comparator: Any other location for chest compressions
- Outcome: Any clinical 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. Physiological outcomes, such as blood pressure, coronary perfusion pressure, or $ETCO_2$, also were considered important.
- 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: SysRev search strategy: All years and all languages were included as long as there was an English abstract.

Consensus on Science

There were no studies reporting the critical outcomes of favorable neurological outcome, survival, or the important outcome of ROSC. For the important outcome of physiological end points, we identified 3 very-low-certainty studies (downgraded for bias, indirectness, and imprecision).[119–121] One crossover study in 17 adults with prolonged resuscitation from nontraumatic cardiac arrest observed improved peak arterial pressure during compression systole (114±51 mm Hg compared with 95±42 mm Hg) and $ETCO_2$ (11.0±6.7 mm Hg compared with 9.6±6.9 mm Hg) when compressions were performed over the lower third of the sternum compared with the center of the chest, but arterial pressure during compression recoil, peak right atrial pressure, and coronary perfusion pressure did not differ.[120] A second crossover study in 30 adults with cardiac arrest observed no difference in $ETCO_2$ values resulting from changes in hand placement.[121] A third crossover study in 10 children observed higher peak systolic pressure and higher mean arterial pressure when compressions were performed on the lower third of the sternum compared with the middle of the sternum.[119]

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[3,4]

We suggest performing chest compressions on the lower half of the sternum on adults in cardiac arrest (weak recommendation, very-low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-6. In making this recommendation, we placed high value on consistency with current treatment recommendations in the absence of compelling clinical data suggesting the need to change the recommended hand placement for performing chest compressions.

Knowledge Gaps

- We did not identify any studies that evaluated the effect of any specific hand position on short- or long-term survival after cardiac arrest; only physiological surrogate outcomes have been reported.
- Imaging studies suggest that there might be important differences in anatomy depending on age, gender, body mass index, presence or absence of chronic heart conditions, and more.
- Important gaps remain in evaluating how to identify optimal hand placement and/or compression point when using physiological feedback during CPR.

Chest Compression Rate, Chest Compression Depth, and Chest Wall Recoil (BLS 366, BLS 367, BLS 343: ScopRev)

Rationale for Review

The BLS Task Force requested a ScopRev related to chest compression rate, chest compression depth, and chest wall recoil to identify any recent published evidence that provided more information on these chest compression components as discrete entities and to assess whether studies have reported interactions among these chest compression components. Therefore, a ScopRev was undertaken to understand whether the science to date has focused on single chest compression components or interactions among chest compression components and identify the evidence related to the chest compression components to determine whether the body of evidence published since the 2015 CoSTR for BLS[3,4] indicates the need for a full SysRev of the evidence related to chest compression components.[122]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with cardiac arrest
- Intervention/Comparator: (1) ≥2 chest compression depths measured in millimeters, centimeters, or inches or (2) ≥2 chest compression rates measured in compressions per minute or (3) ≥2 measures of chest wall recoil or (4) ≥2 measures of leaning or leaning compared with no leaning
- Outcome: Survival to hospital discharge with good neurological outcome and survival to hospital discharge were ranked as critical outcomes. ROSC or survival to a defined time point and physiological measures (eg, blood pressure and $ETCO_2$) were ranked as important outcomes.
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion.
- Time frame: All years and all languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to June 2019.

Summary of Evidence

In addition to the 14 studies identified in the 2015 CoSTR for BLS,[3,4] an additional 8 studies[123–129a] were identified, so a total of 22 studies were included in this ScopRev, which has been published in full.[122] Five observational studies examined both chest compression rate and chest compression depth.[127,128,129a,130,131] One RCT,[124] 1 crossover trial,[132] and 6 observational studies[125,129,133–136] examined chest compression rate only. One RCT[137] and 6 observational studies examined chest compression depth only,[67,138–142] and 2 observational studies examined

chest wall recoil.[123,126] No studies were identified that examined different measures of leaning. This ScopRev (see Supplement Appendix B-2) does highlight significant gaps in the research evidence related to chest compression components, namely a lack of high-level evidence, a paucity of studies of IHCA, and a failure to account for the possibility of interactions between chest compression components.

Task Force Insights

In the evidence identified in this ScopRev, most studies focused on a single chest compression component, whereas several studies suggested the presence of confounding interactions that prompt caution when evaluating any chest compression component in isolation. Most studies identified in this review focused on OHCA, highlighting a major gap in research involving IHCA.

This ScopRev did not identify sufficient new evidence that would justify conducting new SysRevs or reconsideration of current resuscitation guidelines.

Treatment Recommendation

These treatment recommendations (below) are unchanged from 2015.[3,4]

We recommend a manual chest compression rate of 100 to 120/min (strong recommendation, very-low-certainty evidence).

We recommend a chest compression depth of approximately 5 cm (2 in) (strong recommendation, low-certainty evidence) while avoiding excessive chest compression depths (greater than 6 cm [greater than 2.4 in] in an average adult) during manual CPR (weak recommendation, low-certainty evidence).

We suggest that rescuers performing manual CPR avoid leaning on the chest between compressions to allow full chest wall recoil (weak recommendation, very-low-certainty evidence).

Compression-to-Ventilation Ratio (2017 CoSTR BLS 362: SysRev)

Rationale for Review

The first ILCOR review to be performed after the 2015 CoSTR was a large SysRev[63] of compression strategies across different settings and populations. One of these comparisons addressed the optimal compression-to-ventilation ratio. Task force values and preferences can be found in the 2017 CoSTR summary.[5,6]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with OHCA
- Intervention: Any compression-to-ventilation ratio other than 30:2
- Comparator: Compression-to-ventilation ratio of 30:2
- Outcome: The primary outcome was favorable neurological outcomes, measured by cerebral performance or a modified Rankin scale. Secondary outcomes were survival, ROSC, and quality of life.
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Study designs without a comparator group (ie, case series, cross-sectional studies), reviews, and pooled analyses were excluded.
- Time frame: Published studies in English were searched on January 15, 2016.
- PROSPERO registration: CRD42016047811

Treatment Recommendation

We suggest a compression-to-ventilation ratio of 30:2 compared with any other ratio in patients with cardiac arrest (weak recommendation, very-low-quality evidence).[5,6]

Timing of Rhythm Check (BLS 345: SysRev)

Rationale for Review

Adverse outcomes after cardiac arrest have been associated with frequent or prolonged interruptions in chest compressions. Because rhythm checks during resuscitation are frequent causes of pauses in compressions, this SysRev was undertaken to assess the evidence available to identify the optimal timing for rhythm checks.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults with presumed cardiac arrest in in-hospital or out-of-hospital settings receiving a defibrillation attempt during CPR
- Intervention: Checking the cardiac rhythm immediately after defibrillation
- Comparator: Immediate resumption of chest compressions with delayed check of the cardiac rhythm
- Outcome: Critical—survival with good neurological function (ie, at hospital discharge, 1 month, 6 months, 1 year), survival (ie, hospital discharge, 1 month, 6 months, 1 year); important—short-term survival (ROSC, hospital admission), rates of recurrence of fibrillation/refibrillation, CPR quality parameters (ie, compression fraction).
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Animal/laboratory studies, mathematical models, simulation and manikin studies, algorithm studies for rhythm analysis recognition with no outcome data, unpublished studies (eg, conference abstracts, trial protocols), and reviews were excluded.

Table 6. Timing of Rhythm Check

Outcome	Certainty	Studies	No. of Patients	Results
Hospital discharge with favorable neurological outcome	Low (risk of bias, indirectness) Very low (risk of bias, indirectness, imprecision)	1 RCT[145] 3 observational[146–148]	415 763	No difference: Relative risk 0.90 (95% CI, 0.70–1.15), 40 fewer patients/1000 (–119 to 60) Lower survival in immediate rhythm check: Relative risk 0.62 (95% CI, 0.51–0.75), 174 fewer patients/1000 (–224 to –13)
Survival to hospital discharge	Low (serious risk of bias, indirectness) Very low (serious risk of bias, indirectness)	2 RCTs[143,145] 3 observational[146–148]	1 260 3 094	No difference: Relative risk 0.89 (95% CI, 0.72–1.10), 24 fewer patients/1000 (–63 to 23) Lower survival in immediate rhythm check: Relative risk 0.55 (95% CI, 0.45–0.67), 76 fewer patients/1000 (–93 to –56)
Survival to hospital admission	Low (serious risk of bias, indirectness)	2 RCTs[143,145]	1 260	No difference: Relative risk 1.02 (95% CI, 0.91–1.14), 9 more patients/1000 (–43 to 69)
ROSC	Very low (serious risk of bias, indirectness)	2 observational[147,148]	2 969	Lower survival in immediate rhythm check: Relative risk 0.69 (95% CI, 0.61–0.78), 111 fewer patients/1000 (–139 to –80)
VF recurrence	Very low (serious risk of bias, indirectness, imprecision)	2 RCTs[144,145]	551	No difference: Relative risk 1.08 (95% CI, 0.95–1.22), 47 more patients/1000 (–13 to 5)

RCT indicates randomized controlled trial; ROSC, return of spontaneous circulation; and VF, ventricular fibrillation.
Both relative and absolute risks are written as mean values (95% CIs).

- Time frame: All years and all languages were included provided there was an English abstract. The literature search was updated to November 2, 2019.

Consensus on Science

Three RCTs[143–145] and 3 observational studies[146–148] were identified comparing immediate rhythm checks to immediate resumption of chest compressions. Outcomes assessed varied from hospital discharge with favorable neurological outcome to recurrence of VF. The meta-analysis of the RCTs did not demonstrate any differences between immediate rhythm analysis and immediate compressions, but unadjusted analysis of observational data suggested that immediate compressions were associated with better outcomes (Table 6).

Treatment Recommendation

We suggest immediate resumption of chest compressions after shock delivery for adults in cardiac arrest in any setting (weak recommendation, very-low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-7. No change was made to this treatment recommendation. Although there is only very-low-certainty evidence addressing this question, worse short- and long-term outcomes have been reported with immediate rhythm checks after shock delivery. The effect of an immediate rhythm check on the incidence of VF recurrence is unclear. An observational study exploring this specific issue did not find that VF recurrence within 30 seconds of defibrillation (ie, successful shock) was linked to the timing of resumption of chest compressions,[149] and this may not be a major factor affecting outcomes. Protocols including immediate cardiac rhythm check after shock delivery are reported to have reduced chest compression fractions; these increased pauses could be a potential cause of worse outcomes.

Knowledge Gaps

- There were no studies that evaluated this question in the pediatric/in-hospital setting.
- No RCTs compared the specific intervention with standard care in any patient population, although 1 RCT assessed a CPR protocol characterized by different timing of rhythm checks, different compression-to-ventilation ratios, different duration of uninterrupted CPR between shocks, and different ventilation strategies.
- Currently available studies comparing different CPR protocols are characterized not only by different timing of rhythm checks but also by compression-to-ventilation ratios, compression intervals between shocks, and ventilation strategies that differ from standard care. More data are needed comparing groups receiving standard care with differences between control and intervention groups in only the timing of rhythm checks.

Feedback for CPR Quality (BLS 361: SysRev)

Rationale for Review

CPR feedback or prompt devices are intended to improve CPR quality, probability of ROSC, and survival from cardiac arrest. Feedback devices involve technology that can measure various aspects of CPR mechanics, including ventilation rate, chest compression

mechanics (eg, depth, rate, recoil), and measures of flow time (CPR fraction, pre- and postshock pauses). These data can be presented to the provider in real time and/or provided in a summary report at the end of a resuscitation. Real-time displays can involve voice prompts, visual dials, numeric displays, wave forms, verbal prompts, and visual alarms. Visual displays enable the rescuer to see compression-to-compression quality parameters, including compression depth and rate in real time. Audio prompts may guide CPR rate (eg, metronome) and may offer verbal prompts to rescuers (eg, "push harder," "good compressions"). Prompt devices that do not include the measurement and feedback of CPR quality metrics can include audible or visual metronomes set at the recommended rate for compressions or ventilation.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with cardiac arrest
- Intervention: Real-time feedback and prompt devices regarding the mechanics of CPR quality (eg, rate and depth of compressions and/or ventilations)
- Comparator: No feedback
- Outcome: Survival to hospital discharge with good neurological outcome and survival to hospital discharge were ranked as critical outcomes. ROSC, bystander CPR rates, time to first compressions, time to first shock, and CPR quality were ranked as important outcomes.
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Studies involving manikins only or the use of CPR quality data for delayed feedback (eg, debriefing or quality assurance programs) were excluded from this review.
- Time frame: All years and all languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to September 2019.

Consensus on Science

Three discrete forms of real-time CPR guidance devices were identified: (1) digital audiovisual feedback, including corrective audio prompts; (2) analogue audio and tactile "clicker" feedback for chest compression depth and release; and (3) metronome guidance for chest compression rate. The analogue "clicker" device, designed to be placed on the patient's chest under the hands of a CPR provider, involves a mechanism that produces a "click" noise and sensation when sufficient pressure is applied. Because there was considerable clinical heterogeneity across studies with respect to the type of devices used, the mechanism of CPR quality measurement, the mode of feedback, patient types, locations (eg, in-hospital and out-of-hospital), and baseline (control group) CPR quality, we did not conduct any meta-analyses (Tables 7, 8, and 9).

Treatment Recommendations

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 resuscitation systems (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).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-8. There was significant debate among task force members on whether to recommend for or against the use of these devices for real-time feedback on the basis of available data. On one side of the debate, the task force acknowledged that the bulk of higher-certainty data from key studies did not demonstrate a clinically or statistically significant association between real-time feedback and improved patient outcomes and that these devices require additional resources to purchase and implement. On the other side of the debate, we acknowledged several studies that demonstrated clinically important improvements in outcomes associated with the use of feedback devices. Most notable was the study by Goharani et al,[159] newly added to the evidence base considered in 2020, which was an RCT of 900 IHCA patients from Iran. This study demonstrated a +25.6% absolute increase in survival to hospital discharge with the use of an analogue "clicker" device that provided real-time feedback on compression depth and recoil (54% versus 28.4%; $P<0.001$). Task force members did interpret this study to be supportive of the use of feedback devices; however, they also felt that this study represented an outlier. Members felt that replication of this result would be necessary before the task force could make any supportive recommendation for the specific type of device used in the study by Goharani et al.[159]

The task force also considered data from several observational studies demonstrating improvements in favorable neurological outcome that were not statistically significant. In addition, the task force considered statistically significant improvements in various aspects of CPR quality, including CPR rate

Table 7. Real-Time Digital Audiovisual Feedback

Outcome	Studies	No. of Patients	Results
Survival with favorable neurological outcome	1 cluster RCT,[150] low-certainty evidence (downgraded for very serious risk of bias) 4 observational,[151–154] very-low-certainty evidence (downgraded for very serious risk of bias)	1586 1100	No difference: Relative risk 1.02; 95% CI, 0.76–1.36; *P*=0.9 Absolute risk 0.19% (95% CI, −3.18% to 2.82%), or 2 more patients/1000 survived with the intervention (95% CI, 24 fewer patients/1000 to 36 more patients/1000 survived with the intervention) Better outcome with feedback: Adjusted odds ratio 2.69 (95% CI, 1.04–6.94)[153] No difference: Adjusted relative risk 5.75%; 95% CI, −18.51% to 3.85%[152] Adjusted odds ratio 0.92; 95% CI, 0.37–2.30[151] 2/16 versus 0/16; *P*=0.14[154]
Survival to hospital discharge	1 cluster RCT,[150] low-certainty evidence (downgraded for very serious risk of bias) 6 observational: 5 in adults[131,151–153,155] and 1 in children,[156] very-low-certainty evidence (downgraded for very serious risk of bias)	1586 1592	No difference: Relative risk: 0.91 (95% CI, 0.69–1.19); *P*=0.5 Absolute risk: −1.16% (95% CI, −4.37% to 2.02%), or 9 fewer patients/1000 survived with the intervention (95% CI, 31 fewer patients/1000 to 19 more patients/1000 survived with the intervention) No difference: Adjusted odds ratio 0.90; 95% CI, 0.39–2.06; *P*=0.80),[151] Adjusted relative risk −0.91; 95% CI, −11.18 to 12.33),[152] Adjusted relative risk 5.23; 95% CI, −0.49 to 10.89),[153] Adjusted relative risk −0.18; 95% CI, −11.46 to 8.64),[155] Adjusted relative risk 1.37; 95% CI, −2.47 to 6.91),[131] 8 children (ages 1–7 y) with IHCA (1/4 versus 1/4)[156]
Survival to 30 days	1 observational,[157] very-low-certainty evidence (downgraded for serious risk of bias)	196	No difference: Adjusted relative risk −0.84; 95% CI, −13.88 to 14.82; *P*=0.9[157]
Survival to 24 h	1 cluster RCT,[150] low-certainty evidence (downgraded for very serious risk of bias) 2 observational,[152,154] very-low-certainty evidence (downgraded for very serious risk of bias)	1586 219	No difference: Relative risk 0.96 (95% CI, 0.82–1.13; *P*=0.6); ARR, −1.09% (95% CI, −3.35% to 5.50%), or 4 fewer patients/1000 survived with the intervention (95% CI, 18 fewer patients/1000 to 13 more patients/1000 survived with the intervention) No difference: 2/16 versus 0/16[154] Adjusted relative risk 13.13; 95% CI, −0.66 to 28.02[152]
ROSC	1 cluster RCT,[150] low-certainty evidence (downgraded for very serious risk of bias) 8 observational[152,154]: 7 in adults[131,151–155,158] and 1 in children,[156] very-low-certainty evidence (downgraded for very serious risk of bias)	1586 2263	No difference: Relative risk 1.01 (95% CI, 0.91–1.13; *P*=0.9); Adjusted relative risk−0.45% (95% CI, −5.33% to 4.43%), or 1 more patient/1000 survived with the intervention (95% CI, 9 fewer patients/1000 to 13 more patients/1000 survived with the intervention) No benefit 9/16 versus 10/16[154] Adjusted odds ratio 0.62; 95% CI, 0.31–1.22; *P*=0.17),[151] Adjusted relative risk −3.17; 95% CI, −10.73 to 4.35),[153] Adjusted relative risk −4.39; 95% CI, −3.35 to 12.06)[158] Adjusted relative risk 4.55; 95% CI, −11.59 to 19.90)[155] Adjusted relative risk 5.65; 95% CI, −2.89 to 15.09[131] Adjusted relative risk 1.11; 95% CI, −15.56 to 13.69; *P*=0.9,[131,151–155,158] 8 children (ages 1–7 y): 3/4 versus 1/4[156] Better outcome with feedback: Adjusted relative risk 17.55; 95% CI, 1.79–32.46)[152]
Chest compression rate	1 cluster RCT,[150] moderate-certainty evidence 6 observational: 5 in adults[131,151,153–155] and 1 in children,[156] very-low-certainty evidence (downgraded for very serious risk of bias)	1586 1441	Better CPR quality with feedback: Difference of −4.7/min (95% CI, −6.4 to −3.0/min) when feedback was used No difference: One observational study[155] Better CPR quality with feedback: 4 observational studies[131,151,153,154] showed lower compression rates in the group with CPR feedback The pediatric study[156] found a median difference of −10/min with feedback.
Compression depth	1 cluster RCT,[150] very-low-certainty evidence (downgraded for very serious risk of bias) 6 observational: 5 in adults[131,151,153–155] and 1 in children,[156] very-low-certainty evidence (downgraded for very serious risk of bias)	1586 1441	Better CPR quality with feedback: Significant +1.6 mm (95% CI, 0.5–2.7 mm) (cluster-adjusted) difference in chest compression depth with feedback. Better CPR quality with feedback: Three observational studies[131,153,154] showed deeper chest compressions in the groups with CPR feedback[131,153,154] No difference: One observational study[155]; the pediatric study[156] found no difference in median compression depth.

(*Continued*)

Table 7. Continued

Outcome	Studies	No. of Patients	Results
Chest compression fraction	1 cluster RCT,[150] moderate-certainty evidence 6 observational: 5 in adults[131,151,153–155] and 1 in children,[156] very-low-certainty evidence (downgraded for very serious risk of bias)	1586 1441	Better CPR quality with feedback: Difference of +2% (66% compared with 64%; *P*=0.016) Better CPR quality with feedback: 2 studies reported statistically significant increases in CPR fraction associated with feedback[151,155] No difference: 3 studies did not observe a statistically or clinically important difference.[131,153,154] The sample size of the pediatric study[156] was too small to enable inferential statistical analysis.
Ventilation rate	1 cluster RCT,[150] moderate-certainty evidence 3 observational,[131,153,155] very-low-certainty evidence (downgraded for very serious risk of bias)	1586 1001	No difference No difference

ARR indicates adjusted relative risk; CPR, cardiopulmonary resuscitation; RCT, randomized controlled trial; and ROSC, return of spontaneous circulation.

and CPR fraction, associated with the use of feedback devices.

The task force also felt that a permissive recommendation was appropriate because of the role that these devices play in CPR quality monitoring, benchmarking, and quality improvement programs by collecting data across patients treated by a system. These roles were not included in the scope of this PICOST; however, the task force was concerned that a recommendation against the use of these devices for real-time feedback would discourage use for other important activities. The task force also recognized that implementing and maintaining high-quality CPR in hospital and EMS systems would be difficult without the use of these devices to provide an objective method of CPR quality measurement in those systems.

In summary, the task force agreed that CPR feedback devices that measure aspects of CPR quality were reasonable to consider for healthcare systems, given the importance of high-quality CPR. Without any signal of patient harm in the data reviewed, we agreed that a weak recommendation in favor of their use in this manner was appropriate.

We also agreed that there was no consistent signal from the data reviewed indicating that the real-time feedback function of these devices has a significant effect on individual cardiac arrest patient outcomes, suggesting that the devices should not be implemented for this reason alone outside of a comprehensive quality assurance program.

Knowledge Gaps

Current knowledge gaps include but are not limited to the following:

- What is the effect of feedback devices on patient outcomes when used by lay people with AEDs?
- Is there an interaction between the effect of real-time feedback devices and the skill set of the provider (eg, in low-performing services with baseline CPR metrics) that are below recommended values?
- What are the most effective parameters to feedback to users (ie, measures of brain or other tissue perfusion, electrocardiographic characteristics, other physiological measurements)?
- What are the most effective modalities for feedback to be provided to users?

Table 8. Analogue Audio and Tactile "Clicker" Feedback

Outcome	Studies	No. of Patients	Results
Survival to hospital discharge	1 RCT,[159] very-low-certainty evidence (downgraded for serious risk of bias)	900	Better outcome with feedback: Relative risk 1.90 (95% CI, 1.60–2.25; *P*<0.001); Adjusted relative risk 25.56% (95% CI, 19.22%–31.60%), or 91 more patients/1000 survived with the intervention (95% CI, 61 more patients/1000 to 126 more patients/1000 survived with the intervention)
ROSC	2 RCTs,[159,160] very-low-certainty evidence (downgraded for serious risk of bias)	980	Better outcome with feedback: Relative risk 1.57 (95% CI, 1.38–1.78; *P*<0.001); Adjusted relative risk 24.22% (95% CI, 17.79%–30.36%), or 58 more patients/1000 survived with the intervention (95% CI, 38 more patients/1000 to 79 more patients/1000)[159] Relative risk 2.07 (95% CI, 1.20–3.29; *P*<0.001); Adjusted relative risk 37.50% (95% CI, 15.70%–54.68%), or 108 more patients/1000 survived with the intervention (95% CI, 20 more patients/1000 to 232 more patients/1000)[160]

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

Table 9. Metronome Rate Guidance

Outcome	Studies	No. of Patients	Results
Survival to 30 days	1 observational,[157] very-low-certainty evidence (downgraded for serious risk of bias)	196	No difference: Relative risk 1.66; 95% CI, −17.71 to 14.86; *P*=0.8[157]
Survival to 7 days	1 observational,[161] very-low-certainty evidence (downgraded for serious risk of bias)	30	No difference: 3/17 versus 2/13; *P*=ns[161]
ROSC	2 observational,[157,161] very-low-certainty evidence (downgraded for serious risk of bias)	226	No difference: Adjusted relative risk 4.97; 95% CI, −21.11 to 11.76; *P*=0.6[157] 7/13 versus 8/17; *P*=ns[161]

ROSC indicates return of spontaneous circulation.

ALTERNATIVE TECHNIQUES

Alternative Techniques (Cough CPR, Precordial Thump, Fist Pacing) (BLS 374: SysRev)

Rationale for Review

Reports of "cough CPR" circulate on social media, and this technique may be perceived by the public as an effective way of preventing cardiac arrest. Precordial thumping and fist pacing are techniques previously recommended to healthcare professionals. In this review, we update the available evidence for these alternative techniques.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with cardiac arrest
- Intervention: Cough CPR; precordial thump; fist pacing
- Comparator: Standard CPR
- Outcome: Survival with favorable neurological outcome until and beyond hospital discharge or 30 days; survival until and beyond hospital discharge or 30 days; ROSC
- Study design: We included RCTs, nonrandomized studies, and case series with at least 5 cases. We considered papers in all languages provided there was an English language abstract available for review. We excluded unpublished studies, conference abstracts, manikin or simulation studies, narrative reviews, editorials or opinions with no primary data, animal studies, and experimental/laboratory models.
- Time frame: All years and all languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to October 2019.
- PROSPERO registration: CRD42019152925

Consensus on Science

Cough CPR

For the critical outcome of survival to hospital discharge[162] and important outcome of restoration of cardiac output/circulation (at or shortly after the onset of a potentially nonperfusing rhythm in which the patient has not yet lost consciousness or cardiac output),[163–165] we identified only 4 observational studies. All studies were in adult patients only. The overall certainty of evidence was rated as very low for all outcomes as a result of very serious risk of bias. For this reason and because of a high degree of heterogeneity across studies, no meta-analyses could be performed, and individual studies were difficult to interpret. Additional information may be found in Table 10.

Precordial Thump

For the critical outcomes of survival to hospital discharge, we identified 5 observational studies.[162,166–169] Two of these studies, both out-of-hospital, directly compared precordial thump with standard CPR.[166,167] For the important outcome of ROSC, we identified 1 observational study.[170] For the important outcome of restoration of cardiac output/circulation, we identified 10 observational studies.[171–180] All studies were in adult

Table 10. Observational Studies of Cough CPR for Conscious Patients With No Comparator Group

Outcome	Certainty	Studies	No. of Patients	Results
Survival to hospital discharge	Very low (very serious risk of bias)	Caldwell 1985[162]	6 (in-hospital VT)	6/6 (100%), selective reporting of cases achieving outcome
ROSC	Very low (very serious risk of bias)	Marozsan 1990, Nieman 1980[164,165]; Petelenz 1998[163]	20 (in-hospital, 2 studies): n=6 VF, n=13 asystole, n=1 bradycardia; 66 (out-of-hospital, 1 study): rhythms unknown	In-hospital: 18/20 (90%), selective reporting of cases achieving outcome in 1 study (n=7)[165]; out-of-hospital: 66/66 (100%), selective reporting of cases achieving outcome[163]

CPR indicates cardiopulmonary resuscitation; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; and VT, ventricular tachycardia.

patients only. The overall certainty of evidence was rated as very low for all outcomes primarily because of very serious risk of bias. Because of this and a high degree of heterogeneity across the studies, no meta-analyses could be performed, and individual studies were difficult to interpret. Additional information may be found in Tables 11 and 12.

Fist Pacing

For the critical outcome of survival to hospital discharge,[181,182] the important outcome of ROSC,[183] and the important outcome of restoration of cardiac output/circulation,[184] we identified only 4 observational studies. One study included children (age range, 11–84 years).[181] The overall certainty of evidence was rated as very low for all outcomes, mainly because of very serious risk of bias. Because of this and a high degree of heterogeneity, no meta-analyses could be performed, and individual studies were difficult to interpret. Additional information may be found in Table 13.

Treatment Recommendations

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 the 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 the use of a precordial thump for cardiac arrest (strong recommendation, very-low-certainty evidence).

We recommend against fist pacing for cardiac arrest (strong recommendation, very-low-certainty evidence).

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

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-9. This topic was last reviewed in the *2010 International Consensus on CPR and ECC Science With Treatment Recommendations.*[1,2] Although treatment recommendations remain essentially unchanged, the BLS Task Force has tried to update the recommendations with the intention of clarifying the special circumstances when these alternative techniques might be appropriate.

The very-low-quality evidence identified precludes meaningful meta-analysis. Two studies (both on precordial thump) had a direct comparator group (standard CPR), and both had a very serious risk of bias. The others were limited case series or cohorts without comparator groups.

Cough CPR is described as a repeated deep breath followed by a cough every few seconds. There is no evidence for the effectiveness of cough CPR in established cardiac arrest (ie, in an unconscious, pulseless patient), nor is its initiation even feasible under such circumstances. Very-low-quality evidence from 1 study[163] addresses the use of cough CPR for prodromal symptoms of collapse in high-risk patients in whom the cardiac rhythm was not known and the likelihood of progressing to cardiac arrest was uncertain. Suggesting a benefit of cough CPR for the general population would require us to accept that an untrained patient could reliably identify a cardiac arrest rhythm in time to initiate coughing to maintain a cardiac output. This seems highly unlikely.

There are periodic stories (on social media, for example) instructing members of the public to perform cough CPR in case of imminent collapse, so it is important that we address this topic. We should be clear that we do not recommend cough CPR for OHCA. The risks are (1) that it delays effective treatment (early call for help, early CPR and defibrillation if the patient loses consciousness and stops breathing normally) and (2) that members of the public confusing "cardiac arrest" with "heart attack" delay seeking help when suffering chest pain or other symptoms indicating a possible ischemic cardiac event.

There is no evidence to contradict the 2010 CoSTR treatment recommendation[1,2] that providers can consider cough CPR in the exceptional circumstance of monitored, witnessed in IHCAs. The victim must remain conscious and be able to follow instructions for coughing. There is limited very-low-certainty evidence that this may be effective in all arrhythmias that can cause cardiac arrest, not limited to just VF and VT. This evidence is reported for adult patients only. There is some evidence that cough CPR increases aortic, left atrial, and

Table 11. Observational Studies of Precordial Thump With Comparator Group

Outcome	Certainty	Studies	No. of Patients	Results
Survival to hospital discharge	Very low (downgraded for very serious risk of bias)	Nehme 2013,[166] Pellis 2009[167]	797 (n=500 VF/VT, n=101 PEA, n=196 asystole)	No difference: 71% versus 70% (*P*=ns)[166] and 5.6% versus 6.4% (*P*=ns)[167]
ROSC	Very low (downgraded for very serious risk of bias)	Nehme 2013,[166] Pellis 2009[167]	797 (n=500 VF/VT, n=101 PEA, n=196 asystole)	No difference: 93% versus 90% (*P*=ns)[166] and 22% versus 20% (*P*=ns)[167]

ns indicates nonsignificant; PEA, pulseless electric activity; ROSC, return of spontaneous circulation; VT, ventricular tachycardia; and VF, ventricular fibrillation.

Table 12. Observational Studies of Precordial Thump With No Comparator Group

Outcome	Certainty	Studies	No. of Patients	Results
Survival to hospital discharge	Very low (very serious risk of bias)	Caldwell 1985,[162] Gertsch 1992,[168] Rajagopalan 1971[169]; Caldwell 1985[162]	35 (in-hospital, 3 studies): n=29 VT, n=2 VF, n=2 asystole, n=2 unknown; 3 (out-of-hospital, 1 study): n=1 VT, n=2 VF	In-hospital: 20/35 (57%); 2/2 (100%) VF, 14/29 (48%) VT, 2/2 (100%) asystole, 2/2 (100%) unknown; out-of-hospital: 2/3 (67%)
ROSC	Very low (very serious risk of bias)	Miller 1984,[170] Rahner 1978,[171] Cotoi 1980,[172] Pennington 1970,[173] Morgera 1979,[174] Haman 2009,[175] Amir 2007,[176] Befeler 1978,[177] Miller 1985,[178] Nejima 1991,[179] Volkmann 1990[180]	50 (out-of-hospital): n=27 VT, n=23 VF; 366 (in-hospital): n=320 VT, n=38 VF, n=8 Morgagni-Adams-Stokes attack	Out-of-hospital: 23/50 (46%); 11/27 (41%) VT, 12/23 (52%) VF; 88/366 (24%); in-hospital: 80/320 (25%) VT, 8/8 (100%) Morgagni-Adams-Stokes, 0/38 (0%) VF; selective reporting of cases achieving outcome in 3 studies (n=39: n=31 VT, n=8 Morgagni-Adams-Stokes[171–173]

ROSC, return of spontaneous circulation; VF, ventricular fibrillation; and VT, ventricular tachycardia.

left ventricular pressures, but a causative link between cough CPR and termination of malignant arrhythmias is lacking. It would not be appropriate to prioritize cough CPR instead of other measures with proven efficacy, but clinicians may consider it as a temporary measure if there is a delay to defibrillation.

A precordial thump is described as a sharp, high-velocity blow to the middle of the sternum with immediate retraction by the ulnar aspect of the fist. We weighed the potential benefit of precordial thumps against the potential for harm. A precordial thump can potentially interrupt life-threatening VT by generating an electric impulse, resulting in a premature ventricular depolarization. However, there is a risk of deterioration of cardiac rhythm (from VT to VF, akin to an "R on T" phenomenon), reported in some studies,[170,171] and a risk of delaying CPR or defibrillation. Delay to definitive treatment is of particular concern in situations when lay rescuers are providing cardiac arrest interventions.

A causal link between precordial thump and the critical outcomes of survival to hospital discharge and ROSC is lacking. Defibrillation is a more effective treatment for the termination of VF and VT and should be prioritized. There is concern from 1 study (very-low-certainty evidence) that use of precordial thump could compromise first shock success.[166]

In many of the included studies, it is unclear whether the tachyarrhythmia (VT) represents cardiac arrest or impending loss of cardiac output. It is very likely that this is not so for many of the cases included in the studies reviewed.

Across studies, there is a lack of standardization in the technique of precordial thump, the number of times it was used, pharmacological therapy delivered before or after its delivery, and—in some cases—its timing related to the onset of the tachyarrhythmia.

Fist (or percussion) pacing is described as the delivery of serial, rhythmic, relatively low-velocity blows to the sternum by a closed fist. The evidence for the effectiveness of fist pacing is limited to a few small case series (totaling 147 patients among them) suggesting that cardiac output can be maintained if fist pacing is initiated very quickly after onset of asystole or severe bradycardia—and strictly for such rhythms. An electric impulse is generated sufficient to cause myocardial depolarization and contraction. Fist pacing is not used for tachyarrhythmias.

There is no evidence comparing fist pacing with standard CPR (chest compressions) in established bradyasystolic cardiac arrest. We again highlight the importance of prompt, high-quality chest compressions for the treatment of cardiac arrest.

There is no evidence to contradict the 2010 CoSTR treatment recommendation[1,2] that providers can consider fist pacing in the exceptional circumstance of monitored, witnessed IHCA due to bradyasystole. It would not be appropriate to prioritize fist pacing instead of other measures with proven efficacy, but clinicians may consider it as a temporary measure if there is a delay to electric pacing or pharmacological therapies.

Knowledge Gaps

- There are no data directly comparing cough CPR or fist pacing with standard CPR.
- There are no data for any alternative CPR technique assessing survival with a favorable neurological outcome.

Table 13. Observational Studies of Fist Pacing With No Comparator Group

Outcome	Certainty	Studies	No. of Patients	Results
Survival to hospital discharge	Very low (very serious risk of bias)	Klumbies 1988,[181] Scherf 1960[182]	111 (in-hospital): n=51 asystole, n=20 "life-threatening bradycardia," n=29 unclear/delayed monitoring, n=11 "ventricular standstill"	63/111 (57%)
ROSC	Very low (very serious risk of bias)	Iseri 1987[183]; Paliege 1982[184]	5 (in-hospital): all asystole; 42 (in-hospital): n=35 asystole, n=7 "extreme bradycardia"	5/5 (100%); selective reporting of cases achieving outcome; 41/42 (98%)

ROSC indicates return of spontaneous circulation.

- There is limited, very-low quality evidence assessing the critical outcome of survival to hospital discharge.
- There are no data on any outcome after alternative CPR techniques performed in children.

DEFIBRILLATION

Public Access AED Programs (BLS 347: SysRev)

Rationale for Review

This topic was prioritized for review by the BLS Task Force because it had not been updated since 2015.[3,4] Public access AED programs were recommended by ILCOR after review of the evidence before 2015, and since then several additional studies have been published.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with OHCA
- Intervention: Implementation of a public access AED program
- Comparator: Traditional EMS response
- Outcome: Survival to hospital discharge with good neurological outcome and survival to hospital discharge were ranked as critical outcomes. ROSC, bystander CPR rates, time to first compressions, time to first shock, and CPR quality were ranked as important outcomes.
- 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. The literature search was updated to October 2019.

Consensus on Science

SysRevs on the effects of public access defibrillation (PAD) on OHCA survival have been published previously.[185,186] This review is focused on comparing outcomes in systems with public access AED programs versus systems with traditional EMS response and included 1 RCT and 30 observational studies. PAD is defined as defibrillation with an onsite AED by a layperson in the OHCA setting. The PAD group included only patients defibrillated by a lay person using an onsite AED. The control group included all patients not receiving PAD—meaning not treated with an onsite AED by a lay person—and included patients defibrillated by professional first responders, such as police or firefighters.

For the critical outcome of survival to 1 year with favorable neurological outcome, we identified low-certainty evidence (downgraded for risk of bias) from 1 observational trial[187] enrolling 62 patients showing improvement (43% versus 0%; P=0.02) after a PAD program in a subway system.

For the critical outcome of survival to 30 days with favorable neurological outcome, we identified low-certainty evidence (downgraded for risk of bias and inconsistency) from 7 observational studies[188–194] enrolling 43 116 patients demonstrating improved survival with a PAD program (OR, 6.60; 95% CI, 3.54–12.28).

For the critical outcome of survival to hospital discharge with favorable neurological outcome, we identified low-certainty evidence (downgraded for risk of bias) from 8 observational studies. The studies[187,195–201] included 11 837 patients demonstrating improved survival with PAD program (OR, 2.89; 95% CI, 1.79–4.66).

For the critical outcome of survival to 30 days, we identified low-certainty evidence (downgraded for risk of bias) from 8 observational studies[189,190,192,193,202–205] enrolling 85 589 patients demonstrating improved outcome with a PAD program (OR, 3.66; 95% CI, 2.63–5.11).

For the critical outcome of survival to hospital discharge, we identified moderate-certainty evidence (downgraded for risk of bias) from 1 RCT[206] enrolling 235 OHCA patients showing improved survival with PAD compared with no PAD (RR, 2.0; 95% CI, 1.07–3.77) and low-certainty evidence (downgraded for risk of bias) from 16 observational studies enrolling 40 243 patients showing improved survival associated with PAD programs (OR, 3.24; 95% CI, 2.13–4.92).[195–199,201,207–217]

Treatment Recommendation

We recommend the implementation of PAD programs for patients with OHCAs (strong recommendation, low certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-10. PAD programs are implemented at the community level to improve outcomes for patients with OHCA. In making this recommendation, we placed a high value on the potential life-saving capability of an AED for a shockable rhythm and on keeping with the previous treatment recommendation when there were no compelling data suggesting the need to change. We recognize that there are barriers to the implementation of PAD programs. The ILCOR scientific statement on public access defibrillation addresses key interventions (early detection, optimizing availability, signage, novel delivery methods, public awareness, device registration, mobile apps for AED retrieval and personal access defibrillation) that should be considered as part of all PAD programs. Cost-effectiveness of PAD programs may vary according to country. A recent review found cost-effectiveness ratios between 37 200 and 1 152 400 US dollars/quality-adjusted life-years.[185] Another recent cost-effectiveness analysis study[218] from

the United States concluded that public access AEDs are a cost-effective public health intervention.

Among 31 included studies, there was only 1 RCT, which showed improved survival to discharge in the CPR-plus-AED group compared with the CPR-only group. Observational studies were mostly retrospective analyses of data from large registries and generally showed improved survival outcomes associated with PAD. However, there were some inconsistencies among the observational studies, as some were unable to show any significant differences in outcomes.[187,193,196,215] There was also important heterogeneity among studies in the meta-analysis. The location of cardiac arrest was various and included airports,[212] subways,[187] and sports facilities.[200] The population varied, with 2 studies including only children.[190,194] The control group also varied among studies because some patients in control groups received first responder defibrillation, whereas others did not. Some studies were before-and-after studies in which historic controls included periods before PAD implementation[193,215,217] or the initial period of implementation.[187] Despite such heterogeneity, all patients in those studies had OHCA, and most studies showed that implementation of PAD improved survival.

Knowledge Gaps

Current knowledge gaps include but are not limited to the following:

- Optimal placement/location of AEDs
- Optimal role of emergency medical dispatchers in identifying nearest AED and alerting callers to their location
- How AEDs could be most effectively integrated into citizen responder programs

Analysis of Rhythm During Chest Compressions (BLS 373: SysRev)

Rationale for Review

High-quality CPR with few pauses in chest compressions is emphasized in current guidelines and CPR training. Rhythm analysis and pulse checks require pauses in chest compressions, and artifact-filtering algorithms for analysis of electrocardiographic rhythm during CPR have been proposed as a method to reduce pauses in chest compressions.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with cardiac arrest
- Intervention: Analysis of cardiac rhythm during chest compressions
- Comparator: Standard care (analysis of cardiac rhythm during pauses in chest compressions)
- 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. CPR quality metrics, such as time of chest compression fraction, pauses in compressions, compressions per minute, time to commencing CPR, time to first shock, etc, were included as important outcomes.
- 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; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to September 23, 2019.

Consensus on Science

Fourteen full-text papers were identified and reviewed,[219–232] but none assessed any critical or important patient-related outcomes. Most of these studies use previously collected electrocardiographs, electric impedance, and/or accelerometer signals recorded during CPR for cardiac arrest to evaluate the ability of various algorithms[220–229] or machine learning[230] to detect shockable rhythms during chest compressions. Although these studies did not evaluate the effect of the artifact-filtering algorithms on any critical or important outcomes, they provided insights into the feasibility and potential benefits of this technology. We also identified studies evaluating artifact-filtering algorithms in animal models of cardiac arrest[219,231] and simulation studies.[232] Sensitivities and specificities are generally reported in the 90% to 99% range, but none of these studies evaluated the use of this technology during actual cardiac arrest and resuscitation.

Treatment Recommendations

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).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-11. In making a recommendation against routine use, we placed priority on avoiding the costs of introducing a new technology when its effects on patient outcomes and risk of harm remain to be determined.

In making a recommendation for further research; the task force is acknowledging that (1) there is thus far

insufficient evidence to support a decision for or against routine use, (2) further research has potential for reducing uncertainty about the effects, and (3) further research is thought to be of good value for the anticipated costs. This treatment recommendation was changed from a previous weak suggestion that, for EMS systems that had already integrated artifact-filtering algorithms into clinical practice, it would be reasonable to continue with their use.[3,4] The task force acknowledges that some EMS systems may have implemented artifact-filtering algorithms for analysis of electrocardiographic rhythm during CPR and strongly encourages such systems to report their experiences to build the evidence base about the use of these technologies in clinical practice.

Knowledge Gaps

There were no studies identified that evaluated feasibility, efficacy, or effectiveness of artifact-filtering algorithms for analysis of electrocardiographic rhythm during CPR in any setting for any patient population.

CPR Before Defibrillation (BLS 363: SysRev)

Rationale for Review

Previous treatment recommendations for CPR before defibrillation have been based on RCTs, but the results from these trials have been inconsistent, and important uncertainty about the optimal timing of defibrillation remains. This topic has not been reviewed by ILCOR since the 2015 CoSTR[3,4] and therefore was prioritized by the BLS Task Force.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with cardiac arrest and a shockable rhythm at initiation of CPR
- Intervention: A prolonged period of chest compressions before defibrillation (90–180 seconds)
- Comparator: A short period of chest compressions until the defibrillator is ready
- 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.
- Time frame: All years and all languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to October 27, 2019.

Consensus on Science

Five RCTs were identified comparing a shorter with a longer interval of chest compressions before defibrillation.[117,118,233–235] Outcomes assessed varied from 1-year survival with favorable neurological outcome to ROSC. No clear benefit from CPR before defibrillation was found in meta-analysis of any of the critical or important outcomes (Table 14).

Treatment Recommendation

This treatment recommendation (below) is modified slightly from the 2015 CoSTR.[3,4] We suggest a short period of CPR until the defibrillator is ready for analysis and/or defibrillation in unmonitored cardiac arrest. (weak recommendation, low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-12. This topic was prioritized by the

Table 14. CPR Before Defibrillation

Outcome	Certainty	Studies	No. of Patients	Results
1 y with favorable neurological outcome	Low (risk of bias, imprecision)	Wik 2003[117]	200	No difference: Relative risk 1.15 (95% CI, −0.57 to 2.34), 19 more patients/1000 (−54 to 167)
Hospital discharge with favorable neurological outcome	Low (inconsistency, imprecision)	Wik 2003,[117] Baker 2008,[118] Ma 2012,[234] Stiell 2011[235]	10 424	No difference: Relative risk 1.02 (95% CI, −0.01 to 0.01), 1 more patient/1000 (−7 to 11)
Survival to 1 y	Low (risk of bias, imprecision)	Wik 2003,[117] Jacobs 2005[233]	456	No difference: Relative risk 1.19 (95% CI, 0.69–2.04), 18 more patients/1000 (−29 to 98)
Survival to hospital discharge	Low (risk of bias, imprecision)	Wik 2003,[117] Jacobs 2005,[233] Baker 2008,[118] Ma 2012,[234] Stiell 2011[235]	10 680	No difference: Relative risk 1.01 (95% CI, 0.90–1.15), 1 more patient/1000 (−8 to 13)
ROSC	Low (risk of bias, imprecision)	Wik 2003,[117] Jacobs 2005,[233] Baker 2008,[118] Ma 2012,[234] Stiell 2011[235]	10 680	No difference: Relative risk 1.03 (95% CI, 0.97–1.10), 8 more patients/1000 (−9 to 27)

CPR indicates cardiopulmonary resuscitation; and ROSC, return of spontaneous circulation.
Both relative and absolute risks are written as mean values (95% CIs).

BLS Task Force, as it had not been reviewed since the 2015 CoSTR.[3,4] Given the availability of comparative data from several RCTs, we did not include non-RCTs. No new RCTs were identified, and no changes were made to the treatment recommendation; however, because the outcome templates have been altered for the 2020 ILCOR review process, the review has been updated.

In continuing to make the recommendation to provide CPR until the defibrillator is ready for analysis and/or defibrillation in unmonitored cardiac arrest, we placed a high value on being consistent with previous recommendations. The BLS Task Force acknowledges that every change in guidelines comes with a significant risk and cost as CPR educators and providers are asked to change current practice and implement new treatment strategies for complex and high-stress medical emergencies.

Important issues remained in the evaluation of the 5 included RCTs and led the BLS Task Force to downgrade the certainty of the treatment recommendation. The trial by Jacobs et al[233] did not use a random sequence generation and did not conceal randomization before rhythm analysis, leading to potential bias. In all RCTs, the treating EMS personnel could not be blinded to the interventional strategy after randomization. There was also significant heterogeneity in these trials with regard to the duration of CPR provided before defibrillation, with a range of 90 to 180 seconds. For the purposes of this review, the 90 to 180 seconds of CPR was considered a combined group. It is also important to note that the trials were conducted in different countries (Australia, Canada, Norway, Taiwan, United States) with varying EMS system structural configurations (BLS, ALS, physician on scene) as well as response times and treatment protocols. Only 1 of the included trials attempted to document and adjust for the quality of the intervention (or chest compressions) before defibrillation,[235] leaving the possibility that the intervention in the other trials was of varying quality. The studies also included only adult (age ≥18 years) OHCA patients and cannot be generalized to the IHCA or pediatric populations.

Two subgroup analyses were considered in the 2015 CoSTR. One subgroup analysis looked at enrollments based on EMS response interval, comparing those with intervals of less than 4 to 5 minutes versus those with intervals of 4 to ≥5 minutes. Within this subgroup, 1 study[117] found a favorable relationship with CPR for 180 seconds before defibrillation when the response interval was ≥5 minutes, but this relationship was not confirmed in 3 other RCTs.[118,233,235] The second subgroup analysis[236] examined outcomes from early compared with late analysis on the basis of baseline EMS agency VF/pVT survival rates. Among EMS agencies with low baseline survival to hospital discharge (defined as less than 20% for an initial rhythm of VF/pVT), higher neurologically favorable survival was associated with early analysis and shock delivery as opposed to CPR and delayed analysis and shock delivery. Yet, for EMS agencies with higher baseline survival to hospital discharge (greater than 20%), 3 minutes of CPR followed by analysis and defibrillation resulted in higher neurologically favorable survival. These subgroup analyses underscore the difficulty in making "one size fits all" recommendations for resuscitation systems, which may vary considerably in both populations served and treatments offered.

Knowledge Gaps

Current knowledge gaps include but are not limited to the following:

- What effect does the quality of bystander CPR have?
- Can electrocardiographic waveform characteristics be used to determine optimal strategy?
- If a CPR-first strategy is adopted, what is the optimal duration of CPR (90 seconds, 120 seconds, or 180 seconds)?
- What system-level characteristics might influence adopted strategy?

Paddle Size and Placement for Defibrillation (ALS-E-030A: ScopRev)

Rationale for Review

This topic was suggested by the Australian Resuscitation Council. The BLS Task Force was supportive of an updated evidence review because this topic had not been reviewed by ILCOR since 2010.[237,238]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults with cardiac arrest
- Intervention: The use of any specific pad size/orientation and position
- Comparator: Standard resuscitation or other specific paddle/pad size/orientation and 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. Termination of VF and rates of recurrence of fibrillation/refibrillation were included as important outcomes.
- 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. It was anticipated that there would be insufficient studies from which to draw a conclusion; case series were included in the initial search and included as long as they contained at least 5 cases.
- Time frame: Since January 1, 2009: All languages were included as long as there was an English

abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to November 11, 2019.

Summary of Evidence

We did not identify any new evidence that directly addressed this question. See Appendix B-3 for full ScopRev.

Task Force Insights

Key issues from BLS Task Force discussions were as follows:

Although some studies have shown that anteroposterior electrode placement is more effective than the traditional anterolateral position in elective cardioversion of atrial fibrillation, the majority have failed to demonstrate any clear advantage of any specific electrode position. Transmyocardial current during defibrillation is likely to be maximal when the electrodes are placed so that the area of the heart that is fibrillating lies directly between them (ie, ventricles in VF/pVT, atria in atrial fibrillation). Therefore, the optimal electrode position may not be the same for ventricular and atrial arrhythmias.

Recent approaches including double sequential defibrillation, in which differently oriented sequential defibrillations are delivered, have been evaluated by the Advanced Life Support Task Force in a separate evidence review.

This ScopRev was unable to identify any new studies that needed to be added to the previous SysRev. In light of this, we believe that the existing CoSTR does not need to be modified (with the exception of removing reference to "paddles," because modern equipment using self-adhesive pads have replaced paddles).

Treatment Recommendation

These treatment recommendations (below) are unchanged from 2010.[237,238] 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 greater than 8 cm.

SPECIAL CIRCUMSTANCES

CPR During Transport (BLS 1509: ScopRev)

Rationale for Review

This topic has not been reviewed since before 2005.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with OHCA
- Intervention: Transport to hospital
- Comparator: Completing CPR on scene
- Outcome: Critical: survival with good neurological function (ie, at hospital discharge, 1 month, 6 months, 1 year) and survival (ie, hospital discharge, 1 month, 6 months, 1 year); important: short-term survival (ROSC, hospital admission) and CPR quality parameters (ie, compression fraction rate, depth, leaning, etc)
- 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.

Summary of Evidence

This ScopRev is included in Supplement Appendix B-2.

Studies Reporting Survival Among OHCA Patients Transported With CPR in Progress (Arriving at Hospital Without a Pulse)

There were 8 nonrandomized studies[239–246] reporting that ROSC was achieved in the emergency department in approximately 9.5% of cases, with 2.9% surviving to hospital discharge.

Studies Reporting Quality of Manual CPR on Scene Compared With During Transport

There were 5 nonrandomized studies[247–251] comparing the quality of CPR on scene with the quality of CPR during transport to hospital. Two studies[247,250] concluded that the quality of CPR during transport is no worse than the quality of CPR on scene, whereas 2 studies[249,251] concluded that the quality of CPR was poorer during transport than on scene.

There were 4 RCTs[252–255] and 4 nonrandomized studies[256–259] comparing the quality of CPR on scene with the quality of CPR during transport, using manikins. Manikin studies suggest that CPR quality is poorer during transport than when on scene.

Studies Comparing Manual Versus Mechanical CPR During Transport

There were 3 RCTs[260–262] and 3 nonrandomized studies[263–265] reporting survival outcomes for OHCA patients transported with manual CPR compared with mechanical CPR. RCTs showed no benefit from mechanical CPR with respect to ROSC or survival to discharge. The nonrandomized studies reported conflicting results. Two RCTs[260,261] and 3 nonrandomized studies[266–268] suggested variable improvements in physiological parameters with mechanical CPR. Four manikin RCTs[254,255,269,270] and 3 nonrandomized manikin studies[257,271,272] suggested that mechanical CPR provided consistent CPR, whereas the quality of manual CPR declined during transport.

Studies Addressing Duration and/or Distance of Transport on Outcomes

Five nonrandomized studies[246,273–276] suggested that the duration of transport with CPR and the distance transported with CPR does not adversely impact patient outcomes.

There was significant heterogeneity among study populations, study methodologies, outcome measures utilized, and outcomes reported. Findings are grouped into themes, and a narrative analysis is provided.

Task Force Insights

There was considerable task force debate concerning the appropriate outcome for this PICOST:

- Is the quality of CPR during transport better/no different/worse than the quality of CPR on scene?
- Are clinical outcomes affected by the decision to transport with CPR?
- When should the decision to transport with ongoing CPR be made?
- Does the distance of transport affect outcomes of CPR during transport?
- Can we identify which patient groups will/will not benefit from transport with ongoing CPR?
- Should we recommend the use of mechanical CPR during transport?
- What are the risks associated with CPR during transport?

The task force acknowledges several confounding factors when interpreting evidence, such as the use of feedback devices to improve CPR quality during transport and the implementation of high-performance CPR within EMS systems. It was noted that studies of CPR quality reported mean outcome measures and acknowledged that the quality of CPR may fluctuate considerably during transport. Although there is little evidence about risk to providers when performing CPR during transport, there are several reports highlighting the risk of injury when unrestrained in the back of an ambulance. The task force recognizes that performing CPR in the back of a moving ambulance does increase the risk to providers. The decision to transport to hospital or cease in the field might also be dependent on available resources at receiving hospitals—if no additional treatment can be added in the hospital, providers and patients are subjected to additional risk with little potential benefit.

This topic has not been addressed by ILCOR for many years. This ScopRev has identified new evidence addressing this topic. The BLS Task Force recognizes that it may be appropriate to undertake more than 1 SysRev on the basis of these findings. The BLS Task Force will seek public feedback to prioritize the questions to explore in the near future. The BLS Task Force will request as a first priority a SysRev comparing the quality of CPR metrics on scene compared with during transport.

Removal of Foreign-Body Airway Obstruction (BLS 368: SysRev)

Rationale for Review

Foreign-body airway obstruction is a common problem. Many cases are likely resolved easily without the need to involve healthcare providers. Foreign-body airway obstruction is, however, an important cause of early death that typically affects the very young and the elderly or individuals with impaired neurological function/swallowing. Current strategies to relieve foreign-body airway obstruction are well known to many people; delays in treatment increase the risk of death, but interventions themselves can cause harm and death. The topic of relief of foreign-body airway obstruction has not been reviewed since 2010.[1,2] In recent years, manual suction devices (airway clearance devices) that use a vacuum to remove foreign bodies have become commercially available. These devices have not previously been reviewed by ILCOR and are included in this SysRev.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with foreign-body airway obstruction
- Intervention: Interventions to remove foreign-body airway obstruction, such as finger sweep, back slaps or blows, abdominal thrusts, chest thrusts, and suction-based airway clearance devices
- Comparator: No action
- Outcome: Survival with good neurological outcome, survival, ROSC, relief of airway obstruction, harms/complications
- Study design: RCTs, nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies), and case series (≥5 cases) were eligible for inclusion. Case reports of injuries/complications were eligible.
- Time frame: All years and all languages were included as long as there was an English abstract. Unpublished studies (eg, conference abstracts, trial protocols), animal studies, manikin studies, and cadaver studies were excluded. The literature was searched to September 2019.
- PROSPERO registration: CRD42019154784

Consensus on Science

The review focused on studies published in the peer-reviewed literature. All studies identified were observational, consisting mostly of case series. The overall certainty of evidence was very low for all outcomes primarily because of very serious risk of bias and imprecision. Key limitations with interpretation of the case series identified include publication bias (reports of successful use or harm are more likely to be published); lack of information about the denominator (ie, the number of times an intervention was used compared with the number of successes

or harms reported); and, in many reports, more than 1 intervention attempted. For these reasons and because of the high degree of heterogeneity across the case reports, no meta-analyses were performed, and individual studies were difficult to interpret. Evidence relating to the use of back blows, abdominal thrusts, chest compressions, and finger sweeps is presented in Table 15.

Magill Forceps

For the critical outcome of survival with favorable neurological outcome, we identified very-low-certainty evidence from 1 observational study[343] enrolling 240 adults and children with OHCA with foreign-body airway obstruction, which showed benefit associated with the use of Magill forceps by EMS personnel compared with no use (OR, 3.96 [95% CI, 1.21–13.00]; 107 more patients/1000 survived with the intervention [95% CI, 8 more patients/1000 to 324 more patients/1000 survived with the intervention]). This outcome was achieved despite the much lower incidence of bystander CPR provided to the Magill forceps group.

For the critical outcome of survival, we identified very-low-certainty evidence from 1 observational study[343] enrolling 240 patients with OHCA associated with foreign-body airway obstruction. The rate of survival with EMS use of Magill forceps was 27% versus 17% in the control group (P=0.086) despite a lower rate of bystander CPR before EMS arrival (57% versus 80%; P<0.001).

For the important outcome of relief of foreign-body airway obstruction, we identified very-low-certainty evidence from 4 case series studies[278,285,343,344] reporting successful relief of foreign-body airway obstruction in 417 patients treated with Magill forceps.

Airway Clearance Devices

For the critical outcome of survival and the important outcome of relief of foreign-body airway obstruction, we identified a single observational study with very-low-certainty evidence reporting about 9 adult patients with foreign-body airway obstruction who survived after treatment with a suction-based airway clearance device.[345]

Foreign-Body Airway Obstruction Removal by Bystanders

For the critical outcome of survival with good neurological outcome, we identified very-low-certainty evidence downgraded for very serious risk of bias from 1 observational study[278] enrolling 41 patients with foreign-body airway obstruction, which showed benefit from bystander attempts to remove the foreign-body airway obstruction compared with no bystander attempts (intervention versus control, 74% versus 32%; P=0.0075).

Treatment Recommendations

We suggest that back slaps are used initially in adults and children with a foreign-body airway obstruction and an ineffective cough (weak recommendation, very-low-certainty evidence).

We suggest that abdominal thrusts are used in adults and children (older than 1 year) with a foreign-body airway obstruction and an ineffective cough when back

Table 15. Removal of Foreign Body Airway Obstruction

Intervention	Outcome	Studies	No. of Patients	Results
Back blows	Survival	1 observational[277]	13	All 13 patients survived
	Relief of obstruction	3 observational[277–279]	75	All 75 patients had relief of obstruction
	Injury/harm	4 observational[280–282a]	4	3 vascular injuries, 1 thoracic injury
Abdominal thrusts	Survival	2 observational[283,284]	189	All 189 patients survived
	Relief of obstruction	6 observational[277–279,283–285]	417	All 417 patients had relief of obstruction
	Injury/harm	49 observational[281,282a,286–333]	52	17 gastric/esophageal injuries, 15 vascular injuries, 12 thoracic injuries, 8 abdominal injuries
Chest thrusts/compressions	Survival	1 observational[334]	138	All 138 patients survived
	Relief of obstruction	1 observational[279]	28	All 28 patients had relief of obstruction
	Injury/harm	4 observational[280,312,323,326]	5	3 gastric/esophageal injuries, 2 vascular injuries.
Finger sweep	Survival	1 observational[277]	6	All 6 patients survived
	Relief of obstruction	2 observational[277,279]	36	All 36 patients had relief of obstruction
	Injury/harm	8 observational[335–342]	10	5 dislodgement of object, 5 injury to nasopharynx

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 a foreign-body airway obstruction (weak recommendation, very-low-certainty evidence).

We suggest that appropriately skilled healthcare providers use Magill forceps to remove a foreign-body airway obstruction in patients with OHCA from foreign-body airway obstruction (weak recommendation, very-low-certainty evidence).

We suggest that chest thrusts be used in unconscious adults and children with a foreign-body airway obstruction (weak recommendation, very-low-certainty evidence).

We suggest that bystanders undertake interventions to support foreign-body airway obstruction removal as soon as possible after recognition (weak recommendation, very-low-certainty evidence).

We suggest against the routine use of suction-based airway clearance devices (weak recommendation, very-low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-13. The current treatment recommendations are similar to previous recommendations, but the BLS Task Force has provided some additional guidance about the recommended sequence of steps to relieve airway obstruction. The task force recognizes the importance of early removal of a foreign-body airway obstruction to prevent cardiac arrest. Bystanders should be encouraged to assist victims by rapidly attempting to remove the obstruction. The initial response to foreign-body airway obstruction in a conscious individual should be to encourage coughing because this is a normal physiological response that may be effective and is unlikely to cause harm. The sequence of interventions in individuals without an effective cough suggested in treatment recommendations seeks to balance the benefits of early removal of the foreign-body airway obstruction with the potential harms of interventions, such as abdominal thrusts.

We prioritized consistency with current treatment recommendations. We note the difference in methodologic approaches used in this review compared with previous reviews. In particular, previous reviews included cadaver, animal, and manikin studies.

We note that evidence for all outcomes is assessed as very low certainty. Research on foreign-body airway obstruction is challenging because many with a foreign-body airway obstruction are treated immediately and effectively by bystanders or by coughing. It would be difficult if not impossible to perform an RCT of treatments for foreign-body airway obstruction.

The task force distinguished between a situation in which a foreign-body airway obstruction can be seen in the mouth and a situation in which no object can be seen. When an object can be seen in the mouth, the manual removal of the item was considered appropriate. When an object cannot be seen in the mouth, the potential harm associated with the rescuer placing and moving their fingers in the victim's mouth (a blind finger sweep) and the lack of clear benefit to this approach led to a suggestion against the use of blind finger sweeps.

The task force treatment recommendation limits use of abdominal thrusts to adults and children beyond infancy. This was driven by concerns that, in infants, the limited protection of the upper abdominal organs by the lower ribs may mean that the potential harm of abdominal thrusts outweighs any potential benefit. This is consistent with previous treatment recommendations.

The task force treatment recommendation supporting the use of chest thrusts/compressions is based on case series reports of successful relief of foreign-body airway obstruction (unknown whether patients were in cardiac arrest) and an observational study that found that chest compressions improved neurologically intact survival in unresponsive patients with foreign-body airway obstruction. Our current recommendation is consistent with previous treatment recommendations.

The introduction of a treatment recommendation supporting the use of Magill forceps by suitably trained healthcare providers reflects the potential benefit of the intervention and the availability of relevant equipment to trained individuals. The task force expects that these trained healthcare providers will already be skilled in advanced airway management. The treatment recommendation is based on evidence from case series of successful relief in victims with foreign-body airway obstruction (unknown whether patients were in cardiac arrest) and an observational study that found that EMS use of Magill forceps was associated with improved neurologically intact survival in those with OHCA from foreign-body airway obstruction.

The task force acknowledges that there are very limited data in the peer reviewed literature assessing the efficacy of suction-based airway clearance devices (a case series of 9 adults). The task force agreed that the peer-reviewed published data were insufficient to support the implementation of a new technology with an associated financial and training cost. The task force has outlined recommendations for further research in relation to these devices.

We identified no evidence that specifically examined foreign-body airway obstruction removal in pregnant individuals. The task force suggests that abdominal thrusts are avoided in this group due to risk of injury to the fetus.

Knowledge Gaps

- There is a need for high-quality observational studies that accurately describe the incidence of foreign-body

airway obstruction, patient demographics (age, setting, comorbidities, food type, level of consciousness), full range of interventions delivered, who delivered interventions (health professional/lay responder), success rates of interventions, harm of interventions, and outcomes. It is unlikely that such a study can be conducted using only health service data.
- There is a need for further evidence on the benefits and harms of suction-based airway clearance devices. The task force encourages the registration of all device uses. Reports should detail key demographics (eg, age, setting, comorbidities, food type, level of consciousness), full range of interventions provided, who provided the intervention (lay compared with healthcare professional), and outcomes. This evidence initially may come in the form of published case series.

Resuscitation Care for Suspected Opioid-Associated Emergencies (BLS 811: SysRev)

Rationale for Review

Deaths from drug overdose are an increasing public health burden in many countries. In the United States alone, more than 70 000 deaths were attributed to drug overdose in 2017.[345a] Overdose deaths have been increasing since 2013; although there is increasing research into overdose prevention and response education, there is a need for a SysRev to guide development of best practice guidelines for bystander resuscitation in suspected opioid-induced emergencies.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with suspected opioid-associated cardiorespiratory arrest in the prehospital setting
- Intervention: Bystander naloxone administration (intramuscular or intranasal) in addition to standard CPR
- Comparator: Conventional CPR only
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, and controlled before-and-after studies, cohort studies) were eligible for inclusion.
- Time frame: All years and all languages were included as long as there was an English abstract. Unpublished studies (eg, conference abstracts, trial protocols), animal studies, manikin studies, and cadaver studies were excluded. The literature was searched to October 2019.

Consensus on Science

We did not identify any studies reporting any critical or important outcomes for adults or children with suspected opioid-associated cardiorespiratory arrest in any setting, comparing bystander-administered naloxone (intramuscular or intranasal) plus conventional CPR with conventional CPR only.

Treatment Recommendation

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).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-14. There is no direct evidence comparing outcomes for patients with opioid-induced respiratory or cardiac arrest treated with naloxone in addition to standard CPR compared with those treated with CPR alone. Despite this, the BLS Task Force decided to make a suggestion for the use of naloxone on the basis of expert opinion alone, wanting to underline the importance and challenge of the opioid epidemic. Although administering naloxone is unlikely to directly harm the patient, rescuers should be prepared for behavioral changes that may occur after drug administration. Patients who are resuscitated from a narcotic overdose may become agitated and sometimes violent.

Although no evidence directly evaluating the clinical question was identified, we did identify a summary of 4 case series including 66 patients, in which 39 of 39 patients who received naloxone after opioid overdose recovered compared with 24 of 27 who did not receive naloxone after opioid overdose.[346] At the population level, there is evidence to demonstrate improved outcomes in communities after implementation of various naloxone distribution schemes. A recent SysRev identified 22 observational studies evaluating the effect of overdose education and naloxone distribution using Bradford Hill criteria and found a link between implementation of these programs and decreased mortality rates.[347]

Diagnosis of respiratory or cardiac arrest is not always straightforward, and lay rescuers would be expected to have a high suspicion of cardiac or respiratory arrest in any unresponsive person with suspected drug overdose. Administration of naloxone is likely to have preventive effects if given after a drug overdose that has not yet caused respiratory or cardiac arrest, and the potential for desirable effects in a broader population strengthens the suggestion to administer naloxone in this setting. Furthermore, there are very few reports of side effects from naloxone.[348] Although it is possible that bystanders might spend valuable time finding and administering naloxone instead of starting CPR during respiratory or cardiac arrest, lack of reports of harm from large-scale implementation of naloxone distribution schemes indicate that this is unlikely a big problem.

Because there is no formal evaluation of naloxone with CPR compared with CPR alone in opioid overdose, it

is not possible to formally balance desirable and undesirable effects of naloxone administration by laypeople. As a response to the growing epidemic, naloxone has been widely distributed by healthcare authorities to laypeople in various opioid overdose prevention schemes. Overall, these programs report beneficial outcomes at the population level. The BLS Task Force therefore considers it very likely that the desirable effects outweigh undesirable effects and that use of naloxone is acceptable by key stakeholders as well as the general population.

Knowledge Gaps

Current knowledge gaps include but are not limited to the following:

- There is currently no evidence evaluating the role of naloxone use among bystanders attempting CPR in suspected opioid-related respiratory or circulatory arrest.
- Further research is needed to determine the optimal components of resuscitation and the role of naloxone during bystander CPR.

Drowning (BLS 856: SysRev)

Rationale for Review

This question was initiated in response to a request that ILCOR review the evidence for prognostic factors that predict outcome in relation to a drowning incident. Drowning was last reviewed in 2015.[3,4] Drowning is the third leading cause of unintentional injury death worldwide, accounting for over 360 000 deaths annually.[349] Care of a submersion victim in high-resource countries often involves a multiagency approach, with several different organizations independently responsible for different phases of the victim's care, beginning with initial aquatic rescue, through on-scene resuscitation and transfer to hospital, and with in-hospital and rehabilitative care. Attempting to rescue a submerged victim has substantial resource implications and may place rescuers at risk.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children who are submerged in water
- Intervention: Any particular factor in search-and-rescue operations (eg, duration of submersion, salinity of water, water temperature, age of victim)
- Comparator: Compared with no factors
- 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. It was anticipated that there would be insufficient studies from which to draw a conclusion; case series were included in the initial search as long as they contained at least 5 cases.
- Time frame: All years and all languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to October 1, 2019.

Consensus on Science

Age

For the critical outcome of survival with favorable neurological outcome, we identified very-low-certainty evidence from 11 observational studies (downgraded for bias inconsistency, indirectness, and imprecision) comprising 4 105 patients.[350–359,359a] Of the 8 pediatric studies, 6 found that young age, variably defined as less than 3, 4, 5, or 6 years, was not associated with favorable neurological outcome.[350–354,356] A single pediatric study including 166 children less than 15 years of age reported better outcomes in children age less than 5 years (RR, 0.12; 95% CI, 0.03–0.44).[355] Four studies considered drowning victims of all ages; 2 found no association between age and outcome.[357,358]One reported worse outcomes associated with children aged greater than 5 years (RR, 0.66; 95% CI, 0.51–0.85).[359]

For the critical outcome of survival, we identified very-low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 6 observational studies including 1313 patients.[360–365] Three studies found that age was not associated with outcome.[361,363,365] Two reported better outcomes associated with younger ages (less than 58 years: RR, 0.27; 95% CI, 0.08–0.96[362]; less than 46 years: RR, 0.98; 95% CI, 0.99–0.99),[364] and 1 favored older age (≥3 years: RR, 1.51; 95% CI, 1.19–1.9).[360]

EMS Response Interval

For the critical outcome of survival, we identified very-low-certainty evidence (downgraded for risk of bias, indirectness, and imprecision) from 2 observational studies including 746 patients in the Swedish EMS OHCA registry.[362,366] EMS response intervals of less than 10 minutes were associated with better survival (RR,0.29; 95% CI, 0.13–0.66)[366] and a reported OR of 0.44 (95% CI, 0.06–0.83).[362]

Salinity

For the critical outcome of survival with favorable neurological outcome, we identified very-low-certainty evidence (downgraded for risk of bias, indirectness, and imprecision) from 6 observational studies[354,357,359,359a,367,368] 1799 including 3 584 drowning victims, of which 980 occurred in salt water and 2 604 in fresh water. Two reported that drowning in salt water was associated with better outcomes (RRs, 1.3 [95% CI, 1.12–1.5][357] and 1.2 [95% CI, 1.1–1.4],[354] and 4 found no association between water salinity

and outcome (RRs, 1.1 [95% CI, 0.95–1.2],[367] 1.14 [95% CI, 0.9–1.4],[359] 1.1 [95% CI, 0.70–1.72],[368] and 1.15 [95% CI, 0.91–1.45).[359a]

For the critical outcome of survival, we identified very-low-certainty evidence (downgraded for risk of bias imprecision, inconsistency, indirectness, and imprecision) from 5 observational studies.[360,363,368–370] One reported better outcomes associated with salt water submersion (RR, 1.34; 95% CI, 1.19–1.52),[369] 3 showed no association between water salinity and survival (RRs, 1.22 [95% CI, 0.95–1.56],[360] 0.88 [95% CI, 0.40–1.92],[368] and 0.94 [95% CI, 0.62–1.4],[370] and 1 reported worse survival associated with salt water drowning (RR, 0.18; 95% CI, 0.03–1.43).[363]

Submersion Duration

For the purposes of this review, we considered studies in 3 groups. We defined those with short submersion duration (less than 5–6 minutes), those with intermediate duration (less than 10 minutes), and those with prolonged submersion duration (less than 15–25 minutes).

Short Submersion Intervals (Less Than 5–6 Minutes)

For the critical outcome of survival with favorable neurological outcome, we identified moderate-certainty evidence from 15 observational studies (downgraded for bias and indirectness, upgraded for dose response) including 2 746 drowning victims.[350,352–356,359,359a,371–377] All studies noted worse outcomes associated with submersion durations exceeding 5 minutes (RRs between 0.05[359] and 0.61.[355] The 943/1 075 patients (87.7%) who had outcome information available and were submerged for short durations had good outcomes compared with the 139/1 238 (11.2%) who had longer submersion durations.

For the critical outcome of survival, we identified low-certainty evidence (downgraded for risk of bias, indirectness, and imprecision; upgraded for dose response) from 6 observational studies comprising 392 cases.[360,361,369,375,378,379] All studies noted an association between worse outcomes with prolonged compared with short submersion durations (RRs between 0.27[378] and 0.83.[379] The 204/217 patients (94.0%) submerged for short durations had good outcomes compared with the 54/98 (55.1%) who had longer submersion durations.

Intermediate Submersion Intervals (Less Than 10 Minutes).

For the critical outcome of survival with favorable neurological outcome, we identified moderate-certainty evidence (downgraded for bias, indirectness, and imprecision; upgraded for dose response) from 9 observational studies including 2 453 victims of drowning.[352,354,355,359,371,372,374,380,381] All studies noted an association between worse outcomes and prolonged submersion durations compared with intermediate submersion durations (RRs between 0.02.[359] and 0.45.[355,372] The 787/1 019 patients (77.2%) submerged for intermediate durations had good outcomes compared with the 36/962 (3.7%) who had longer submersion durations.

For the critical outcome of survival, we identified low-certainty evidence (downgraded for bias, indirectness and imprecision; upgraded for dose response) from 2 observational studies[369,382] reporting about 121 victims of drowning. In the first study,[369] 56/73 (77%) submerged for less than10 minutes survived compared with none of the 7 patients who were submerged for more prolonged periods survived (RR, not estimable; absolute difference, 76.7%; 95% CI, 39.7%–94.9%). The second study[382] also noted better survival rates associated with a submersion duration of less than 10 minutes (46/50 [96%] survived) compared with submersion duration of more than 10 minutes (2/5 [40%] survived).[382]

Prolonged Submersion Intervals (Less Than 15–25 Minutes).

For the critical outcome of survival with favorable neurological outcome, we identified low-certainty evidence (downgraded for bias and imprecision, upgraded for dose response) from 3 observational studies including reports of 739 victims of drowning.[352,354,374] In 1 study (n=398),[354] submersion for less than 20 minutes was associated with better outcomes (289/370 [78%] compared with 1/27 [4%] survived; RR, 0.05; 95% CI, 0.01–0.31). The second series[352] reported better outcomes associated with a submersion duration of less than 25 minutes (68/101 survivors, or a 67% survival rate) compared with a submersion duration longer than 25 minutes (0/4 survivors, or a 0% survival rate).[352] In the third study, which included hypothermic children in cardiac arrest, 12/66 (18%) submerged for less than 25 minutes survived compared with 0/39 who were submerged for more than 25 minutes.[374]

For the critical outcome of survival, we identified very-low-certainty evidence (downgraded for bias, indirectness, and imprecision) from a single study[378] comprising 49 patients. Those with a submersion duration of less than 15 minutes had an overall survival rate of 82% (33/39) compared with none of the 2 victims whose submersion duration exceeded 15 minutes (RR, not estimable; absolute difference, 84.6%; 95% CI, 17.3%–92.8%).

Water Temperature

For the critical outcome of survival with favorable neurological outcome, we identified very-low-certainty evidence (downgraded for bias, inconsistency, indirectness, and imprecision) from 2 studies[359,374] including 1254 victims of drowning. The largest study (n=1094) included all unintentional drownings in open waters (lakes, ponds, rivers, ocean) in a single large region, collected from medical examiners, EMS systems, and all regional hospitals.[359] Water temperatures were measured within a month of the drowning incident. Univariable analysis according to temperatures less than or greater than 6°C or less than or

greater than 16°C did not find any association between water temperature and neurological survival. Multivariable analysis also showed no association between water temperature and outcome. The second study included 160 children who required resuscitation and were hypothermic after submersion.[374] Water temperatures were estimated on the basis of the season. Submersion in the winter, with water temperature estimated as 0°C to 8°C, was associated with better outcomes than submersion in spring or summer, with water temperature estimated at 6°C to 28°C (univariable OR, 4.55; 95% CI, 1.37–15.09).

For the critical outcome of survival, we identified very-low-certainty evidence (downgraded for risk of bias, indirectness, and imprecision) from a single study[362] including 250 victims of drowning. This study included only those who had OHCA and received EMS care, and it included those with intentional (suicide and homicide) drowning. This study found no relationship between water temperature less than or greater than 15°C and outcome (RR, 0.94; 95% CI, 0.34–2.62; absolute difference, 0.36%; 95% CI, –6.4% to 6.5%).

Witnessed Status

The definition of witnessed compared with unwitnessed drowning was inconsistently defined in the studies reviewed. It was often unclear if the term "witnessed" related to the submersion or the cardiac arrest.

For the critical outcome of survival with favorable neurological outcome, we found very-low-certainty evidence (downgraded for indirectness and imprecision) from 3 observational studies[358,359a,383] involving 2 707 patients. Two studies reported better neurological outcomes associated with a witness to the event (unadjusted odds ratio, 16.33 [95% CI, 5.58–47.77]; AOR, 11.8 [95% CI, 2.84–49.08][358]; and unadjusted odds ratio, 2.6 [95% CI, 1.69–4.01]; AOR, 3.27 [95% CI, 2.0–5.36][383]). Neither of the analyses included submersion duration, which several studies have reported as an independent predictor.

For the critical outcome of survival, we found low-certainty evidence (downgraded for risk of bias, indirectness, and imprecision) from 4 studies[358,363,364,366] involving 2 857 victims. Two studies[362,364] were from the same EMS system, and both used multivariable analysis. The smaller study (n=255) showed that witnessed status was not associated with improved survival (RR, 0.55; 95% CI, 0.17–1.75; absolute difference, 3%; 95% CI, –3.1% to 11.2%).[362] However, in the larger subsequent study from that same EMS system, witnessed status predicted better outcome (reported univariable analysis: *P*=0.05; AOR, 2.5; 95% CI, 1.38–4.52).[364] Another study[363] found no association between witnessed status and improved survival (RR, 0.82; 95% CI, 0.26–2.59). A large observational study from Japan[358] reported an UAOR of 7.38 (95% CI, 3.81–14.3) and an AOR of 6.5 (95% CI, 2.81–15.02) with witnessed compared with unwitnessed drowning, although the unusual population of much older victims, most drowning in bathtubs, and a very low rate of favorable outcomes limited the generalizability of these findings.

Treatment Recommendations

These treatment recommendations are unchanged from 2015.[3,4] We recommend that submersion duration be used as a prognostic indicator when making decisions surrounding 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.

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-15. The 2015 CoSTR benefited from significant feedback from ILCOR task forces as well as through public consultation and input from the drowning research and clinical communities.[3,4] In making the original recommendations, the task force placed priority on producing simple guidance that may assist those responsible for managing search and rescue operations. The public comments highlighted the difficult moral dilemmas facing the rescuer in an emotionally charged and fast-moving environment requiring dynamic risk assessments that consider the likelihood of a favorable outcome with the risks posed to those undertaking the rescue. It must also be noted that there is substantial difficulty inherent in determining the submersion duration and the bias of studies using it as a predictive variable. The key finding of the 2015 review was that submersion durations of less than 10 minutes are associated with a very high chance of favorable outcome, and submersion durations more than 25 minutes are associated with a low chance of favorable outcomes.[3,4]

The findings from the 6 new papers identified in this update[359a,368,370,375,376,383] are consistent with the 2015 treatment recommendation.[3,4] The previously identified limitations of this review (exclusion of factors after the victim is rescued, for example, bystander CPR[383–385]; specialist interventions, such as the use of extracorporeal membrane oxygenation[386–393]; and the lack of prospective validation of submersion duration as a clinical decision rule) persist. Similarly, continued reports of rare survival after prolonged (more than 30 minutes) submersion[387,392,394] highlight the need for case-by-case decisions that balance risk and potential for benefit.

Knowledge Gaps

Submersion duration should be assessed in all future drowning studies and be part of multivariable analyses.

To better clarify the value of this predictor, studies should include all victims rescued from the water and not only subcategories.

POTENTIAL HARM FROM CPR

Harm From CPR to Victims Not in Cardiac Arrest (BLS 353: SysRev)

Rationale for Review

Many lay rescuers are reluctant to begin CPR even when a victim is in cardiac arrest because of concern that delivering chest compressions to a person who is not in cardiac arrest could cause serious harm. Case reports and case series of serious harm to persons receiving CPR who are not in cardiac arrest are likely to be published because they are of general interest to a broad group of healthcare providers. A lack of reported cases demonstrating serious harm could strengthen arguments that desirable effects will far outweigh undesirable effects. This topic was last reviewed in 2015.[3,4]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children without OHCA
- Intervention: Provision of chest compressions from lay rescuers
- Comparator: No use of chest compressions
- Outcome: Change in survival with favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; harm (eg, rib fracture); complications; major bleeding; risk of complications (eg, aspiration); survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to admission
- 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. It was anticipated that there would be insufficient studies from which to draw a conclusion; case series and case reports were included in the initial search.
- Time frame: All years and all languages were included as long as there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to October 13, 2019.

Consensus on Science

For the important outcome of harm, we identified very-low-certainty evidence (downgraded for risk of bias and imprecision) from 4 observational studies enrolling 762 patients who were not in cardiac arrest but received CPR by lay rescuers out-of-hospital. Three of the studies[395–397] reviewed the medical records to identify harm, and 1 included follow-up telephone interviews.[395] Pooled data from the first 3 studies, encompassing 345 patients, found an incidence of rhabdomyolysis of 0.3% (n=1), bone fracture (ribs and clavicle) of 1.7% (95% CI, 0.4%–3.1%), pain in the area of chest compression of 8.7% (95% CI, 5.7%–11.7%), and no clinically relevant visceral injury. The fourth study[34] relied on fire department observations at the scene; there were no reported injuries in 417 patients.

Treatment Recommendation

This treatment recommendation is unchanged from 2015.[3,4] We recommend that lay people initiate CPR for presumed cardiac arrest without concerns of harm to patients not in cardiac arrest (strong recommendation, very-low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-16. No change was made to this treatment recommendation. In continuing to make this discordant recommendation (strong recommendation based on very-low-certainty evidence), the BLS Task Force placed a much higher value on the potential survival benefits of CPR initiated by lay persons for patients in cardiac arrest and a lower value on the low risk of injury to patients not in cardiac arrest. The intention of this recommendation is to strongly encourage and support lay rescuers who are willing to initiate CPR in any setting when they believe someone is in cardiac arrest. The intention is also to support emergency medical dispatchers in their efforts to provide DA-CPR instructions in suspected cardiac arrest calls.

Knowledge Gaps

- Studies are needed to identify harm and provide follow-up after hospital discharge. Many of the conditions prompting initiation of CPR for persons not in cardiac arrest are associated with reduced responsiveness and have poor prognoses. Whether chest compressions and rescue breaths could accentuate these conditions independent of physical injury is not known at the present time.
- The incidence of chest wall fractures was substantially lower than the incidence reported after CPR in patients who were in cardiac arrest. This is likely the result of a shorter duration of CPR (approximately 6 minutes) initiated by lay persons but stopped by professional rescuers and the younger patient age in the studies reviewed. However, it is possible that the lack of systematic follow-up leads to under-reporting of these injuries, and additional research is warranted.

- Could the accuracy of DA protocol be enhanced to reduce the frequency of CPR performed on patients not in cardiac arrest without compromising the initiation of CPR on patients in cardiac arrest?

Harm to Rescuers From CPR (BLS 354: ScopRev)

Rationale for Review

The BLS Task Force prioritized an updated evidence review because this topic had not been reviewed by ILCOR since 2010, and that review addressed only injury from CPR to victims who are not in cardiac arrest.[1,2] This 2020 review focused on any potential harm to the rescuers during CPR, including harm during chest compressions, during mouth-to-mouth ventilation, and with the use of defibrillators.

Summary of Evidence

The complete ScopRev is included in Supplement Appendix B-5. The review identified 5 experimental studies and 1 case report published since 2008. The 5 experimental studies reported the perception of rescuers in an experimental setting during shock administration for elective cardioversion. In these studies, the authors also measured current flow and the average leakage current in different experiments.

Task Force Insights

We identified many gaps in the published literature. No RCTs were identified that met our inclusion criteria. Most identified studies addressed safety of shock delivery during chest compressions when rescuers wore gloves.

Despite limited evidence evaluating rescuer safety, there was broad agreement within the BLS Task Force that the lack of published evidence supports the interpretation that CPR is generally safe for rescuers. A few reports demonstrate the possibility of disease transmission in the course of performing mouth-to-mouth ventilation. The isolated reports of adverse effects resulting from the widespread and frequent use of CPR suggest that performing CPR is relatively safe. Delivery of a defibrillator shock with an AED during BLS is also safe. The incidence and morbidity of defibrillator-related injuries in the rescuers are low.

The BLS Task Force considers the overall body of new evidence identified by this ScopRev insufficient to warrant a full SysRev. The few reports of harm to rescuers from performing CPR and defibrillation are supportive of general recommendations that lay rescuers may safely perform CPR and use an AED.

Treatment Recommendation

Evidence supporting rescuer safety during CPR is limited. The few isolated reports of adverse effects resulting from the widespread and frequent use of CPR suggest that performing CPR is relatively safe. Delivery of a defibrillator shock with an AED during BLS is also safe. The incidence and morbidity of defibrillator-related injuries in the rescuers are low.

TOPICS NOT REVIEWED IN 2020

Topics not reviewed or updated are the following:

- BLS 352: Passive ventilation technique
- BLS 358: Minimizing pauses in chest compressions

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Disclosures

Appendix 1. Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Theresa M. Olasveengen	Oslo University Hospital (Norway)	Zoll Foundation*; Laerdal Foundation*	None	None	None	None	None	None
Mary E. Mancini	University of Texas at Arlington	None	None	Stryker*	None	None	None	None
Gavin D. Perkins	Warwick Medical School and University Hospitals NHS Foundation Trust (United Kingdom)	National Institute for Health Research (Institutional funding relating to cardiac arrest research)†; British Heart Foundation (Institutional funding relating to cardiac arrest research)†; Resuscitation Council UK (Institutional funding relating to cardiac arrest research)†	None	None	None	None	None	None
Suzanne Avis	Ms School of Medicine (Australia)	None	None	None	None	None	None	None
Steven Brooks	Queen's University, Kingston General Hospital	Canadian Institutes of Health Research (Peer-reviewed funding to study the PulsePoint mobile device application)†	None	None	Borden-Ladner-Gervais†	None	Heart and Stroke Foundation of Canada (member of the Resuscitation Advisory Committee and receive travel reimbursement)*	None
Maaret Castrén	Helsinki University Hospital (Finland)	None	None	None	None	None	None	None
Sung Phil Chung	Yonsei University (Republic of Korea)	None	None	None	None	None	None	None
Julie Considine	Deakin University	None	None	None	None	None	None	Salary: Deakin University†; Eastern Health†; College of Emergency Nursing Australasia*
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Raffo Escalante	Inter-American Heart Foundation (Peru)	None	None	None	None	None	None	None
Tetsuo Hatanaka	Emergency Life Saving Technique Academy (Japan)	None	None	None	None	None	None	None
Mary Fran Hazinski	Vanderbilt University	None	None	None	None	None	American Heart Association†	None
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(*Continued*)

Appendix 1. Continued

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Jerry P. Nolan	Warwick Medical School (United Kingdom)	None	None	None	None	None	None	None
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Christopher M. Smith	University of Warwick, Warwick Medical School (United Kingdom)	Resuscitation Council UK (Grant of £23890 to conduct a simulation study into delivery of AEDs by drone. Awarded January 2020)*	None	None	None	None	None	None
Michael A. Smyth	University of Warwick (United Kingdom)	None	None	None	None	None	None	None
Christian Vaillancourt	University of Ottawa, The Ottawa Hospital (Canada)	Cardiac Arrhythmia Network of Canada (CANet) (PI on study on telecommunication-assisted CPR)†; Canadian Institutes of Health Research (Co-PI for Canadian Resuscitation Outcomes Consortium (CanROC))†; Heart and Stroke Foundation of Canada (Co-PI for Canadian Resuscitation Outcomes Consortium (CanROC))†	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.

Appendix 2. Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
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*Significant.

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Circulation

Adult Advanced Life Support

2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

ABSTRACT: This *2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations* for advanced life support includes updates on multiple advanced life support topics addressed with 3 different types of reviews. Topics were prioritized on the basis of both recent interest within the resuscitation community and the amount of new evidence available since any previous review. Systematic reviews addressed higher-priority topics, and included double-sequential defibrillation, intravenous versus intraosseous route for drug administration during cardiac arrest, point-of-care echocardiography for intra-arrest prognostication, cardiac arrest caused by pulmonary embolism, postresuscitation oxygenation and ventilation, prophylactic antibiotics after resuscitation, postresuscitation seizure prophylaxis and treatment, and neuroprognostication. New or updated treatment recommendations on these topics are presented. Scoping reviews were conducted for anticipatory charging and monitoring of physiological parameters during cardiopulmonary resuscitation. Topics for which systematic reviews and new Consensuses on Science With Treatment Recommendations were completed since 2015 are also summarized here. All remaining topics reviewed were addressed with evidence updates to identify any new evidence and to help determine which topics should be the highest priority for systematic reviews in the next 1 to 2 years.

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Key Words: AHA Scientific Statements ■ cardiopulmonary arrest ■ cardiopulmonary resuscitation and emergency cardiac care ■ echocardiography ■ post–cardiac arrest care ■ prognostication ■ sudden cardiac arrest ■ ventricular fibrillation

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CONTENTS

OVERVIEW

The *International Consensus on Cardiopulmonary Resuscitation (*CPR) *and Emergency Cardiovascular Care* (ECC) *Science With Treatment Recommendations* (CoSTR) is the fourth in a series of annual International Liaison Committee on Resuscitation (ILCOR) publications. This 2020 CoSTR for advanced life support (ALS) includes new topics addressed by systematic reviews performed within the past 12 months and prioritized by the ALS Task Force. In addition, it includes updates of the ALS treatment recommendations that were

published from 2010 through 2019,[1–8] as needed, and were based on additional evidence evaluations. As a result, this 2020 CoSTR for ALS is the most comprehensive update since 2010. The 3 major types of evidence evaluation supporting this 2020 publication are the systematic review (SysRev), the scoping review (ScopRev), and the evidence update (EvUp).

The SysRev is a rigorous process following strict methodology to answer a specific question, and each of these ultimately resulted in generation of the task force CoSTR included in this publication. The SysRevs were performed by a Knowledge Synthesis Unit, an Expert Systematic Reviewer, or by the ALS Task Force, and many resulted in separate published SysRevs.

To begin the SysRev, the question to be answered was phrased in terms of the population, intervention, comparator, outcome, study design, time frame (PICOST) format. The methodology used to *identify* the evidence was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[9] The approach used to *evaluate* the evidence was based on the one proposed by the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) working group.[10] Using this approach, the task force rated as high, moderate, low, or very low the certainty/confidence in the estimates of effect of an intervention or assessment across a body of evidence for each of the predefined outcomes. Randomized controlled trials (RCTs) generally began the analysis as high-certainty evidence, and observational studies generally began the analysis as low-certainty evidence; examination of the evidence by using the GRADE approach could result in downgrading or upgrading of the certainty of evidence. For additional information, refer to "Part 2: Evidence Evaluation Process and Guidelines Development in this supplement."[11,11a]

When we have quoted unchanged treatment recommendations from the 2010 CoSTR, the language used differs from that in the GRADE approach because GRADE was not used before 2015.[12,13]

Draft 2020 CoSTRs for ALS were posted on the ILCOR website[14] for public comment between January 3 and January 4, 2020, with comments accepted through January 18, 2020. These new draft 2020 CoSTR statements for ALS were viewed a total of 4205 times with 11 comments received.

This summary statement contains the final wording of the CoSTR statements as approved by the ILCOR task forces and by the ILCOR member councils after review and consideration of comments posted online in response to the draft 2020 CoSTRs. Within this publication, each topic includes the PICOST as well as the CoSTR, an expanded Justification and Evidence-to-Decision Framework Highlights section, and a list of knowledge gaps requiring future research studies. An evidence-to-decision table is included for each CoSTR in Appendix A in the Supplemental Materials of this publication.

The second major type of evidence evaluation performed to support this 2020 CoSTR for ALS is a ScopRev, which identifies the extent, range, and nature of evidence on a topic or a question. The ScopRevs were performed by topic experts in consultation with the ALS Task Force. The task force analyzed the identified evidence and determined its value and implications for resuscitation practice or research. The rationale for the ScopRev, the summary of evidence, and task force insights are all highlighted in the body of this publication. The most recent treatment recommendation is included. The task force notes whether the ScopRev identified substantive evidence that may result in a change in ILCOR treatment recommendations. If sufficient evidence was identified, the task force suggested consideration of a future systematic review to supply sufficient detail to support the development of an updated CoSTR. All ScopRevs are included in their entirety in Appendix B in the Supplemental Materials of this publication.

The third type of evidence evaluation supporting this 2020 CoSTR for ALS is an EvUp. EvUps are generally performed for topics previously reviewed by ILCOR to identify new studies published after the most recent ILCOR evidence evaluation, typically through use of search terms and methodologies from previous reviews. These EvUps were performed by task force members, collaborating experts, or by members of council writing groups. The EvUps are cited in the body of this publication with reiteration of the original PICOST (if available) and a note as to whether the evidence suggested the need to consider a SysRev; the existing ILCOR treatment recommendation is quoted. In this publication, no change in ILCOR treatment recommendations resulted from an EvUp; if substantial new evidence was identified, the task force recommended consideration of a SysRev. All EvUps are included in Appendix C in the Supplemental Materials of this publication.

The ALS Task Force considered the availability of new evidence as well as the evidence needed to create, confirm, or revise treatment recommendations. The chapter topics are organized in sections according to the approximate order of the steps of resuscitation, postresuscitation care, and prognostication. For each reviewed topic, the method of review (SysRev, ScopRev, EvUp) is clearly labeled, with links to the relevant review documents in the Appendix.

TOPICS REVIEWED IN THIS 2020 ALS CoSTR

Note: As indicated above, the ALS CoSTR evidence reviews were all completed by January 18, 2020. As a result, this document does not address the topic of

potential influence of coronavirus disease 2019 (COVID-19) on resuscitation practice. In the spring of 2020, an ILCOR writing group was assembled to identify and evaluate the published evidence regarding risks of aerosol generation and infection transmission during attempted resuscitation of adults, children, and infants. This group developed a consensus on science with treatment recommendations and task force insights. This statement is published as a separate document.[15] As new evidence emerges, the ILCOR task forces will review and update this statement, so the reader is referred to the ILCOR website[14] for the most up-to-date recommendations.

Defibrillation Strategies for Ventricular Fibrillation or Pulseless Ventricular Tachycardia

- Anticipatory defibrillator charging (ALS 2001: ScopRev)
- Double sequential defibrillation (ALS 2003: SysRev)
- Automated external defibrillator versus manual defibrillator (ALS 495: EvUp)
- Waveform analysis for predicting successful defibrillation (ALS 601: EvUp)

Airway, Oxygenation, and Ventilation During CPR

- Airway management during cardiac arrest (ALS 576, 783, 432, 496, 711, 714: 2019 SysRev, CoSTR update)
- Confirmation of correct tracheal tube placement (ALS 469: EvUp)
- Oxygen dose during CPR (ALS 889: EvUp)
- Automatic ventilators versus manual ventilation during CPR (ALS 490: EvUp)

Circulatory Support During CPR

- ECPR versus manual or mechanical CPR (ALS 723: 2018 SysRev, 2019 CoSTR)

Physiological Monitoring During CPR

- Monitoring physiological parameters during CPR (ALS 656: Adopted From Pediatric Task Force ScopRev)

Drugs During CPR, Including Timing of Administration

- Vasopressors during cardiac arrest (ALS 788, 659, 789, 784, 778: 2019 SysRev, CoSTR)
- Antiarrhythmic drugs for cardiac arrest (ALS 428, 493: 2018 SysRev, CoSTR)
- Intravenous versus intraosseous drug delivery (ALS 2046: SysRev)
- Steroids during cardiac arrest (ALS 433: EvUp)
- Buffering agents for cardiac arrest (ALS 483: EvUp)
- Drugs for torsades de pointes (ALS 457: EvUp)

Intra-arrest Prognostication

- Point-of-care echocardiography for prognostication during CPR (ALS 658: SysRev)
- $ETCO_2$ to predict outcome of cardiac arrest (ALS 459: EvUp)

Cardiac Arrest in Special Circumstances

- Cardiac arrest associated with pulmonary embolism (ALS 435, 581: SysRev)
- Cardiac arrest in pregnancy (ALS 436: EvUp)
- Opioid toxicity (ALS 441: EvUp)

Postresuscitation Care

- Oxygen dose after return of spontaneous circulation (ROSC) in adults (ALS 448: SysRev)
- Ventilation strategy after ROSC in adults (ALS 571: SysRev)
- Postresuscitation hemodynamic support (ALS 570: EvUp)
- Postresuscitation steroids (ALS 446: EvUp)
- Prophylactic antibiotics after cardiac arrest (ALS 2000: SysRev)
- Post–cardiac arrest seizure prophylaxis and treatment (ALS 431, 868: SysRev)
- Targeted temperature management (ALS 455, 790, 791, 802, 879: EvUp)

Prognostication in Comatose Patients After Resuscitation From Cardiac Arrest

- Clinical examination for prognostication (ALS 450, 713, 487: SysRev)
- Neurophysiological tests for prognostication (ALS 450, 713, 460: SysRev)
- Blood biomarkers for prognostication (ALS 450, 713, 484: SysRev)
- Imaging for prognostication (ALS 450, 713, 458: SysRev)

DEFIBRILLATION STRATEGIES FOR VENTRICULAR FIBRILLATION OR PULSELESS VENTRICULAR TACHYCARDIA

The task force restricted its review to 2 new topics that were based on trends in current clinical practice. These deal primarily with manual defibrillation in adults. The CoSTRs for the use of automated external defibrillators for adults can be found in Adult Basic Life Support, and for infants and children in Pediatric Life Support.

Anticipatory Defibrillator Charging (ALS 2001: ScopRev)

Rationale for Review

This topic was chosen because the timing of the rhythm check in relation to manual defibrillator charging varies by country and region. The standard method described in the *2010 American Heart Association Guidelines for CPR and ECC*[16] and the 2015 European Resuscitation Guidelines[17] consists of briefly pausing compressions to analyze the rhythm then resuming compressions while charging the defibrillator, then pausing compressions

briefly to deliver the shock. With the anticipatory method, the defibrillator is charged near the end of a compression cycle but before the rhythm is checked; then, compressions are paused briefly both to analyze the rhythm and deliver a shock. The ScopRev methodology was chosen given the limited published evidence.[18]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults with cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: Charging the defibrillator before rhythm analysis during manual defibrillation
- Comparator: Charging the defibrillator after rhythm analysis during manual defibrillation
- Outcome: Survival with favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC were defined as critical or important outcomes. Other outcomes were termination of arrhythmia, defibrillation success, preshock pause, postshock pause, perishock pause, hands-off time, hands-on time, compression fraction, inappropriate shocks, shocks during chest compression (shock to rescuer), or any other defibrillation measure.
- Study design: Human and manikin studies were included. 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. In addition, gray literature (evidence not published in traditional journals) was included in this ScopRev.[19,20]
- Time frame: All years and languages were included. Studies without a title in English were excluded. MEDLINE, Embase, and Cochrane databases were updated to October 7, 2019.

Summary of Evidence

We identified no clinical studies addressing the critical or important outcomes specified in the PICOST question. Three manikin and 1 multicenter retrospective human study were identified. In the only human study,[21] both methods resulted in relatively short pre- and postshock pauses, whereas anticipatory charging was associated with a shorter total hands-off time in the 30 seconds preceding shock delivery. The results of the 3 manikin studies showed reduced overall pause duration during the compression cycle, but increased pre, post, and perishock pause duration with anticipatory charging.[22–24]

Task Force Insights

The ScopRev is included in Supplement Appendix B-1. The task force noted that although anticipatory charging can reduce overall chest compression pause duration during the compression cycle, it can increase pre, post, and perishock pause duration. The clinical relevance of these findings is undetermined. Further high-quality evidence is required to evaluate the relative importance of the different types of pause duration for critical and important patient outcomes, and the role of new defibrillator technologies and methods. There are insufficient data for a SysRev to be of use at this time.

Treatment Recommendation

There was no treatment recommendation on timing of defibrillator charging previously, and in the absence of sufficient evidence, none was added.

Double Sequential Defibrillation (ALS 2003: SysRev)

Rationale for Review

This is a new topic in response to the increasing use of double (dual) sequential defibrillation (DSD). At least 20% of patients with ventricular fibrillation (VF)/pulseless ventricular tachycardia (pVT) will remain in a shockable rhythm after 3 shocks.[25–28] Survival decreases as the number of defibrillation attempts required increases. DSD, or the use of 2 defibrillators to deliver 2 overlapping shocks or 2 rapid sequential shocks, one with standard pad placement and the other with either anteroposterior or additional anterolateral pad placement, has been suggested as a possible means of increasing VF termination rates.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults with cardiac arrest in any setting (in-hospital or out-of-hospital) with a shockable rhythm
- Intervention: DSD
- Comparator: Standard defibrillation
- Outcome: Favorable neurological outcome at hospital discharge, survival to hospital discharge or admission, ROSC, or termination of VF
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies with 5 patients or more) are eligible for inclusion.
- Time frame: There was no date restriction, and the literature search was updated to September 27, 2019.
- International Prospective Register of Systematic Reviews (PROSPERO) Registration: CRD42020152575

Consensus on Science

For the critical outcomes of survival with favorable neurological outcome[29–31] and survival to hospital discharge[29–34] and the important outcomes of survival to hospital admission,[29,30,32,33] ROSC,[29–35] and termination of VF,[31,34,35] we identified only observational studies. The overall certainty of evidence was rated as very low for all outcomes, primarily because of a very serious risk

of bias. The individual studies were all at a critical or serious risk of bias because of confounding (due to inadequate adjustment for cardiac arrest characteristics and other factors). Because of this and a high degree of heterogeneity, no meta-analyses could be performed, and individual studies were difficult to interpret.[36]

Treatment Recommendation

We suggest against routine use of a DSD strategy in comparison with a standard defibrillation strategy for cardiac arrest with a shockable rhythm (weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-1. There is no strong evidence to favor one intervention compared with the other. The evidence available (very low certainty) suggests lower rates of survival and neurological outcome for patients treated with DSD, but any odds ratios (ORs) or other results reported are difficult to interpret given the very high risk of bias.[36] There is no consensus standardized approach to double defibrillation, in that a double-dose strategy could be 2 overlapping shocks or 2 sequential shocks. The ALS Task Force discussed whether any potential benefit might arise from increased shock energy, the fact that 2 shocks were delivered sequentially, different pad placement and vector for the second shock, or some other reason. The task force is aware of recently published data from a small pilot RCT comparing standard defibrillation to DSD (adding a second set of defibrillator pads in the anteroposterior position) or to vector change defibrillation (replacing anterolateral pads with anteroposterior pads).[37] The study found differences in VF termination (DSD 76%, vector change 82%, and standard placement 66%) and ROSC (DSD 40%, vector change 39%, and standard defibrillation 25%). This pilot RCT was not designed to formally test differences between the groups, and no survival data were reported. These results have informed a larger, ongoing RCT (NCT04080986) that will provide further data about DSD.

Implementation of DSD requires training of staff and availability of defibrillators. It is important to monitor the intervention to determine effectiveness, and to track adverse events such as harm to the patient, defibrillator damage, and the increase in resource utilization.

Knowledge Gap

- High-quality studies comparing DSD with standard defibrillation in terms of survival and neurological outcome at hospital discharge

Automated External Defibrillator Versus Manual Defibrillator (ALS 495: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Adults who are in cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: Use of an automated external defibrillator or a multifunctional defibrillator in automatic mode
- Comparator: Standard resuscitation (using a manual defibrillator)
- Outcome: Favorable neurological outcome at hospital discharge, survival to hospital discharge or admission, ROSC, or termination of VF
- This topic was last reviewed in 2010.[43,44] The evidence update is included in Supplement Appendix C-1 and the search conducted was limited to January 2008 to December 2019. We identified 5 observational studies (only 2 of which included a comparison group) and no randomized trials.[38–42] After consideration, a SysRev was not suggested.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[43,44]

No significant survival differences have been demonstrated between defibrillation in semiautomatic and manual modes during out-of-hospital or in-hospital resuscitation; however, the semiautomatic mode is preferred because it is easier to use and may deliver fewer inappropriate shocks.

Trained personnel may deliver defibrillation in manual mode. Use of the manual mode enables chest compressions to be continued during charging, thereby minimizing the preshock pause. When using the defibrillator in manual mode, frequent team training and ECG recognition skills are essential.

The defibrillation mode that results in the best outcome will be influenced by the system of care and by provider skills, training, and ECG recognition.

Waveform Analysis for Predicting Successful Defibrillation (ALS 601: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Adults with cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: Use of techniques for prediction of the likelihood of success of defibrillation (analysis of VF, etc)
- Comparator: Standard resuscitation (without such prediction)
- Outcome: Survival with favorable neurological/functional outcome at discharge, 30 days, 60 days,

180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC; termination of VF
- This topic was last reviewed in 2010.[43,44] Two EvUps were completed for 2020 and are included in Supplement Appendix C-2a and C-2b. The evidence updates restricted the search to January 2008 to January 2020 and identified one large RCT conducted in 2013[45] and 20 observational studies.[46–65] In addition, there is an ongoing multicenter RCT of real-time amplitude spectrum area to guide defibrillation (NCT03237910). Although the VF waveform analyses and outcomes studied were highly heterogeneous, given the amount of data available, an updated SysRev was suggested.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[43,44]

There is insufficient evidence to support routine use of VF waveform analysis to guide defibrillation management in adult cardiac arrest in- or out-of-hospital.

AIRWAY, OXYGENATION, AND VENTILATION DURING CPR

Airway Management During Cardiac Arrest (ALS 576, 783, 432, 496, 711, 714: 2019 SysRev, CoSTR Update)

Airway management during cardiac arrest was addressed by a 2019 SysRev[66] and a 2019 CoSTR summary.[2,3] Consensus on science, justification and evidence-to-decision highlights, and knowledge gaps can be found in the 2019 CoSTR summary.[2,3]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults with cardiac arrest from any cause and in any setting (in-hospital or out-of-hospital)
- Intervention: A specific advanced airway management method (eg, tracheal intubation or a supraglottic airway) during cardiac arrest
- Comparator: A different advanced airway management method or no advanced airway management method (eg, bag-mask ventilation) during cardiac arrest
- Outcome: ROSC, survival, or survival with favorable neurological outcome at discharge/28 days or longer
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) that compared at least 2 airway strategies were eligible for inclusion. Studies with 10 or fewer patients in either group were excluded.
- Time frame: All years and languages were included; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to October 30, 2018.

Treatment Recommendations

We suggest using bag-mask ventilation or an advanced airway strategy during CPR for adults with cardiac arrest in any setting (weak recommendation, low to moderate certainty of evidence).

If an advanced airway is used, we suggest a supraglottic airway for adults with out-of-hospital cardiac arrest (OHCA) in settings with a low tracheal intubation success rate (weak recommendation, low-certainty evidence).

If an advanced airway is used, we suggest a supraglottic airway or tracheal intubation for adults with OHCA in settings with a high tracheal intubation success rate (weak recommendation, very low-certainty evidence).

If an advanced airway is used, we suggest a supraglottic airway or tracheal intubation for adults with in-hospital cardiac arrest (IHCA) (weak recommendation, very low-certainty evidence).[2,3]

Confirmation of Correct Tracheal Tube Placement (ALS 469: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Adults with cardiac arrest in any setting (in-hospital or out-of-hospital) requiring tracheal intubation
- Intervention: Use of devices (eg, waveform capnography, CO_2 detection device, esophageal detector device, or tracheal ultrasound)
- Comparator: Not using these devices
- Outcome: Tracheal intubation success
- This topic was last reviewed in 2015.[1,7] This EvUp is included in Supplement Appendix C-3. An updated SysRev was not considered necessary.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[1,7]

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).

We recommend that if waveform capnography is not available, a nonwaveform CO_2 detector, esophageal detector device, or ultrasound in addition to clinical assessment is an alternative (strong recommendation, low-quality evidence).[1,7]

Oxygen Dose During CPR (ALS 889: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Adults with cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: Administering a maximal oxygen concentration (eg, 100% by face mask or closed circuit)
- Comparator: No supplemental oxygen (room air) or an alternative supplemental oxygen concentration (eg, 40% to 50%)
- Outcome: Survival with favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC
- This topic was last reviewed in 2015.[1,7] This EvUp is included in Supplement Appendix C-4 and the search was conducted from October 30, 2013, to December 2, 2019. The search identified 2 observational studies relevant to this topic published since 2015.[67,68] There are no adult studies of oxygen titration during CPR. An updated SysRev was not considered necessary.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[1,7]

We suggest using the highest possible inspired oxygen concentration during CPR (weak recommendation, very low-certainty evidence).

Automatic Ventilators Versus Manual Ventilation During CPR (ALS 490: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Adults and children in cardiac arrest in any setting (in-hospital or out-of-hospital) and who have advanced airways in place
- Intervention: The use of automatic ventilators
- Comparator: Use of manual ventilation
- Outcome: Ventilation, oxygenation, hands-off time, continuous compressions, survival
- This topic was last reviewed in 2010.[6,8] An evidence update is included in Supplement Appendix C-5. A search restricted to January 1, 2008, to December 7, 2019, identified 1 very small RCT and 3 observational studies.[69–72] An updated SysRev was not considered necessary.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[6,8]

There is insufficient evidence to support or refute the use of an automatic transport ventilator over manual ventilation during resuscitation of the cardiac arrest victim with an advanced airway.

CIRCULATORY SUPPORT DURING CPR

ECPR Versus Manual or Mechanical CPR (ALS 723: 2018 SysRev, 2019 CoSTR)

Extracorporeal CPR (ECPR) was addressed by a 2018 SysRev[73] and a 2019 published CoSTR summary.[2,3] Consensus on Science, Values, Preferences, and Task Force Insights and Knowledge Gaps can be found in the 2019 CoSTR summary.[2,3]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults (18 years or older) and children (younger than 18 years) with cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: ECPR, including extracorporeal membrane oxygenation or cardiopulmonary bypass, during cardiac arrest
- Comparator: Manual CPR and/or mechanical CPR
- Outcome: Short-term survival and neurological outcomes (eg, hospital discharge, 28 days, 30 days, and 1 month) and long-term survival and neurological outcomes (eg, 3 months, 6 months, and 1 year)
- Study design: Randomized trials, non-RCTs, and observational studies (cohort studies and case-control studies) with a control group were included. Animal studies, ecological studies, case series, case reports, reviews, abstracts, editorials, comments, and letters to the editor were not included.
- Time frame: All years and languages were included up to May 22, 2018.

Treatment Recommendations

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).[2,3]

PHYSIOLOGICAL MONITORING DURING CPR

The ability to monitor physiological variables and tailor ALS interventions to the patient's precise physiological state is appealing and hence the ongoing interest in this area.

Monitoring Physiological Parameters During CPR (ALS 656: Adopted From Pediatric Task Force ScopRev)

Rationale for Review

Physiological monitoring during CPR, including measurement of end-tidal CO_2 ($ETCO_2$) and arterial blood pressure among other parameters, is growing in popularity. There is limited evidence to-date on whether use of such parameters improves outcomes. This topic was last updated in 2015.[1,7] A Pediatric Task Force ScopRev of physiological monitoring during CPR for 2020 also included review of the adult evidence. The adult portion of the ScopRev was included in this update.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults who are in cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: The use of physiological feedback in regard to CPR quality (eg, arterial catheter, $ETCO_2$ monitoring, Spo_2 waveforms, or others)
- Comparator: No use of physiological feedback
- Outcome: Survival with favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies). If it is anticipated that there will be insufficient studies from which to draw a conclusion, case series may be included. The minimum number of cases for a case series to be included was set by the task-force at 5. Unpublished studies (eg, conference abstracts, trial protocols) are excluded.
- Time frame: For Step 1, all languages are included if there is an English abstract. We searched articles from 2015 onward. For Step 2, if a SysRev or ScopRev of high quality (as per AMSTAR 2 tool: https://amstar.ca/Amstar-2.php) is identified, the search can be limited to beyond data and/or scope of that review.

Summary of Evidence

$ETCO_2$ or Arterial Blood Pressure Monitoring

The ScopRev is included in Supplement Appendix B-2a and 2b. We identified 1 observational propensity-matched cohort study of adult IHCA by using data from the AHA Get With the Guidelines-Resuscitation registry.[74] In this study, 3032 physiologically monitored patients (either by $ETCO_2$ or arterial catheter) were compared with 6064 patients without such monitoring. Those monitored showed a higher rate of ROSC (OR, 1.22 [95% CI, 1.04; 1.43]) but not survival to discharge (OR, 1.04 [95% CI, 0.91; 1.18]) nor survival with favorable neurological outcome. The study did not specifically look at diastolic blood pressure. Even when an arterial catheter was in place, only about one third reported using the diastolic blood pressure to guide their CPR efforts.

Near-Infrared Spectroscopy

The ScopRev is included in Supplement Appendix B-2c. Two SysRevs were identified; the latest was published in 2018 and comprised studies published before February 2017. The SysRevs concluded that a higher cerebral oxygen saturation measured with near-infrared spectroscopy (NIRS) is associated with a higher chance of ROSC and survival and a lower NIRS is associated with an increased mortality.[75,76] However, there is no consensus on specific thresholds of cerebral oxygen saturation.[75] There was a wide overlap of mean or median cerebral oxygen saturation values between patients with and without ROSC, and this was also reflected in the cohort studies.[77–79] Only 1 observational study[80] compared the rates of ROSC with and without NIRS monitoring and found no difference between the groups. All other studies compared NIRS values in patients who achieved ROSC with those without ROSC. Many different NIRS devices with noninterchangeable saturation indices were used across the studies, complicating comparisons.[81] The findings of the observational studies published since February 2017 correlate with those published in both SysRevs.

The ScopRev did not suggest the existence of sufficient new data to proceed to a SysRev.

Task Force Insights

Physiological monitoring during CPR is increasingly popular and potentially useful for both outcome prediction and real-time improvement in CPR quality. The heterogeneity and observational nature of available studies continues to limit the task force's ability to make specific recommendations. The 2015 treatment recommendation is therefore unchanged.[1,7]

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[1,7]

We make no treatment recommendation for any particular physiological measure to guide CPR because the available evidence would make any estimate of effect speculative.

DRUGS DURING CPR, INCLUDING TIMING OF ADMINISTRATION

Since the 2015 CoSTR, there have been RCTs of antiarrhythmics and vasopressors during CPR[82,83] and subsequent publications comparing the intravenous (IV) and intraosseous (IO) route for drugs.[84,85]

Vasopressors During Cardiac Arrest (ALS 788, 659, 789, 784, 778: 2019 SysRev, 2019 CoSTR)

The topic of vasopressors during cardiac arrest was addressed by a 2019 SysRev[86] and a published CoSTR summary. Consensus on science, justification and evidence to decision highlights, and knowledge gaps can be found in the 2019 CoSTR summary.[2,3]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults (older than 18 years) with cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: Any vasopressor or combination of vasopressors provided intravenously or intraosseously during CPR
- Comparator: No vasopressor, a different vasopressor, or a combination of vasopressors provided intravenously or intraosseously during CPR
- Outcome: Short-term survival (ROSC and survival to hospital admission), midterm survival (survival to hospital discharge, 28 days, 30 days, or 1 month), midterm favorable neurological outcomes (Cerebral Performance Category [CPC] 1–2 or modified Rankin Scale [mRS] score 0–3 at hospital discharge, 28 days, 30 days, or 1 month), and long-term unfavorable and poor (mRS score 4–5) neurological outcomes (after 1 month)
- Study design: Randomized trials, nonrandomized trials, and observational studies (cohort and case-control studies) with a comparison group were included.
- Time frame: All years and languages were included if there was an English abstract to November 23, 2018.

Treatment Recommendations

We recommend administration of epinephrine during CPR (strong recommendation, low to moderate certainty of evidence).

For nonshockable rhythms (pulseless electric activity/asystole), we recommend administration of epinephrine as soon as feasible during CPR (strong recommendation, very low-certainty evidence).

For shockable rhythms (VF/pVT), we suggest administration of epinephrine after initial defibrillation attempts are unsuccessful during CPR (weak recommendation, very low-certainty evidence).

We suggest against the administration of vasopressin in place of epinephrine during CPR (weak recommendation, very low-certainty evidence).

We suggest against the addition of vasopressin to epinephrine during CPR (weak recommendation, low-certainty evidence).[2,3]

Additional Task Force Commentary

Concerns have been expressed about epinephrine increasing the number of survivors with unfavorable neurological outcome in the PARAMEDIC2 trial (Pre-Hospital Assessment of the Role of Adrenaline: Measuring the Effectiveness of Drug Administration in Cardiac Arrest). The opinion of the ALS Task Force, however, is that any drug that increases the rate of ROSC and survival, but is given after several minutes of cardiac arrest when some degree of neurological damage may already have occurred, will likely increase the number of survivors with both favorable and unfavorable neurological outcome. Determining the likelihood of favorable or unfavorable neurological outcome at the time of starting resuscitation is currently not feasible. Therefore, the task force consensus is that continuing to use a drug that increases survival and focusing efforts on providing earlier CPR, earlier drug administration, and improved postresuscitation care for all patients is likely to increase survival with a favorable neurological outcome.

Antiarrhythmic Drugs for Cardiac Arrest (ALS 428, 493: 2018 SysRev, CoSTR)

This topic was addressed by a 2018 SysRev[87] and a published 2018 CoSTR summary.[4,5] Consensus on Science, Values and Preferences, Task Force Insights, and Knowledge Gaps can be found in the 2018 CoSTR summary.[4,5]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children in cardiac arrest in any setting (in-hospital or out-of-hospital) and a shockable rhythm at any time during CPR or immediately after ROSC
- Intervention: Administration (intravenously or intraosseously) of an antiarrhythmic drug during CPR or immediately (within 1 hour) after ROSC
- Comparator: Administration of another antiarrhythmic drug or placebo or no drug during CPR or immediately after ROSC
- Outcome: Survival to hospital discharge with good neurologic outcome and survival to hospital discharge were ranked as critical outcomes. ROSC was ranked as an important outcome. For antiarrhythmic drugs after ROSC, rearrest was included as an important outcome.
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion.
- Time frame: All years and languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to August 15, 2017.

Treatment Recommendations

We suggest the use of amiodarone or lidocaine in adults with shock-refractory VF/pVT (weak recommendation, low certainty evidence).

We suggest against the routine use of magnesium in adults with shock-refractory VF/pVT (weak recommendation, very low-certainty evidence).

The confidence in effect estimates is currently too low to support an ALS Task Force recommendation about the use of bretylium, nifekalant, or sotalol in the treatment of adults in cardiac arrest with shock refractory VF/pVT.

The confidence in effect estimates is currently too low to support an ALS Task Force recommendation about the use of prophylactic antiarrhythmic drugs immediately after ROSC in adults with VF/pVT cardiac arrest.[4,5]

IV Versus IO Drug Delivery (ALS 2046: SysRev)

Rationale for Review

This is a new ALS question that was based on the increasing use of IO access during adult resuscitation. It can often be difficult to obtain IV access, especially in the prehospital setting. IO access as an alternative to IV access is increasingly used during cardiac arrest. However, whether drugs are as effective when administered intraosseously versus intravenously is unknown. This 2020 CoSTR is informed by a 2020 SysRev.[88]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults with cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: Placement of an IO cannula and drug administration through this IO during cardiac arrest
- Comparator: Placement of an IV cannula and drug administration through this IV during cardiac arrest
- Outcome: ROSC, or survival/survival with a favorable neurological outcome at hospital discharge, 30 days, or longer
- Study design: Randomized trials, non-RCTs, and observational studies (cohort studies and case-control studies) comparing IO with IV administration of drugs were included. Randomized trials assessing the effect of specific drugs (ie, epinephrine and amiodarone/lidocaine) in subgroups related to IO versus IV administration were also included. Ecological studies, case series, case reports, reviews, abstracts, editorials, comments, letters to the editor, and unpublished studies were not included. Studies assessing cost-effectiveness were included for a descriptive summary.
- Time frame: The literature search was performed on September 12, 2019, and updated on December 17, 2019, with no date restrictions.
- PROSPERO Registration: CRD42020150877

Consensus on Science

For the important outcome of ROSC, we identified very low-certainty evidence (downgraded for risk of bias and inconsistency) from 4 observational studies[89–92] including 70419 adults with OHCA, demonstrating an association of worse outcomes with the use of IO access when compared with IV access (adjusted OR, 0.72 [95% CI, 0.68–0.76]; *P*<0.00001; absolute risk difference, –6.1% [95% CI, –7.1 to –5.2] or 61 fewer per 1000 cardiac arrests had ROSC with IO access compared with IV access [95% CI, 71 fewer to 52 fewer]).

For the critical outcome of survival to hospital discharge, we identified very low-certainty evidence (downgraded for risk of bias and inconsistency) from 4 observational studies[89–92] including 70419 adult OHCAs, demonstrating an association of worse outcomes with the use of IO access when compared with IV access (adjusted OR, 0.71 [95% CI, 0.63–0.79]; *P*<0.00001; absolute risk difference, –2.0% [95% CI, –2.5 to –1.4] or 20 fewer per 1000 cardiac arrests with survival to hospital discharge with use of IO access compared with IV access [95% CI, 25 fewer to 14 fewer]).

For the critical outcome of survival to hospital discharge with a favorable neurological outcome, we identified very low-certainty evidence (downgraded for risk of bias and inconsistency) from 3 observational studies[89,91,92] including 68619 adult OHCAs, demonstrating an association of worse outcomes with the use of IO access when compared with IV access (adjusted OR, 0.60 [95% CI, 0.52–0.69]; *P*<0.00001; absolute risk difference, –1.9% [95% CI, –2.3 to –1.5] or 19 fewer per 1000 cardiac arrests with survival to hospital discharge with a favorable neurological outcome with use of IO access compared with IV access [95% CI, 23 fewer to 15 fewer]).

In addition to these findings from observational studies, we identified 2 RCTs of drug administration during cardiac arrest that performed subgroup analyses according to IO versus IV route of administration.[84,85] None of the comparisons showed statistically significant effect modification. The point estimates generally favored IV access as compared with IO access, except for the outcome of ROSC in the PARAMEDIC2 trial where the effect of epinephrine was similar when given IV or IO. These 2 trials were underpowered to assess such interactions for any outcomes other than ROSC.

Treatment Recommendations

We suggest IV access as compared with IO access as the first attempt for drug administration during adult cardiac arrest (weak recommendation, very low-certainty evidence).

If attempts at IV access are unsuccessful or IV access is not feasible, we suggest IO access as a route for drug administration during adult cardiac arrest (weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-2. Although the overall certainty in the evidence is very low, the current evidence suggests that outcomes might be better with IV versus IO drug administration. The task force discussed the possibility of unaccounted-for confounders in comparing patients for whom an IV could be obtained with those who required IO placement for access. The task force also discussed that 2015 council guidelines suggest that IO access should be used only if IV access is "difficult or impossible"[17] or "not readily available."[93] The included studies did not enable meaningful analyses of specific subgroups. The documented IO site was primarily tibial, but the site was often not documented. As such, no statements can be made about difference between tibial and humeral (or other) IO sites. All studies were conducted in OHCA patients. Although IHCA patients are likely to have existing IV access, this is not universally true. Although there might be differences in provider skills and patient characteristics between OHCA and IHCA, we consider it unlikely that these would lead to substantial effect modification. As such, the above recommendations apply to both IHCA and OHCA.

Knowledge Gap

- The overall certainty in the evidence is very low. As such, there is clinical equipoise for additional trials related to IV versus IO drug administration during cardiac arrest. These could include trials that directly compare IV to different sites of IO access (eg, tibial, humeral).

Steroids During CPR (ALS 433: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Adults who are in cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: Corticosteroid or mineralocorticoid administration during CPR
- Comparator: Not using steroids
- Outcome: Survival with favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC
- Intra-arrest steroid use was last reviewed in 2015.[1,7] The EvUp for intra-arrest steroid use is included in Supplement Appendix C-6. The search identified 2 large, population-based observational studies published since the 2015 CoSTR,[94,95] both of which suggest a possible association between the use of corticosteroids during CPR and improved survival. Three ongoing clinical trials on this topic were also identified (NCT02790788, NCT03640949, NCT03317197). The task force will prioritize a SysRev when the results of these trials become available.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[1,7]

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).

Buffering Agents for Cardiac Arrest (ALS 483: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Adults with cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: The use of buffering agents alone or combination with other drugs
- Comparator: Not using drugs (or a standard drug regimen)
- Outcome: ROSC, survival, survival with favorable neurological outcome
- This topic was last reviewed in 2010.[6,8] An EvUp was completed for 2020 and is included in Supplement Appendix C-7. One small RCT and 4 observational studies were identified.[96–100] An updated SysRev was not considered necessary.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[6,8]

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

Drugs for Torsades de Pointes (ALS 457: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Adults with torsades de pointes in any setting (in-hospital or out-of-hospital)
- Intervention: Any drug or combination of drugs
- Comparator: Not using drugs or alternative drugs
- Outcome: ROSC, survival, or survival with favorable neurological outcome
- This PICO was last reviewed in 2010.[6,8] An EvUp is included in Supplement Appendix C-8. No studies meeting inclusion criteria were identified, and thus consideration of an updated SysRev was not suggested.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[6,8]

Polymorphic wide-complex tachycardia associated with familial long QT may be treated with IV magnesium, pacing, and/or beta blockers; however, isoprenaline should be avoided.

Polymorphic wide-complex tachycardia associated with acquired long QT may be treated with IV magnesium.

Addition of pacing or IV isoprenaline may be considered when polymorphic wide-complex tachycardia is accompanied by bradycardia or appears to be precipitated by pauses in rhythm.

INTRA-ARREST PROGNOSTICATION

Point-of-Care Echocardiography for Prognostication During CPR (ALS 658: SysRev)

Rationale for Review

In 2015, the question of whether the use of cardiac ultrasound during CPR changed outcomes was reviewed.[1,7] This question has not been reviewed for the 2020 CoSTR for ALS, and the 2015 CoSTR currently remains: We suggest that if cardiac ultrasound can be performed without interfering with standard advanced cardiovascular life support protocols, it may be considered as an additional diagnostic tool to identify potentially reversible causes (weak recommendation, very low-quality evidence).[1,7]

The current question is different from that mentioned above and was prioritized by the ALS Task Force due to the increasing popularity of the use of point-of-care echocardiography during cardiac arrest as a prognostic tool, as well as concern about potential pitfalls for misinterpretation of ultrasound findings. A task force–led SysRev of the intra-arrest prognostic capabilities of point-of-care echocardiography was performed to inform the 2020 CoSTR for ALS.[101]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults with cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: A particular finding on point-of-care echocardiography during CPR
- Comparator: The absence of that finding or a different finding on point-of-care echocardiography during CPR
- Outcome: Clinical outcomes include, but are not necessarily limited to, ROSC and survival to hospital admission (both important) and the critical outcomes of survival/survival with a favorable neurological outcome at hospital discharge and survival/survival with a favorable neurological outcome beyond hospital discharge.
- Study design: Randomized trials, non-RCTs, observational studies (cohort studies and case-control studies), registries, and prognosis studies. Ecological studies, case series, case reports, reviews, abstracts, editorials, comments, letters to the editor, or unpublished studies will not be included.
- Time frame: All years and languages were included if there was an English abstract, and there were no date restrictions. The literature search was updated to September 18, 2019.
- PROSPERO Registration: CRD42020150677.

Consensus on Science

The SysRev identified no RCTs and 15 relevant observational studies.[102–116] The overall certainty of evidence was rated as very low for all outcomes primarily due to risk of bias, inconsistency, and/or imprecision. There was a substantial risk of bias due to prognostic factor measurement, outcome measurement, adjustment for prognostic factors, or confounding. Because of this and a high degree of clinical heterogeneity, no meta-analyses could be performed, and individual studies are difficult to interpret. The consensus on science is summarized in Table 1. The summary of each outcome is separated by the ultrasonographic finding (organized contractility versus nonorganized and/or unspecified motion) and timing of image acquisition (initial, every, any, or subsequent evaluation; or unspecified) because these also varied considerably across studies.

Treatment Recommendation

We suggest against the use of point-of-care echocardiography for prognostication during CPR (weak recommendation, very low-certainty evidence)

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-3. This CoSTR specifically addresses the role of ultrasound in prognostication, and in particular prognostication of a favorable outcome that is based on the presence of cardiac motion. In 2015, the task force stated that ultrasound had a potential role in diagnosing reversible causes of cardiac arrest if it could be done without interfering with high-quality CPR, and this recommendation was not reassessed for 2020.[1,7]

Given the increasing popularity of the use of point-of-care echocardiography for prognostication during attempted resuscitation after cardiac arrest, this comprehensive and rigorous summary of its intra-arrest prognostic capabilities provides valuable information to both the resuscitation science community and bedside clinicians. In making these recommendations, the ALS Task Force considered the following:

Table 1. Estimated Prognostic Test Performance and Prognostic Association for Sonographic Findings on Point-of-Care Echocardiography During Cardiac Arrest to Predict Clinical Outcomes

Outcome	Author, Year	Total Subjects (n), IHCA or OHCA	Sensitivity (Range or 95% CI)	Specificity (Range or 95% CI)	Odds Ratio (Range or 95% CI)
Organized Cardiac Motion (Unspecified Timing of Echocardiography)					
Survival 180 d	Flato, 2015[113]	49, IHCA	1.0 (95% CI, 0.4–1.0)	0.49 (95% CI, 0.34–0.64)	8.62 (95% CI, 0.44–169.38)
Survival to hospital discharge	Atkinson, 2019[108] Flato, 2015[113]	229, IHCA and OHCA	0.67–1.00	0.51–0.89	13.60–16.63
Survival to hospital admission	Atkinson, 2019[108] Blaivas, 2001[109]	349, OHCA	0.39–1.00	0.91–0.91	6.73–414.56
ROSC	Atkinson, 2019[108] Flato, 2015[113]	229, IHCA and OHCA	0.34–0.79	0.68–0.96	8.07–13.21
Nonorganized and/or Unspecified Cardiac Motion on Initial Echocardiogram					
Good neurological outcome at discharge	Aichinger, 2012[107]	42, OHCA	1.00 (95% CI, 0.03–1.00)	0.78 (95% CI, 0.62–0.89)	10.26 (95% CI, 0.39–273.09)
Survival to hospital discharge	Gaspari, 2016[114] Varriale, 1997[106] Zengin, 2016[116]	1171,† IHCA and OHCA	0.06–0.91	0.49–0.94	0.38–17.00
Survival to hospital admission	Aichinger, 2012[107] Gaspari, 2016[114] Salen, 2001[104] Zengin, 2016[116]	1295,† IHCA and OHCA	0.11–0.92	0.55–0.85	0.75–27.56
ROSC	Gaspari, 2016[114] Kim, 2016[115] Varriale, 1997[106]	861, IHCA and OHCA	0.25–0.64	0.78–1.00	6.33–16.11
Nonorganized and/or Unspecified Cardiac Motion on Every Echocardiogram					
Survival to hospital admission	Aichinger, 2012[107] Salen, 2001[104]	134,* OHCA	0.50–0.80	0.92–1.00	45.33–148.20
Nonorganized and/or Unspecified Cardiac Motion (Unspecified Timing of Echocardiography)					
Good neurological outcome at 180 days	Flato, 2015[113]	49, IHCA	1.00 (95% CI, 0.40–1.00)	0.49 (95% CI, 0.34–0.64)	8.62 (95% CI, 0.44–169.38)
Good neurological outcome at discharge	Salen, 2005[103]	70, OHCA	1.00 (95% CI, 0.03–1.00)	0.86 (95% CI, 0.75–0.93)	17.00 (95% CI, 0.65–446.02)
Survival to hospital discharge	Lien, 2018[102]	177, OHCA	0.48 (95% CI, 0.28–0.69)	0.77 (95% CI, 0.69–0.83)	3.09 (95% CI, 1.29–7.37)
Survival to hospital admission	Breitkreutz, 2010[110] Chua, 2017[112] Salen, 2001[104]	291,* OHCA	0.72–0.86	0.60–0.84	9.14–14.00
ROSC	Chardoli, 2012[111] Lien, 2018[102] Salen, 2005[103] Tayal, 2003[105]	317, OHCA	0.62–1.00	0.33–0.98	23.18–289.00
Return of Organized Cardiac Motion on Subsequent Echocardiogram					
Survival to hospital discharge	Varriale, 1997[106]	20, IHCA	0.50 (95% CI, 0.01–0.99)	0.79 (95% CI, 0.54–0.94)	3.75 (95% CI, 0.19–74.06)
ROSC	Varriale, 1997[106]	20, IHCA	0.67 (95% CI, 0.22–0.96)	1.00 (95% CI, 0.77–1.00)	52.50 (95% CI, 2.10–1300.33)
Coalescent Echo Contrast (ie, Visible Clotted Intra-Cardiac Blood) After 20–30 min of CPR					
Survival to hospital discharge	Varriale, 1997[106]	20, IHCA	0.00 (95% CI, 0.00–0.84)	0.45 (95% CI, 0.23–0.68)	0.13 (95% CI, 0.01–3.11)
ROSC	Varriale, 1997[106]	20, IHCA	0.00 (95% CI, 0.00–0.46)	0.21 (95% CI, 0.05–0.51)	0.02 (95% CI, 0.00–0.53)
Sonographic Evidence of Treatable Pathology					
Survival to hospital discharge	Gaspari, 2016[114] Varriale, 1997[106] Zengin, 2016[116]	1130,† IHCA and OHCA	0.00–0.15	0.89–0.98	1.32–4.25

(*Continued*)

Table 1. Continued

Outcome	Author, Year	Total Subjects (n), IHCA or OHCA	Sensitivity (Range or 95% CI)	Specificity (Range or 95% CI)	Odds Ratio (Range or 95% CI)
Survival to hospital admission	Zengin, 2016[116]	531,† IHCA and OHCA	0.03–0.04	0.95–0.99	0.61–4.70
ROSC	Chardoli, 2012[111] Lien, 2018[102] Tayal, 2003[105] Varriale, 1997[106]	317,† IHCA and OHCA	0.00–1.00	0.84–0.94	0.38–125.00

IHCA indicates in-hospital cardiac arrest; OHCA, out-of-hospital cardiac arrest; and ROSC, return of spontaneous circulation.
*Studies did not report these data for all enrolled subjects; n is lower than the total of all subjects enrolled.
†Gaspari et al and Zengin et al report multiple sonographic findings within a given category on the same subjects; n reflects composite variable "subject-assessments."

There were inconsistent definitions and terminology about the sonographic evidence of cardiac motion. This included wide variation in the classification of anatomy, type of motion, and timing of point-of-care echocardiogram. The task force encourages the establishment of uniform definitions and terminology to describe sonographic findings of cardiac activity during cardiac arrest.

Most of the identified studies suffer from high risk of bias related to prognostic factor measurement, outcome measurement, lack of adjustment for other prognostic factors, and confounding from self-fulfilling prophecy and unspecified timing of point-of-care echocardiography. Because the risk of bias and heterogeneity across studies was high, no meta-analyses were performed. The evidence supporting use of point-of-care echocardiography as a prognostic tool during cardiac arrest is uniformly of very low certainty. Clinicians should interpret sonographic findings during cardiac arrest in light of these limitations. The task force encourages subsequent investigators studying point-of-care echocardiography during cardiac arrest to identify methodology that mitigates these risks of bias.

Only 2 studies[113,114] reported estimates of inter-rater reliability (Kappa 0.63 and 0.93). More uniform reporting of inter-rater reliability of point-of-care echocardiography interpretation in future investigations is important.

No sonographic finding had sufficient and/or consistent sensitivity for any clinical outcome for its absence to be used as a sole criterion to stop resuscitation, but the certainty of this evidence is very low.

Some sonographic findings had higher ranges of specificity for clinical outcomes, but the certainty of this evidence is very low.

The impact of ECPR on the prognostic accuracy of point-of-care echocardiography is uncertain.

Point-of-care echocardiography may still be useful to diagnose treatable etiologies of cardiac arrest or to intermittently assess response to resuscitative treatments. These applications are not within the scope of this particular PICOST question. We do, however, caution against overinterpreting the finding of right-ventricular dilation in isolation as a diagnostic indicator of massive pulmonary embolism. Right-ventricular dilation begins a few minutes after onset of cardiac arrest as blood shifts from the systemic circulation to the right heart along a pressure gradient.[117,118] Right-ventricular dilation was uniformly observed in a porcine model of cardiac arrest across etiologies of hypovolemia, hyperkalemia, and primary arrhythmia.[119]

Clinicians should be cautious about potentially prolonging interruptions in chest compressions when using point-of-care echocardiography during cardiac arrest.[120,121] Several strategies to minimize these interruptions have been proposed.[122,123]

Point-of-care echocardiography is subject to availability of equipment and skilled operators.

Knowledge Gaps

- There is no standardized or uniform definition of cardiac motion visualized on point-of-care echocardiography during cardiac arrest.
- There are very few prognostic factor studies of point-of-care echocardiography during cardiac arrest performed with methodology that minimizes risk of bias.
- The inter-rater reliability of point-of-care echocardiography during cardiac arrest is uncertain.
- The relative roles and feasibility of transesophageal versus transthoracic echocardiography during CPR require research.

$ETCO_2$ to Predict Outcome of Cardiac Arrest (ALS 459: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Adults who are in cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: Any $ETCO_2$ level value, when present
- Comparator: Any $ETCO_2$ level below that value
- Outcome: ROSC, survival, survival with favorable neurological outcome
- This topic was last updated in a published 2015 CoSTR,[1,7] and the SysRev that informed this CoSTR was published in 2018.[124] The 2 EvUps are included in Supplement Appendix C-9a and C-9b. A search

from December 2013 to November 2019 identified 7 new observational studies[74,80,125–129] in addition to the previous SysRev.[124] The task force discussed the low likelihood of an updated SysRev leading to a change in treatment recommendations based on the available studies, and therefore did not prioritize this topic for a SysRev at this time. Future studies and SysRevs should consider trends and changes in $ETCO_2$ values during CPR in addition to the significance of single $ETCO_2$ values. The 2015 treatment recommendations remain unchanged.[1,7]

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[1,7]

We recommend against using $ETCO_2$ cutoff values alone as a mortality predictor or for the decision to stop a resuscitation attempt (strong recommendation, low-quality evidence).

We suggest that an $ETCO_2$ of 10 mm Hg or greater measured after tracheal intubation or after 20 minutes of resuscitation may be a predictor of ROSC (weak recommendation, low-quality evidence).

We suggest that an $ETCO_2$ of 10 mm Hg or greater measured after tracheal intubation, or an $ETCO_2$ of 20 mm Hg or greater measured after 20 minutes of resuscitation, may be a predictor of survival to discharge (weak recommendation, moderate-quality evidence).

CARDIAC ARREST IN SPECIAL CIRCUMSTANCES

Cardiac Arrest Associated With Pulmonary Embolism (ALS 435, 581: SysRev)

Rationale for Review

Pulmonary embolism (PE) is a potentially reversible cause of cardiac arrest. Whether chances for ROSC and survival may be significantly higher if a PE is present and can be treated is not well established because research has been limited to-date. This topic was last reviewed in 2015.[1,7] The specific role of ECPR was not addressed in this updated SysRev because ECPR was addressed in the previous 2019 CoSTR summary.[2,3] The role of ECPR for the treatment of PE and cardiac arrest is discussed in the justification section that follows.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults in cardiac arrest due to PE or suspected PE in any setting (in-hospital or out-of-hospital)
- Intervention: Any specific alteration in the ALS treatment algorithm (eg, fibrinolytics or any other)
- Comparator: Standard ALS care
- Outcome: Survival with favorable neurological outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival at discharge, 30 days, 60 days, 180 days, and/or 1 year (all critical); ROSC (important)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) are excluded.
- Time frame: All years and languages were included if there was an English abstract. Literature search was updated to October 2019.
- PROSPERO Registration: Registered with ILCOR Science Advisory Committee October 6, 2019. This SysRev was done as an update of the 2015 CoSTR SysRev and PROSPERO registration was not done.

Consensus on Science

Fibrinolysis

For the critical outcome of survival with favorable neurological outcome at 30 days, we identified very low-certainty evidence (downgraded for serious imprecision and very serious risk of bias) from a subgroup of 37 patients with confirmed PE from 1 RCT comparing fibrinolytics with placebo during cardiac arrest[130] finding no difference between groups [tenecteplase 2/15, (13.3%) versus placebo, 0/22 (0%)] [risk ratio (RR), 7.19; 95% CI, 0.37–139.9]. We also identified very low-certainty evidence (downgraded for risk of bias) from a single observational study that found no difference (10% with fibrinolysis versus 5% without; adjusted RR [ARR], 1.97; 95% CI, 0.70–5.56).[131]

For the critical outcome of survival at 30 days, very low-certainty evidence (downgraded for risk of bias) from one observational study showed an association between improved survival and administration of fibrinolysis (16% with fibrinolysis versus 6% without; P=0.005).[131]

For the critical outcome of survival to hospital discharge, very low-certainty evidence (downgraded for very serious risk of bias and imprecision) from 3 retrospective observational studies showed no association between administration of fibrinolysis and survival (10.5% survival with fibrinolysis versus 8.7% without;[132] 9.5% survival with fibrinolysis versus 4.8% without[133] and 19.4% survival with fibrinolysis versus 6.7% without (RR, 2.9; 95% CI, 0.75–13.8).[134]

For the important outcome of ROSC, very low-certainty evidence from 1 study (downgraded for very serious risk of bias) showed benefit associated with the use of fibrinolytic drugs compared with no fibrinolytic drugs in patients with PE (81.0% with fibrinolysis versus 42.9% without; P=0.03).[133] Two other studies provided very low-certainty evidence (downgraded for very serious risk of bias) of no difference in ROSC (66.7% with fibrinolysis versus 43.3% without [RR, 1.5; 95%

CI, 0.8–8.6] and 47.4% with fibrinolysis versus 47.8% without; *P*=0.98).[132,134]

For the outcome of survival at 24 hours, very low-certainty evidence (downgraded for risk of bias) from 1 observational study showed no difference associated with fibrinolysis (66% with fibrinolysis versus 63% without; *P*=0.76),[131] whereas another study showed benefit associated with fibrinolysis (52.8% with fibrinolysis versus 23.3% without; RR, 2.3; 95% CI, 1.1–4.7).[134]

Surgical Embolectomy

We found very low-certainty evidence (downgraded for very serious risk of bias) from 2 case series[135,136] with no control groups and a total of 21 patients requiring CPR with a 30-day survival rate of 12.5% and 71.4%, respectively.

Percutaneous Mechanical Thrombectomy

For the important outcome of ROSC, very low-certainty evidence (downgraded for very serious risk of bias and very serious imprecision) from 1 case series of 7 patients with cardiac arrest with no control group,[137] ROSC was achieved in 6 of 7 patients (85.7%) treated with percutaneous mechanical thrombectomy.

The overall certainty of evidence was rated as very low primarily due to a very serious risk of bias and inconsistency. For this reason, no meta-analyses were performed.

Treatment Recommendations

These recommendations (below) are unchanged from 2015.[1,7] We suggest administering fibrinolytic drugs for cardiac arrest when PE is the suspected cause of cardiac arrest (weak recommendation, very low-certainty evidence).

We suggest the use of fibrinolytic drugs or surgical embolectomy or percutaneous mechanical thrombectomy for cardiac arrest when PE is the known cause of cardiac arrest (weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-4. The task force considered that mechanical or surgical thrombectomy would be used only if the patient had a confirmed PE. No RCTs were identified and no meta-analysis was undertaken given the limited evidence.

The task force considered that 2% to 7% of patients with OHCA have a PE,[130,131] and this figure is probably higher for patients with IHCA. The task force acknowledged that ECPR techniques are now frequently used in patients with cardiac arrest from suspected PE in those settings where it is feasible. This role of ECPR for advanced life support was addressed by the 2019 CoSTR summary, and the considered studies included patients with PE.[2,3] Specifically in patients with PE, ECPR may potentially facilitate the use of fibrinolysis or mechanical or surgical embolectomy, but the evidence is of very low certainty.

The task force considered the increased risk of bleeding from fibrinolysis if it is administered to patients without PE. The Thrombolysis in Cardiac Arrest (TROICA) Study—which is the largest study of thrombolysis during cardiac arrest—showed an increased risk of bleeding in the thrombolysis group (any intracranial hemorrhage, 2.7% versus 0.4%; RR, 6.95 [95% CI, 1.59–30.41]; *P*=0.006), but major bleeding complications did not occur more often (symptomatic intracranial hemorrhage, 0.8% versus 0%; RR, 8.93 [95% CI, 0.48–165.45]; *P*=0.13; major nonintracranial hemorrhage, 7.7% versus 6.4; RR, 1.21 [95% CI, 0.77–1.88]; *P*=0.48; ischemic stroke, 0.8% versus 0.6%; RR, 1.32 [95% CI, 0.30–5.88]; *P*=1.00).[130] Patients are far more likely to die from the cardiac arrest than from the treatment.

Knowledge Gap

- Optimal drug and dosing strategy for fibrinolysis during CPR with a suspected or actual PE
- Intra-arrest prediction of PE during CPR

Cardiac Arrest in Pregnancy (ALS 436: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Pregnant women who are in cardiac arrest in any setting
- Intervention: Any specific intervention(s)
- Comparator: Standard care (usual resuscitation practice)
- Outcome: ROSC; survival to discharge, 30 days, or longer; survival with favorable neurological outcome at discharge, 30 days, or longer
- An EvUp is included in Supplement Appendix C-10. Since the 2015 CoSTR,[1,7] 7 new small observational studies were identified, 5 of which focused on association of timing of delivery with outcome of cardiac arrest and other factors associated with maternal and fetal mortality.[138–142] Due to the very small size of most studies, an updated SysRev was not suggested. The 2015 treatment recommendation remains unchanged.[1,7]

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[1,7]

We suggest delivery of the fetus by perimortem cesarean delivery for women in cardiac arrest in the second half of pregnancy (weak recommendation, very low-quality evidence).

There is insufficient evidence to define a specific time interval by which delivery should begin.

High-quality usual resuscitation care and therapeutic interventions that target the most likely cause(s) of cardiac arrest remain important in this population.

There is insufficient evidence to make a recommendation about the use of left-lateral tilt and/or uterine displacement during CPR in the pregnant patient.

Opioid Toxicity (ALS 441: EvUp)

Death from opioid toxicity is an important public health issue in many countries. The issue of first aid education for opioid toxicity has been addressed by the EIT Task Force ScopRev 891.[142a,142b]

Population, Intervention, Comparator, and Outcome

- Population: Adults who are in cardiac arrest or respiratory arrest due to opioid toxicity in any setting (in-hospital or out-of-hospital)
- Intervention: Any specific therapy (eg, naloxone, bicarbonate, or other drugs)
- Comparator: Usual ALS care
- Outcome: Survival with favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; ROSC were defined as critical or important outcomes
- This topic was last reviewed in 2015.[1,7] The EvUp is included in Supplement Appendix C-11. The search was conducted for studies published from September 1, 2013, to September 13, 2019. There was insufficient evidence to support consideration of a stand-alone ALS SysRev, but an updated SysRev with other task forces was suggested.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[1,7]

We recommend the use of naloxone by IV, intramuscular, subcutaneous, IO, or intranasal routes in respiratory arrest associated with opioid toxicity (strong recommendation, very low-quality evidence). The dose of naloxone required will depend on the route.

We can make no recommendation about the modification of standard ALS in opioid-induced cardiac arrest.

POSTRESUSCITATION CARE

The last update of postresuscitation care was published in the 2015 CoSTR.[1,7] Since that publication, there have been many reported studies of postresuscitation care.[143]

Oxygen Dose After ROSC in Adults (ALS 448: SysRev)

Rationale for Review

Both hypoxemia and hyperoxemia during postresuscitation care have been associated with worse outcomes. Hypoxemia may worsen ischemic brain injury and injury to other organs, and hyperoxemia may lead to increased oxidative stress and organ damage after reperfusion. A SysRev was conducted to inform this 2020 CoSTR for ALS.[144]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Unresponsive adults with sustained ROSC after cardiac arrest in any setting
- Intervention: A ventilation strategy targeting a specific oxygen saturation and/or Pa_{O_2}
- Comparator: Treatment without specific targets or with an alternate target to the intervention
- Outcome: Critical outcomes include survival/survival with a favorable neurological outcome at hospital discharge or 30 days; and survival/survival with a favorable neurological outcome after hospital discharge or 30 days (eg, 90 days, 180 days, 1 year).
- Study design: Randomized trials, non-RCTs, and observational studies (cohort studies and case-control studies) with a control group (ie, patients treated with no specific oxygen saturation and/or Pa_{O_2} targets or an alternative target to the intervention) were included. Animal studies, ecological studies, case series, case reports, reviews, abstracts, editorials, comments, and letters to the editor were not included. There were no limitations on publication period or study language, if there was an English abstract. The population included patients with IHCA or OHCA of any origin. Unpublished studies (eg, conference abstracts, trial protocols) were excluded. The cited SysRev[144] was performed without age restriction, and the evidence from adult studies (generally defined as older than 16 years or 18 years or older) is included here.
- Time frame: All years and languages were included. The literature search was updated to August 22, 2019.
- PROSPERO Registration: CRD42020150877

Consensus on Science

The evidence from the 6 RCTs identified in the SysRev is summarized in Table 2. Trials generally failed to show a benefit of a titrated (lower percentage of oxygen) approach compared with standard care (higher percentage of oxygen). A subgroup analysis of postresuscitation patients in one larger RCT, however, found better survival in patients for whom hyperoxemia was aggressively avoided.[145] In addition, results from 10 observational studies rated as having only serious risk of bias were inconsistent. Four[146–149] found an association between hyperoxemia (variable definitions, but most often Pa_{O_2} greater than 300 mm Hg) and either worse survival or worse survival with neurological outcome, whereas the other 6[150–155] found

Table 2. Overview of Included Randomized Trials

Study, Year	Country	Years of Inclusion	Number of Patients	Intervention	Comparator	Relative Risk [95% CI]	Absolute Risk Reduction [95% CI]	Certainty
Favorable Neurological Outcome at 6 mo*—ICU Initiation								
Jakkula, 2018[156]	Finland and Denmark	2016–2017	120	Normoxia for 36 h (10–15 kPa)	Moderate hyperoxia for 36 h (20–25 kPa)	1.13 [0.87–1.47]	79 more per 1000 [79 fewer to 287 more]	Moderate†
Mackle, 2019[145]	Australia and New Zealand	2015–2018	164	Conservative oxygen (O_2 Sat 90%–97%)	Standard oxygen (O_2 Sat >90%)	1.40 [0.93–2.13]	128 more per 1000 [22 fewer to 361 more]	Very low‡
Survival to Hospital Discharge With Favorable Neurological Outcome#—Prehospital Initiation								
Young, 2014[157]	New Zealand	2012–2013	17	Titrated oxygen for 72 h (O_2 Sat 90%–94%)	Standard oxygen for 72 h (O_2 Sat >95%)	0.56 [0.14–2.29]	196 fewer per 1000 [382 fewer to 573 more]	Very low¶
Kuisma, 2006[158]	Finland	Not recorded	28	Low oxygen prehospital (30%)	High oxygen prehospital (100%)	1.33 [0.63–2.84]	141 more per 1000 [159 fewer to 789 more]	Low§
Survival to Hospital Discharge—ICU Initiation								
Jakkula, 2018[156]	Finland and Denmark	2016–2017	120	Normoxia for 36 h (10–15 kPa)	Moderate hyperoxia for 36 h (20–25 kPa)	1.07 [0.84–1.36]	46 more per 1000 [106 fewer to 238 more]	Moderate§
Survival to 90 Days—ICU Initiation								
Mackle, 2019[145]	Australia and New Zealand	2015–2018	164	Conservative oxygen (O_2 Sat 90%–97%)	Standard oxygen (O_2 Sat >90%)	1.39 [1.01–1.92]	160 more per 1000 [4 more to 377 more]	Low††
Survival to Hospital Discharge—Prehospital Initiation								
Meta-analysis Kuisma 2006[158]/ Bray, 2018[159]	Finland, Australia	Not recorded,[158] 2015–2017[159]	89	Low oxygen prehospital (30% or 2–4 L/min)	High oxygen prehospital (100% or ≥10 L/min)	0.97 [0.68– 1.37]	18 fewer per 1000 [194 fewer to 224 more]	Very low§
Thomas, 2019[160]	United Kingdom	2014–2015	35	Titrated oxygen prehospital (O_2 Sat 94%–98%)	Standard oxygen prehospital (O_2 Sat 100%)	3.15 [1.04–9.52]	379 more per 1000 [7 more to 1000 more]	Very low¶
Young,** 2014[157]	New Zealand	2012–2013	17	Titrated oxygen for 72 h (O_2 Sat 90%–94%)	Standard oxygen for 72 h (O_2 Sat >95%)	1.13 [0.41–3.08]	58 more per 1000 [262 fewer to 924 more]	Very low¶

ICU indicates intensive care unit; and Sat, saturation.
*Defined as either Cerebral Performance Category (CPC) 1–2 or Extended Glasgow Outcome Score of 5–8.
†Downgraded for imprecision.
‡Downgraded for risk of bias and imprecision.
§Downgraded 2 levels for imprecision.
¶Downgraded for indirectness and 2 levels for imprecision.
#Defined as CPC 1–2 or discharge to home.
**Intervention initiated prehospital but continued after admission.
††Downgraded 2 levels for risk of bias.

no such association. Hypoxemia was found to be associated with worse outcome in adjusted analysis in 1 of these studies.[149]

Treatment Recommendations

We suggest the use of 100% inspired oxygen until the arterial oxygen saturation or the partial pressure of arterial oxygen can be measured reliably in adults with ROSC after cardiac arrest in any setting (weak recommendation, very low-certainty evidence).

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).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-5. In making the recommendation to avoid hypoxemia, the task force acknowledges that the evidence is of very low certainty. The task force concluded that the known harm that can result from hypoxia justifies its avoidance, and detection of hypoxemia may be the best surrogate for or precursor of tissue hypoxia. The

suggestion to avoid hyperoxemia is based on low- to moderate-certainty evidence that showed either harm or no benefit from hyperoxemia. The definitions used for hyperoxemia varied, ranging from an oxygen saturation greater than 97% measured by pulse oximeter to a Pa_{O_2} up to 20 to 25 kPa (150–188 mm Hg) in the available RCTs. In light of the possible benefit and lack of evidence for harm, the task force suggests targeting normoxemia and avoiding hyperoxemia. The task force acknowledges that the primary randomized trial evidence suggesting benefit from avoiding hyperoxemia is from a subgroup analysis only, and data from the 3 ongoing trials (NCT03138005, NCT03653325, NCT03141099) will be helpful.

The task force felt that titration of oxygen should not be attempted until oxygen levels (peripheral oxygen saturation or partial pressure of oxygen in arterial blood) could be measured reliably. Some of the randomized trials conducted in the prehospital setting, although very small, reported more desaturation of arterial blood in the lower oxygen group, which reinforces the task force suggestion to administer 100% oxygen until reliable measurement of oxygen level is possible. This is likely to be more important in the prehospital setting.

Knowledge Gap

- Randomized trials comparing lower oxygen target strategies with higher oxygen target strategies or usual care in postarrest patients have thus far been small and therefore inconclusive. More trials are needed, and 3 trials are underway currently (NCT03138005, NCT03653325, NCT03141099).

Ventilation Strategy After ROSC in Adults (ALS 571: SysRev)

Rationale for Review

Hypocapnia causes cerebral vasoconstriction and hypercapnia leads to cerebral vasodilation. Exactly how variations in $Paco_2$ affect intracranial pressure and perfusion in the brains of postarrest patients, and whether this affects outcome, remains unclear.[161] This topic was last reviewed in 2015.[1,7] A SysRev[144] was conducted to inform this 2020 ALS CoSTR.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Unresponsive adults with sustained ROSC after cardiac arrest in any setting
- Intervention: A ventilation strategy targeting a specific $Paco_2$
- Comparator: Treatment without specific targets or with an alternate target to the intervention
- Outcome: Critical outcomes include survival/survival with a favorable neurological outcome at hospital discharge or 30 days; and survival/survival with a favorable neurological outcome after hospital discharge or 30 days (eg, 90 days, 180 days, 1 year).
- Study design: Randomized trials, non-RCTs, and observational studies (cohort studies and case-control studies) with a control group (ie, patients treated with no specific $Paco_2$ targets or an alternative target to the intervention) were included. Animal studies, ecological studies, case series, case reports, reviews, abstracts, editorials, comments, and letters to the editor were not included. There were no limitations on publication period or study language, if there was an English abstract. The population included patients with IHCA or OHCA of any origin. Unpublished studies (eg, conference abstracts, trial protocols) were excluded. The cited SysRev[144] was done without age restriction, and the evidence from adult studies (generally defined as older than 16 years or 18 years or older) is included here.
- Time frame: All years and languages were included. The literature search was updated to August 22, 2019.
- PROSPERO Registration: CRD42020150877

Consensus on Science

The task force concluded that differences in the $Paco_2$ targets used in the arms of the 2 RCTs identified[156,162] precluded meta-analysis.

For the critical outcome of favorable neurological outcome (defined as CPC 1–2) at 6 months, we identified low-certainty evidence from 1 RCT enrolling 120 patients and comparing a ventilation strategy targeting high-normal $Paco_2$ (5.8–6.0 kPa/43.5–45 mmHg) with one targeting low-normal $Paco_2$ (4.5–4.7/kPa/33.7–35.2 mmHg) and failing to show benefit from the higher $Paco_2$ strategy (RR, 0.84; 95% CI, 0.64–1.10; ARR, 113 fewer per 1000; 95% CI, from 254 fewer to 70 more).[156] For the critical outcome of favorable neurological outcome (defined as an extended Glasgow Outcomes Scale ≥5) at 6 months, we identified low-certainty evidence (downgraded for inconsistency and imprecision) from 1 RCT enrolling 83 patients and comparing a ventilation strategy targeting moderate hypercapnia ($Paco_2$ 50–55 mm Hg/6.7–7.3 kPa) with one targeting normocapnia ($Paco_2$ 35–45 mm Hg/4.7–6.0 kPa) and failing to show benefit from the higher $Paco_2$ strategy (RR, 1.28; 95% CI, 0.83–1.96; ARR, 129 more per 1000; 95% CI, from 78 fewer to 443 more).[162]

For the critical outcome of survival to 30 days we identified low-certainty evidence (downgraded for inconsistency and imprecision) from 1 RCT enrolling 120 patients and comparing a ventilation strategy targeting high-normal $Paco_2$ (5.8–6.0 kPa/43.5–45 mmHg) with one targeting low-normal $Paco_2$ (4.5–4.7 kPa/33.7–35.2 mmHg) and failing to show benefit from the higher

$Paco_2$ strategy (RR, 0.81; 95% CI, 0.63–1.05; ARR, 143 fewer per 1000; 95% CI, from 279 fewer to 38 more).[156]

For the critical outcome of survival to discharge we identified low-certainty evidence (downgraded for inconsistency and imprecision) from 1 RCT enrolling 83 patients and comparing a ventilation strategy targeting moderate hypercapnia ($Paco_2$ 50–55 mm Hg/6.7–7.3 kPa) with one targeting normocapnia ($Paco_2$ 35–45 mm Hg/4.7–6.0 kPa) and failing to show benefit from the higher $Paco_2$ strategy (RR, 1.16; 95% CI, 0.87–1.56; ARR, 101 more per 1000; 95% CI, from 82 fewer to 355 more).[162]

Results were inconsistent across the 6 observational studies rated as having less than critical risk of bias. Hypercapnia was associated with improved outcomes in 2 studies[155,163] and worse outcomes in 2 studies.[149,164] There was no association between hypercapnia and outcomes in the remaining 2 studies.[152,165] Results were similar for hypocapnia although no studies found an association with improved outcomes.

Treatment Recommendations

There is insufficient evidence to suggest for or against targeting mild hypercapnia compared with normocapnia in adults with ROSC after cardiac arrest.

We suggest against routinely targeting hypocapnia in adults with ROSC after cardiac arrest (weak recommendation, low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-6. Evidence from existing randomized trials and observational studies is very inconsistent. Both randomized trials failed to show any effect from different $Paco_2$ targets, but the trials were small and used different target ranges, precluding meta-analysis. Observational studies were evenly distributed in showing benefit, harm or no effect associated with hypercapnia. Hypocapnia results were also inconsistent, although no studies found an association with benefit. In light of the lack of evidence for benefit, and lack of consistent evidence for harm from $Paco_2$ levels higher than normal, the task force did not think there was sufficient evidence to suggest for or against targeting mild hypercapnia compared with normocapnia. An ongoing trial investigating this comparison may bring clarity to this issue (NCT03114033).

For hypocapnia, very limited evidence suggests either no benefit or harm, supporting the task force's suggestion against targeting hypocapnia.

Although the task force discussed whether patients with baseline chronic lung disease and chronic CO_2 retention might respond differently to different $Paco_2$ targets, no evidence addressing this subgroup was found. The task force agreed it would be reasonable to adjust $Paco_2$ targets in patients with known chronic CO_2 retention, but this is expert opinion only because no evidence was identified on this topic.

The prior treatment recommendation (2015[1,7]) was a suggestion to maintain normocapnia. The updated treatment recommendation allows for continuing this approach, while emphasizing that we do not currently know if targeting normocapnia is beneficial, harmful, or equal in comparison to targeting hypercapnia. The task force discussed the possible complication of acidemia from hypercapnia. The presence or absence of metabolic acidosis requires consideration when choosing a ventilation strategy and $Paco_2$ target, and metabolic acidosis is common in postarrest patients. The $Paco_2$ targets or ranges also differed somewhat across studies. For this reason, the task force chose not to define specific numeric targets because no optimal target or range has been made clear. Additionally, opinions vary on whether arterial blood gas analysis in patients receiving targeted temperature management (TTM) should be adjusted for temperature. Once again, trials differed in their approach. Approaches to blood gas interpretation in regard to temperature also varied across the observational studies. These variations in methodology and in definitions of target ranges prohibit the task force from being able to recommend specific numbers or a specific method for blood gas analysis for systems implementing these recommendations.

Knowledge Gaps

- Randomized trials comparing strategies targeting mild hypercapnia with strategies targeting normocapnia have thus far been small and therefore inconclusive. A much larger randomized trial is currently underway (NCT03114033).
- How $Paco_2$ targets should be adjusted in those with chronic CO_2 retention is unknown.

Postresuscitation Hemodynamic Support (ALS 570: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Adults with ROSC after cardiac arrest in any setting
- Intervention: Titration of therapy to achieve a specific hemodynamic goal (eg, mean arterial pressure greater than 65 mm Hg)
- Comparator: No hemodynamic goal
- Outcome: Any clinical outcome
- An EvUp for this topic was performed and is included in Supplement Appendix C-12. Two RCTs completed since 2015[156,166] did not find that targeting a specific mean arterial pressure affected outcome, although the studies were not powered for clinical outcomes of survival or neurological outcome. In the absence of ongoing RCTs, and

controversy about the targeting of higher blood pressure, the task force suggests that this topic be considered for a SysRev.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[1,7]

We suggest hemodynamic goals (eg, mean arterial pressure, systolic blood pressure) be considered during postresuscitation care and as part of any bundle of postresuscitation interventions (weak recommendation, low-certainty evidence).

There is insufficient evidence to recommend specific hemodynamic goals; such goals should be considered on an individual patient basis and are likely to be influenced by post–cardiac arrest status and preexisting comorbidities (weak recommendation, low-certainty evidence).

Postresuscitation Steroids (ALS 446: EvUp)

Population, Intervention, Comparator, and Outcome

- Population: Adult patients with ROSC after cardiac arrest (prehospital or in-hospital)
- Intervention: Treatment with corticosteroids
- Comparator: Standard care
- Outcome: Survival to hospital discharge with good neurological outcome or survival to hospital discharge (± time to shock reversal/shock reversal)
- The 2010 CoSTR addressed steroid use both intra-arrest and postresuscitation.[6,8] The 2015 CoSTR included only intra-arrest steroid use.[1,7] The EvUp for postresuscitation steroid use is included in Supplement Appendix C-13. Three small RCTs and a large observational study were identified.[94,167–169] Two of the RCTs used steroids both during CPR and after ROSC.[167,168] One recently completed trial that is not yet published was also identified (NCT02790788). The task force recommends a SysRev be undertaken once the recently completed trial is published.

Treatment Recommendations

This treatment (below) is unchanged from 2010.[6,8]

There is insufficient evidence to support or refute the use of corticosteroids for patients with ROSC after cardiac arrest.

Prophylactic Antibiotics After Cardiac Arrest (ALS 2000: SysRev)

Rationale for Review

This is a new topic prioritized by the ALS Task Force. Infective complications are common in patients admitted to intensive care units (ICUs). After cardiac arrest, pneumonia has been reported in 50% to 60% of patients,[170,171] which is thought to result in part from aspiration during the cardiac arrest and resuscitation. In these patients, early and accurate identification of infection is challenging. Standard criteria for identifying infection are affected by patient treatment (ie, TTM) and the pathophysiology of the post–cardiac arrest syndrome (ie, including the systemic inflammatory response). The decision to treat a possible infection needs to be balanced by the need for prudent antibiotic administration to avoid antibiotic resistance. This new topic was prioritized by the ALS Task Force due to the recent publication of a SysRev on the topic.[172] The published SysRev was updated by using the ADOLOPMENT process.[173]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adult patients after ROSC from cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: Early/prophylactic administration of antibiotics
- Comparator: Delayed/clinically driven administration
- Outcome: Survival or survival with good neurological outcome at hospital discharge or longer (critical), and important outcomes of critical care length of stay, infective complications, or duration of mechanical ventilation
- Study design: Observational and interventional studies if they compared the effect of administration of early or prophylactic antibiotics with delayed or clinically driven administration of antibiotics in adult patients after cardiac arrest. All study types that included a control group were included. Case reports and case series were not eligible for inclusion. There was no restriction on language.
- Time frame: There was no restriction on publication date, and the literature search was completed/updated in October 2019.
- PROSPERO Registration: CRD42016039358 for the original SysRev.[172]

Consensus on Science

For the critical outcome of survival with favorable neurological outcome at ICU discharge or 30 days, we identified low-certainty evidence (downgraded for serious risk of bias and serious imprecision) from 2 RCTs[171,174] enrolling 254 patients, which showed no benefit of early/prophylactic antibiotic administration (RR, 0.89; 95% CI, 0.71–1.12; *P*=0.31; risk difference, –0.06; 95% CI, –0.19 to 0.06; *P*=0.30).

For the critical outcome of survival at ICU discharge or 30 days, we identified low-certainty evidence (downgraded for serious risk of bias and serious imprecision) from 2 RCTs[171,174] enrolling 254 patients, which showed no benefit (RR, 0.95; 95% CI, 0.79–1.14; *P*=0.60; risk difference, –0.03; 95% CI, –0.15 to 0.08; *P*=0.58). We also identified very low-certainty evidence (downgraded for serious indirectness) from 2 observational

studies. One study[175] enrolling 1604 patients showed no benefit associated with early or prophylactic antibiotic administration compared with delayed/clinically driven administration (OR, 1.16; 95% CI, 0.94 to 1.13; *P*=0.18). The second observational study[176] enrolling 138 patients showed a benefit (data presentation precludes reporting of OR, *P*=0.01).

For the important outcome of infective complications (pneumonia) we identified low-certainty evidence (downgraded for serious risk of bias and serious imprecision) from 2 RCTs[171,174] enrolling 254 patients, which showed no benefit (RR, 0.75; 95% CI, 0.43 to 1.32; *P*=0.32; risk difference, –0.12; 95% CI, –0.23 to 0.00; *P*=0.05). There were differences between the studies in methods used to diagnose pneumonia. We found very low-certainty evidence (downgraded for serious risk of bias, serious indirectness, and serious imprecision) from 2 observational studies[175,177] enrolling 2245 patients, which showed no association between early/prophylactic administration compared with delayed/clinically driven administration (OR, 0.61; 95% CI, 0.61 to 1.62; *P*=0.98). These studies, too, differed in methods used to diagnose pneumonia.

For the important outcome of critical care length of stay we identified low-certainty evidence (downgraded for serious risk of bias and serious imprecision) from 2 RCTs[171,174] enrolling 248 patients, which showed no benefit (mean difference, 0.47 days; 95% CI, –1.31 to 2.24; *P*=0.61).

For the important outcome of duration of mechanical ventilation we identified very low-certainty evidence (downgraded for very serious risk of bias and serious imprecision) from 1 RCT[174] enrolling 60 patients, which showed no benefit (mean difference, 0.20 days; 95% CI, –1.53 to 1.93; *P*=0.82).

Treatment Recommendation

We suggest against the use of prophylactic antibiotics in patients after ROSC (weak recommendation, low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-7. Meta-analyses of both randomized trials and observational studies showed no overall benefit in the use of prophylactic antibiotics during post–cardiac arrest care. The task force did review the findings of 1 RCT at low overall risk of bias that reported reduced incidence of early pneumonia in patients treated with prophylactic antibiotics.[171] Although this study demonstrated the potential efficacy of prophylactic antibiotics, there was no improvement in other clinical outcomes, such as survival or critical care length of stay. Pneumonia affects approximately 50% of ICU patients after cardiac arrest, but this is unlikely to contribute to mortality because most deaths are attributable to neurological failure, cardiovascular failure, or multiorgan failure.[170,171] A strategy of prophylactic antibiotic use would likely expose a large number of patients to antibiotics with no specific benefit and increase the risk of development of resistant organisms. The decision to administer antibiotics after cardiac arrest, particularly in the context of gastric aspiration, is challenging and clinicians may have different clinical thresholds for prescribing antibiotics. We did not identify any RCTs enrolling patients after IHCA.

Knowledge Gaps

- Studies of post-ROSC antibiotics after IHCA.
- RCTs that evaluate this question in patients treated with TTM at temperatures other than 32°C to 34°C.
- RCTs powered to determine the effect of prophylactic antibiotics on outcomes such as critical care length of stay or duration of mechanical ventilation.

Post–Cardiac Arrest Seizure Prophylaxis and Treatment (ALS 431, 868: SysRev)

Rationale for Review

Hypoxic-ischemic brain injury is a common cause of death in comatose cardiac arrest survivors. Clinical convulsions and epileptiform activity in the electroencephalogram (EEG) are common, with substantial overlap and an approximate incidence of 20% to 30%.[178–181] The prognosis for patients with clinical and electrographic seizures is usually poor, but some patients recover and may ultimately have a good neurological outcome.[180,181] This CoSTR is based on an update of the 2015 SysRev and CoSTR[1,7] for seizure prophylaxis and treatment in cardiac arrest survivors.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Unresponsive adults (older than 18 years) with sustained ROSC after cardiac arrest in any setting (in-hospital or out-of-hospital)
- Intervention: One strategy for seizure prophylaxis or treatment
- Comparator: Another strategy or no seizure prophylaxis or treatment
- Outcome: Survival with favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival at discharge, 30 days, 60 days, 180 days, and/or 1 year (all critical); and the important outcome of seizure incidence during index hospitalization (for seizure prophylaxis only)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) are excluded.

- Time frame: All years and languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to September 26, 2019.
- PROSPERO Registration: Registered with ILCOR Science Advisory Committee October 3, 2019. This SysRev was done as an update of the 2015 CoSTR SysRev and PROSPERO registration was not done.

Consensus on Science

Post–Cardiac Arrest Seizure Prophylaxis

For the critical outcomes of survival with favorable neurological outcome to discharge/30 days or longer, and survival to discharge/30 days or longer, 2 prospective RCTs involving a total of 562 subjects provided very low-certainty evidence (downgraded for risk of bias, indirectness and imprecision)[182,183] of no benefit from seizure prophylaxis. One nonrandomized prospective clinical trial with 107 subjects that used historic controls provided very low-certainty evidence (downgraded for risk of bias, indirectness, and imprecision) of no benefit.[184]

For the important outcome of seizure prevention, we identified very low-certainty evidence (downgraded for risk of bias and indirectness and imprecision) from 2 prospective double-blinded RCTs[182,183] showing no benefit of seizure prophylaxis.

Post–Cardiac Arrest Seizure Treatment

For the critical outcomes of survival with favorable neurological outcome or survival at discharge/30 days or longer, we identified no RCTs or nonrandomized studies that addressed the effect of post–cardiac arrest seizure treatment, compared with no seizure treatment, on outcomes.

Treatment Recommendations

This treatment recommendation has been updated from 2015.[1,7]

We suggest against seizure prophylaxis in adult post–cardiac arrest survivors (weak recommendation, very low-certainty evidence).

We suggest treatment of seizures in adult post–cardiac arrest survivors (weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-8. The task force decision to suggest against post–cardiac arrest seizure prophylaxis was primarily based on the absence of direct evidence that prophylactic therapy with antiepileptic drugs prevents seizures or improves important outcomes in adult comatose cardiac arrest survivors. However, the task force did recognize the very low certainty of the evidence from RCTs. The task force also considered that seizure prophylaxis in other forms of acute brain injury is not associated with improved outcomes, and that most drugs used for seizure prophylaxis can have significant side effects. Finally, the task force acknowledged that most comatose cardiac arrest survivors routinely receive sedatives such as propofol or benzodiazepines that are known to have antiepileptic effects. However, the task force identified no controlled studies that examined whether different sedation strategies or choices of sedation drugs had an impact on the incidence of post–cardiac arrest seizures.

The task force decision to suggest treatment of seizures in post–cardiac arrest survivors takes into consideration the absence of direct evidence that seizure treatment improves critical outcomes in this patient population. However, there are no published controlled clinical studies. Therefore, the task force weighed the fact that ongoing seizures have the potential to worsen brain injury, and treatment of recurrent seizures and status epilepticus constitutes "standard of care" in other patient populations. A large randomized trial is currently underway investigating the benefit of systematic antiepileptic drug therapy with the goal of suppressing all epileptiform activity on the EEG versus standard treatment of clinical seizures only in post–cardiac arrest status epilepticus. (TELSTAR trial [Treatment of Electroencephalographic Status Epilepticus After Cardiopulmonary Resuscitation], NCT02056236)

Indirect evidence from case series suggests that sedatives such as propofol are effective in suppressing both clinical convulsions and epileptiform activity on EEG in these patients.[185–187] A recent retrospective study provides some evidence that conventional antiepileptic drugs (specifically valproate and levetiracetam) also have an effect in suppressing epileptiform activity in the EEG.[188] In a recent comparison of valproate, levetiracetam, and fosphenytoin for convulsive status epilepticus, the 3 drugs were equally effective but fosphenytoin caused more episodes of hypotension and need for tracheal intubation.[189] However, it is important to note that this study excluded post–cardiac arrest patients. On the basis of these results, the task force discussed using valproate and levetiracetam as first-line drugs in post–cardiac arrest seizure treatment.

There is no direct evidence of undesirable effects of antiepileptic drug therapy in comatose post–cardiac arrest survivors. Treatment with sedatives and conventional antiepileptic drugs in high doses has the potential to cause delayed awakening, prolonged need for mechanical ventilation, and increased critical care days. Importantly, generalized myoclonus in combination with epileptiform discharges may be manifestations of Lance-Adams syndrome, which is compatible with a good outcome.[187,190] In such cases, overly aggressive

sedation and treatment with high doses of conventional antiepileptic drugs may confound the clinical examination and lead to overly pessimistic prognostication.

The relative benefit of continuous EEG compared with intermittent EEG monitoring was not specifically reviewed. Continuous EEG monitoring is labor intensive and likely to add significant cost to patient care. The net cost-effectiveness of this approach is controversial and may depend substantially on the setting.[191,192] The task force also discussed the potential cost of delayed neurological prognostication and prolonged ICU care associated with active treatment of seizures because of the need to continue sedation.

Knowledge Gaps

- There is no high-certainty evidence of a positive effect of antiepileptic drugs on the outcome of post–cardiac arrest patients with seizures.
- There are no RCTs specifically designed to evaluate the impact of post–cardiac arrest seizure prophylaxis on the incidence of seizures and on neurological outcome.
- There are inadequate data about the timing, duration, dosing, and choice of antiepileptic drugs for seizure prophylaxis in comatose post–cardiac arrest patients.
- The utility of continuous EEG versus intermittent EEG monitoring in the diagnosis and treatment of seizures in comatose postcardiac arrest patients remains controversial.
- The threshold for treating epileptiform activity other than convulsive seizures (eg, generalized epileptiform discharges) is poorly defined.
- Standardized terminology for classification of epileptiform activity in the EEG of comatose post-cardiac arrest patients is increasingly used. There remains a need to develop consensus on the definition of post–cardiac arrest status epilepticus.
- The value of using volatile anesthetics to treat refractory status epilepticus on post–cardiac arrest patients is currently unknown.

Targeted Temperature Management (ALS 455, 790, 791, 802, 879: EvUp)

A comprehensive SysRev of TTM[193,194] was conducted for the 2015 CoSTR.[1,7] The task force chose to delay updating this SysRev until the completion and publication of the Targeted Hypothermia Versus Targeted Normothermia After Out-of-Hospital Cardiac Arrest (TTM2) RCT (NCT02908308). EvUps for use of TTM and TTM duration were completed and appear in Supplement Appendix C-14 and C-15.

The results of the HYPERION trial (Therapeutic Hypothermia After Cardiac Arrest in Nonshockable Rhythm) were recently published.[195] In this French trial, 581 adult patients who were comatose after resuscitation from either an IHCA or OHCA with an initial nonshockable rhythm were randomized to either TTM with a target temperature of 33°C or TTM with a temperature of 37°C, both for 24 hours. The primary outcome (the proportion of patients with a CPC of either 1 or 2 at 90 days after the cardiac arrest) significantly favored the 33°C group. At 90 days, 29 of 284 patients (10.2%) in the 33°C group were alive with a CPC of 1 or 2, as compared with 17 of 297 (5.7%) in the normothermia group (risk difference, 4.5%; 95% CI, 0.1–8.9; P=0.04). There was no difference in mortality at 90 days (81.3% versus 83.2%; risk difference, –1.9%; 95% CI, –8.0 to 4.3).

This trial does not lead to any immediate changes to the 2015 ILCOR treatment recommendations[1,7] but reinforces the suggestion to consider TTM, targeting a constant temperature between 32°C and 36°C, in patients who remain comatose after resuscitation from either IHCA or OHCA with an initial nonshockable rhythm.

Treatment Recommendations

These treatment recommendations are unchanged from 2015.[1,7]

We recommend selecting and maintaining a constant target temperature between 32°C and 36°C for those patients in whom temperature control is used (strong recommendation, moderate-quality evidence). Whether certain subpopulations of cardiac arrest patients may benefit from lower (32°C–34°C) or higher (36°C) temperatures remains unknown, and further research may help elucidate this.

We recommend TTM as opposed to no TTM for adults with OHCA with an initial shockable rhythm who remain unresponsive after ROSC (strong recommendation, low-quality evidence).

We suggest TTM as opposed to no TTM for adults with OHCA with an initial nonshockable rhythm who remain unresponsive after ROSC (weak recommendation, very low-quality evidence).

We suggest TTM as opposed to no TTM for adults with IHCA with any initial rhythm who remain unresponsive after ROSC (weak recommendation, very low-quality evidence).

We suggest that if TTM is used, duration should be at least 24 hours (weak recommendation, very low-quality evidence).

We recommend against routine use of prehospital cooling with rapid infusion of large volumes of cold IV fluid immediately after ROSC (strong recommendation, moderate-quality evidence).

We suggest prevention and treatment of fever in persistently comatose adults after completion of TTM between 32°C and 36°C (weak recommendation, very low-quality evidence).

Prognostication in Comatose Patients After Resuscitation From Cardiac Arrest

Combined Prognostic Systematic Reviews

Many comatose post–cardiac arrest patients will not survive or will survive with an unfavorable neurological outcome. In some regions, family and treating teams may limit or withdraw life-sustaining treatment when unfavorable neurological outcomes are expected. Therefore, reliable strategies for timely prognostication are a critical component of any cardiac arrest system of care. The 2015 CoSTR distinguished between studies of prognostication among patients treated with or without hypothermia. For this 2020 CoSTR for ALS, these treatment recommendations apply regardless of the TTM strategy used. The reason for this is that in all of the studies we assessed, the population included a mix of TTM-treated and non–TTM-treated patients, and the potential impact of TTM on prognostication could not be assessed separately.

On May 31, 2013, a new search was launched, using the search strategies used for previous SysRevs on neuroprognostication. For the SysRev informing the 2020 CoSTRs, the search included studies published from January 1, 2013, to December 31, 2019 [PROSPERO Registration: CRD42019141169].

This review identified clinical signs, neurophysiological measurements, blood biomarkers, and imaging studies that had high specificity for poor neurological outcome, defined as CPC score of 3 to 5 or mRS score of 4 to 6 at hospital discharge, 1 month, or later.

The decision to limit treatment of comatose post–cardiac arrest patients should never rely on a single prognostication element. The consensus of the task force was that in patients who remain comatose in the absence of confounders (eg, sedative drugs), a multimodal approach should be used, with all supplementary tests considered in the context of the clinical examination. The most reliable combination and timing for each assessment are still to be determined and require further research.

The SysRevs supporting this CoSTR defined prediction as imprecise when the upper limit of 95% CIs for false-positive rate was above 5%.[196] However, there is no universal consensus on what the acceptable limits for imprecision should be. In a recent survey of 640 medical providers, Steinberg et al[197] reported that 56% considered an acceptable false-positive rate for withdrawal of life sustaining treatment from patients who might otherwise have recovered was 0.1% or less. In addition, 59% of respondents felt that an acceptable false-positive rate threshold for continuing life-sustaining treatment in patients with unrecognized unrecoverable injury was 1% or less.

Clinical Examination for Prognostication (ALS 450, 713, 487: SysRev)

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults who are comatose after resuscitation from cardiac arrest (either in-hospital or out-of-hospital), regardless of target temperature
- Intervention: Pupillary light reflex (PLR), pupillometry, corneal reflex, myoclonus, and status myoclonus assessed within 1 week after cardiac arrest
- Comparator: None
- Outcome: Prediction of poor neurological outcome defined as CPC 3 to 5 or mRS 4 to 6 at hospital discharge, 1 month, or later
- Study design: Prognostic accuracy studies where the 2×2 contingency table (ie, the number of true/false negatives and positives for prediction of poor outcome) was reported, or where those variables could be calculated from reported data, are eligible for inclusion. Unpublished studies, reviews, case reports, case series, studies including fewer than 10 patients, letters, editorials, conference abstracts, and studies published in abstract form were excluded.
- Time frame: In 2015, an ILCOR evidence review identified 4 categories of predictors of neurological outcome after cardiac arrest, namely clinical examination, biomarkers, electrophysiology, and imaging. In the last 4 years, several studies have been published and new predictors have been identified, therefore the topic needs an update.
- The most recent search of the previous SysRevs on neuroprognostication was launched on May 31, 2013. We searched studies published from January 1, 2013, to December 31, 2019.
- PROSPERO Registration: CRD42019141169

Consensus on Science

Pupillary Reflex

The association of a bilaterally absent standard PLR, measured at various time points, with outcome was investigated in 17 observational studies.[198–214] Although all of this evidence was rated as very low certainty, studies that evaluated the prognostic value of absent standard PLR at time points of 72 hours or more after ROSC had greater specificity (ranging from 90% to 100%) for unfavorable neurological outcome at time points from discharge to 12 months than studies that used the absence of PLR at less than 72 hours (specificity ranging from 48% to 92%). Sensitivity appeared to decrease when using a time point of 72 hours or more, but specificity was identified as the higher priority given the critical importance of avoiding false positives.

Pupillometry

Automated assessment of PLR can be made by measuring either of the following variables:

- The percent reduction in pupillary size, which is reported as qPLR, or
- The neurological pupil index (NPi), which is based on several variables such as pupillary size, percentage of constriction, constriction velocity, and latency.

Automated Pupillometry Using Percent of Pupillary Size Reduction (qPLR). In 3 observational studies using various time points,[209,215,216] qPLR from 0% to 13% at 24 hours predicted poor neurological outcome from 3 months to 12 months with specificity ranging from 77.8% to 98.9% and sensitivity from 17% to 66% (certainty of evidence from moderate to very low). When evaluated at 48 hours, specificity ranged from 95.7% to 100% and sensitivity from 18.1% to 58.5% (certainty of evidence from low to very low). In 1 study of 234 patients[209] qPLR=0% at 72 hours predicted poor neurological outcome at 3 months with 100% specificity and 4.9% sensitivity (moderate certainty of evidence).

Automated Pupillometry Using Multiple Variables (NPi). In 3 observational studies,[209,217,218] NPi from 0 to 2.40 within 24 hours predicted poor neurological outcome from hospital discharge to 3 months with 100% specificity and sensitivity ranging from 22% to 43.9% (certainty of evidence from moderate to very low). For the same outcome, 1 study with 361 patients[209] found that NPi 2 or less at 48 hours had 100% specificity and 18.8% sensitivity, and NPi 2 or less at 72 hours had 100% specificity, and 16.9% sensitivity (moderate certainty of evidence).

Corneal Reflex

Corneal reflex at various time points was investigated in 11 observational studies.[198,200,202,204–206,210,211,213,214,219] Although all of the evidence was rated as very low certainty, studies that evaluated the prognostic value of absent corneal reflex at time points of 72 hours or more after ROSC had greater specificity (ranging from 89% to 100%) for unfavorable neurological outcome from hospital discharge to 12 months after ROSC than studies that used the absence of corneal reflex at less than 72 hours (specificity ranging from 25% to 89%). Sensitivity appeared to decrease when using a time point of 72 hours or more, but specificity was determined to be a higher priority given the critical importance of avoiding false positives.

Myoclonus

Presence of myoclonus within 96 hours after ROSC was investigated in 6 studies[200,210,219–222] and predicted poor neurological outcome from hospital discharge to 6 months with specificity ranging from 77.8% to 100% and sensitivity ranging from 18.2% to 44.4% (very low-certainty evidence). However, definitions of myoclonus were provided in only 1 study.[220]

Status Myoclonus

Presence of status myoclonus within 72 hours after ROSC was investigated in 2 studies[178,223] and predicted poor neurological outcome from hospital discharge to 6 months with specificity ranging from 99.8% to 100% and sensitivity ranging from 12.2% to 49.1% (very low-certainty evidence). The definitions of status myoclonus differed between these 2 studies.

Treatment Recommendations

We recommend that neuroprognostication always be undertaken by using a multimodal approach because no single test has sufficient specificity to eliminate false positives (strong recommendation, very low-certainty evidence).

We suggest using PLR at 72 hours or more 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 72 hours or more 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 72 hours or more 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 days 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).

Justification and Evidence-to-Decision Framework Highlights

As noted in the previous CoSTR on this topic in 2015,[1,7] the task force consensus is that a multimodal approach should be used in all cases with all supplementary tests considered in the context of the clinical examination.

The evidence-to-decision tables are included in Supplement Appendixes A-9, 10, 11, and 12. For standard PLR, NPi, and corneal reflex, the suggestion to use these findings at 72 hours or more after ROSC was based both on the specificity found in different studies and on the perceived importance of eliminating confounding effects of sedatives or muscle relaxants as much as possible. Only some of the included studies specifically excluded the presence of residual sedation at the time the pupillary or corneal reflex was assessed.

For assessment of the pupillary reflex, the task force felt that NPi has the potential for being more accurate and less prone to bias and subjectivity. This benefit,

however, may be counterbalanced by the need for more equipment and specialized training to obtain the NPi.

Results of clinical examination usually cannot be concealed from the treating team. Therefore, a risk of self-fulfilling prophecy exists even when index tests that are based on clinical examination are not explicitly included in the criteria for withdrawal of life-sustaining therapy.

Although definitions of both myoclonus and status myoclonus are missing from most studies and are inconsistent in others, the presence of myoclonus is associated with poor outcome in patients who are comatose after ROSC from cardiac arrest and the finding may be useful within the context of a multimodal prognostic assessment. Myoclonus and status myoclonus are inconsistently associated with epileptiform activity on the EEG. Importantly, generalized myoclonus associated with favorable clinical features, such as a continuous or reactive EEG background or preserved brain stem reflexes, may be manifestations of Lance-Adams syndrome, which is compatible with a good outcome.[187,190]

Knowledge Gaps

- Absence of residual effects from sedatives must be specifically assessed in studies evaluating the accuracy of predictors on the basis of clinical examination after cardiac arrest.
- The interrater agreement for the assessment of standard PLR, corneal reflex, and myoclonus/status myoclonus in patients resuscitated from cardiac arrest deserves investigation.
- The number of studies documenting pupillometry for predicting poor outcome after cardiac arrest is still low. A consistent threshold for 100% specificity has not been identified for qPLR or NPi.
- Achieving a uniform and consensus-based definition of both myoclonus and status myoclonus is necessary. The role of EEG as an additional tool to investigate the nature and the prognostic significance of myoclonus deserves investigation.
- The most reliable combination and timing for each assessment remains to be determined.
- The potential impact of TTM on prognostication remains to be determined.

Neurophysiological Tests for Prognostication (ALS 450, 713, 460: SysRev)

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults who are comatose after resuscitation from cardiac arrest in any setting (in-hospital or out-of-hospital) and regardless of target temperature
- Intervention: Electrophysiology studies assessed within 1 week after cardiac arrest
- Comparator: None
- Outcome: Prediction of unfavorable neurological outcome defined as CPC 3 to 5 or mRS 4 to 6 at hospital discharge, 1 month, or later
- Study design: Prognostic accuracy studies where the 2×2 contingency table (ie, the number of true/false negatives and positives for prediction of poor outcome) was reported, or where those variables could be calculated from reported data, are eligible for inclusion. Unpublished studies, reviews, case reports, case series, studies including fewer than 10 patients, letters, editorials, conference abstracts, and studies published in abstract form are excluded.
- Time frame: In 2015,[1,7] an ILCOR evidence review identified 4 categories of predictors of neurological outcome after cardiac arrest, namely clinical examination, biomarkers, electrophysiology, and imaging. In the last 4 years, several studies have been published and new predictors have been identified, therefore the topic needs an update.
- The most recent search of the previous SysRevs on neuroprognostication was launched on May 31, 2013. We searched studies published from January 1, 2013, to December 31, 2019.
- PROSPERO Registration: CRD42019141169

Consensus on Science

Somatosensory Evoked Potentials

The prognostic value of somatosensory evoked potentials (SSEPs) was investigated in 14 observational studies.[199,205,208–211,214,224–230] In 4 studies,[205,224,228,229] bilaterally absent N20 SSEP wave within 24 hours after ROSC predicted poor neurological outcome from hospital discharge to 6 months. Specificity was 100% and sensitivity ranged from 33.3% to 57.7% (very low-certainty evidence). In 1 study,[199] an absent N20 wave on one side and an absent or low-voltage N20 wave on the other side within 24 hours after ROSC predicted poor neurological outcome at 6 months. Specificity was 100% and sensitivity was 49.6% (very low-certainty evidence).

In 12 studies,[205,208–211,214,225–230] bilaterally absent N20 SSEP wave at 24 to 96 hours after ROSC predicted poor neurological outcome from hospital discharge to 6 months. Specificity ranged from 50% to 100% and sensitivity ranged from 18.2% to 69.1% (very low-certainty evidence).

Unreactive EEG

The prognostic value of an unreactive EEG was investigated in 10 observational studies.[210,219,229,231–237] In 9 of these studies,[210,219,229,232–237] an unreactive EEG within 72 hours after ROSC predicted poor neurological outcome from hospital discharge to 6 months. Specificity ranged from 41.7% to 100% and sensitivity ranged from 50% to 97.1% (certainty of evidence from moderate to very

low). Specificity was below 90% in most of these studies, reaching 100% in only 2 of them.

In 1 study,[231] an unreactive EEG at a median of 77 hours after ROSC (interquartile range [IQR], 53–102) predicted poor neurological outcome at 6 months with 70% specificity and 88.1% sensitivity (very low-certainty evidence).

Rhythmic/Periodic Discharges

The prognostic value of rhythmic/periodic discharges were investigated in 9 observational studies.[199,210,228,231,237–241]

In 2 studies,[199,238] rhythmic/periodic discharges within 24 hours after ROSC predicted poor neurological outcome from 3 months to 6 months. Specificity was 100% and sensitivity ranged from 2.4% to 7.9% (certainty of evidence from moderate to very low).

In 4 studies,[210,228,238,239] rhythmic/periodic discharges within 48 hours after ROSC predicted poor neurological outcome from 3 months to 6 months. Specificity ranged from 97.2% to 100% and sensitivity ranged from 8.1% to 42.9% (certainty of evidence from moderate to very low).

In 3 studies,[228,237,239] rhythmic/periodic discharges at 48 to 72 hours after ROSC predicted poor neurological outcome from 1 month to 6 months. Specificity ranged from 66.7% to 96.1% and sensitivity ranged from 11.4% to 50.8% (certainty of evidence from low to very low).

In 2 studies,[231,240] rhythmic/periodic discharges at the median time of 76 to 77 hours after ROSC predicted poor neurological outcome at 6 months. Specificity ranged from 97% to 100% and sensitivity ranged from 5% to 40% (certainty of evidence from low to very low).

In 1 study,[241] rhythmic/periodic discharges within 5 days after ROSC predicted poor neurological outcome at 6 months. Specificity was 100% and sensitivity was 15.7% (moderate certainty of evidence).

Sporadic, Nonrhythmic/Periodic Discharges

The prognostic value of sporadic, nonrhythmic/periodic discharges was investigated in 5 observational studies.[199,226,228,237,238] In 3 studies,[199,226,238] sporadic, nonrhythmic/periodic discharges within 24 hours after ROSC predicted poor neurological outcome from 3 months to 6 months. Specificity ranged from 84.6% to 100% and sensitivity ranged from 0.5% to 7.9% (certainty of evidence from moderate to very low).

In 3 studies,[226,228,238] sporadic, nonrhythmic/periodic discharges within 48 hours predicted poor neurological outcome from 3 months to 6 months. Specificity ranged from 95.8% to 99.5% and sensitivity ranged from 0.4% to 13.3% (certainty of evidence from moderate to very low).

In 3 studies,[226,228,237] sporadic, nonrhythmic/periodic discharges at 48 to 72 hours predicted poor neurological outcome from 1 month to 6 months. Specificity ranged from 88.9% to 97.3% and sensitivity ranging from 0.6% to 38.5% (certainty of evidence from low to very low).

In 1 study,[226] sporadic, nonrhythmic/periodic discharges at 96 to 120 hours predicted poor neurological outcome at 6 months. Specificity ranged from 66.7% to 82.1% and sensitivity ranged from 17.6% to 21.3% (very low-certainty evidence).

Seizures

The prognostic implications of seizures were investigated in 5 observational studies.[220,231,236–238] In 4 of these studies, seizures were recorded within 72 hours after ROSC, and in 1 study,[231] they were recorded at a median of 77 (53–102) hours after ROSC. In these studies, the presence of seizures predicted poor neurological outcome from hospital discharge to 6 months with 100% specificity and sensitivity ranging from 0.6% to 26.8% (certainty of evidence from moderate to very low).

The prognostic implications of status epilepticus were investigated in 6 studies.[202,225,236,241–243] The definitions of status epilepticus were inconsistent across studies. In these studies, status epilepticus within 5 days after ROSC predicted poor neurological outcome from hospital discharge to 6 months. Specificity ranged from 82.6% to 100% and sensitivity ranged from 1.8% to 50% (certainty of evidence low to very low).

In 3 of these studies,[202,225,236] EEG was recorded within 72 hours after ROSC and specificity was 100%. In another study,[243] specificity was 100% only when status epilepticus originated from a discontinuous or burst-suppression background.

Burst Suppression

The possible prognostic value of burst suppression was investigated in 6 observational studies.[202,220,225,231,233,240] In 2 studies,[220,233] burst suppression within 24 hours after ROSC predicted poor neurological outcome to hospital discharge with 50% to 100% specificity and 50% to 51.5% sensitivity (certainty of evidence very low).

In 5 studies,[202,225,231,233,240] burst suppression at 24 to 120 hours after ROSC predicted poor neurological outcome at hospital discharge to 6 months. Specificity ranged from 91.7% to 100% and sensitivity ranged from 13.9% to 55.6% (certainty of evidence from low to very low).

Definitions of burst suppression used in these studies varied when they were included at all. In 2 studies,[231,240] the American Clinical Neurophysiology Society definition[244] was used. In 1 study, a non-American Clinical Neurophysiology Society definition was used, while in the remaining studies, no specific definition was used.

Synchronous Burst Suppression. In 1 study,[226] a synchronous burst suppression at 6 to 96 hours after ROSC

predicted poor neurological outcome at 6 months with 100% specificity and sensitivity ranging from 1.1% to 31.7% (certainty of evidence from moderate to low).

Heterogeneous Burst Suppression. In 1 study,[226] heterogeneous burst suppression at 6 to 120 hours after ROSC predicted poor neurological outcome at 6 months. Specificity ranged from 90.7% to 100% and sensitivity ranged from 1.1% to 16.2% (certainty of evidence from moderate to very low).

Treatment Recommendations

We recommend that neuroprognostication always be undertaken by using a multimodal approach because no single test has sufficient specificity to eliminate false positives (strong recommendation, very low-certainty evidence).

We suggest using a bilaterally absent N20 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).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision tables are included in Supplement Appendixes A-13, 14, 15, 16, and 17.

In making a recommendation about use of SSEPs for prognostication, the task force considered that SSEPs have a low risk of confounding from TTM or sedation and a large size of effect (high precision). However, to limit the risk of self-fulfilling prophecy, combining evaluation of SSEPs with other indices of poor neurological outcome is prudent.

In almost all studies, we included the specificity of unreactive EEG background for predicting poor outcome, and its precision was low. In addition, both definitions of and stimuli to induce EEG reactivity were inconsistent across studies.

In most of the studies, we reported the specificity of rhythmic/periodic epileptiform activity for predicting poor outcome as 100%. Specificity was lower for sporadic epileptiform discharges.

In all studies, we included the specificity of American Clinical Neurophysiology Society-defined seizures on EEG for predicting poor outcome as 100%.[244] This specificity was consistent throughout the first 72 hours after ROSC.

Specificity of status epilepticus for predicting poor outcome was 100% in only half of the studies we included. An additional challenge for use of studies of status epilepticus for prognostication is the inconsistency of its definitions in reported studies.

In all studies we included, the presence of burst suppression on EEG predicted poor neurological outcome with a specificity above 90%, and in most studies, the specificity was 100%. Because sedative agents can affect the EEG, the most prudent strategy is to assess burst suppression for prognostication when any effects of sedation medications have cleared.

Knowledge Gaps

- Further studies are needed to evaluate the added value of assessing SSEPs in combination with other predictors of poor neurological outcome after cardiac arrest.
- It is desirable that future studies adopt a standard definition of background EEG reactivity. An international consensus statement on EEG reactivity testing (eg, stimulus protocol) has been proposed.[245]
- It is desirable that future studies adopt a standard definition of epileptiform discharges.
- The specific predictive value of the different epileptiform subtypes, their prevalence, and their combination with background EEG deserves further investigation.
- Precision was low or very low in most studies of the association of seizures with outcome. Further studies are needed to confirm the predictive value of seizures for poor outcome after cardiac arrest.
- A standard definition of status epilepticus is urgently needed.
- It is desirable that future studies adopt a standard definition of burst suppression, such as the one included in the American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology.[244]
- The accuracy of synchronous burst suppression for prognostication (identical/highly epileptiform bursts) deserves further investigation.
- It is desirable to achieve a consensus definition of the term, "highly malignant EEG patterns"

in patients who are comatose after resuscitation from cardiac arrest.
- The potential impact of TTM on prognostication remains to be determined.

Blood Biomarkers for Prognostication (ALS 450, 713, 484: SysRev)

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults who are comatose after resuscitation from cardiac arrest in any setting (in-hospital or out-of-hospital) and regardless of target temperature
- Intervention: The use of neuron-specific enolase (NSE), S-100B, glial fibrillary acidic protein, serum tau protein, and neurofilament light chain assessed within 1 week after cardiac arrest
- Comparator: None
- Outcome: Prediction of unfavorable neurological outcome, defined as CPC 3 to 5 or mRS 4 to 6 at hospital discharge, 1 month, or later
- Study design: Prognostic accuracy studies where the 2×2 contingency table (ie, the number of true/false negatives and positives for prediction of poor outcome) was reported, or where those variables could be calculated from reported data, are eligible for inclusion. Unpublished studies, reviews, case reports, case series, studies including fewer than 10 patients, letters, editorials, conference abstracts, and studies published in abstract form were excluded.
- Time frame: In 2015, an ILCOR evidence review[1,7] identified 4 categories of predictors of neurological outcome after cardiac arrest, namely clinical examination, biomarkers, electrophysiology, and imaging. In the last 4 years, several studies have been published and new predictors have been identified, therefore the topic needs an update.
- The most recent search of the previous SysRevs on neuroprognostication was launched on May 31, 2013. We searched studies published from January 1, 2013, to December 31, 2019.
- PROSPERO Registration: CRD42019141169

Consensus on Science

Neuron-Specific Enolase

The prognostic value of NSE was investigated in 12 observational studies.[202,206,208,214,239,246–252] In these studies, NSE with thresholds ranging from 33 to 120 µg/L within 72 hours after ROSC predicted poor neurological outcome from hospital discharge to 6 months. Specificity ranged from 75% to 100% and sensitivity ranged from 7.8% to 83.6% (certainty of evidence from moderate to very low).

In 1 study,[248] NSE with a threshold of 50.2 µg/L at day 4 (after ROSC) predicted poor neurological outcome at 1 month with 100% specificity and 42.1% sensitivity (moderate certainty of evidence).

S-100B

The accuracy of S-100B protein in predicting poor outcome in patients with ROSC after cardiac arrest was investigated in 3 observational studies.[251,253,254]

In 2 studies,[251,254] S-100B protein with threshold ranging from 3.58 to 16.6 µg/L immediately after ROSC predicted poor neurological outcome from 3 to 6 months with 100% specificity and sensitivity ranging from 2.8% to 26.9% (certainty of evidence from moderate to very low).

In 3 studies,[251,253,254] S-100B protein with a threshold ranging from 0.193 to 2.59 µg/L at 24 hours after ROSC predicted poor neurological outcome from 3 to 6 months with 100% specificity and sensitivity ranging from 10.1% to 77.6% (certainty of evidence from moderate to very low). In the same 3 studies,[251,253,254] S-100B protein with a threshold ranging from 0.159 to 3.67 µg/L at 48 hours after ROSC predicted poor neurological outcome from 3 to 6 months with 100% specificity and sensitivity ranging from 5% to 77.6% (certainty of evidence from moderate to very low). In the same 3 studies,[251,253,254] S-100B protein with a threshold ranging from 0.202 to 1.83 µg/L at 72 hours after ROSC predicted poor neurological outcome from 3 to 6 months with 100% specificity and sensitivity ranging from 5% to 61.2% (certainty of evidence from moderate to very low).

Glial Fibrillary Acidic Protein

In 1 study,[252] glial fibrillary acidic protein with a threshold of 0.08 µg/L at 48±12 hours after ROSC predicted poor neurological outcome at 1 month with 100% specificity and 21.3% sensitivity (low-certainty evidence).

Serum Tau Protein

In 1 study with 667 patients,[255] serum tau protein with a threshold ranging from 72.7 to 874.5 ng/L at 24 to 72 hours after ROSC predicted poor neurological outcome at 6 months with 100% specificity and sensitivity ranging from 4% to 42% (very low-certainty evidence).

Serum Neurofilament Light Chain

In 1 study,[256] serum neurofilament light chain with a threshold ranging from 1539 to 12317 pg/mL at 24 to 72 hours after ROSC predicted poor neurological outcome at 6 months with 100% specificity and sensitivity ranging from 53.1% to 65% (moderate certainty of evidence).

In 1 study,[257] serum neurofilament light chain with a threshold ranging from 252 to 405 pg/mL from day 1 to day 7 after ROSC predicted poor neurological outcome (CPC 4–5) at 6 months with 100% specificity and sensitivity ranging from 55.6% to 94.4% (very low-certainty evidence).

Treatment Recommendations

We recommend that neuroprognostication always be undertaken by using a multimodal approach because no single test has sufficient specificity to eliminate false positives (strong recommendation, very low-certainty evidence).

We suggest using NSE within 72 hours 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).

Justification and Evidence-to-Decision Framework Highlights

As was noted in the information addressing this topic in the 2015 CoSTR,[1,7] the task force opinion is that a multimodal approach should be used in all cases with all supplementary tests considered in the context of prognostication.

The evidence-to-decision tables are included in Supplement Appendixes A-18, 19, and 20.

Limited evidence suggests that high concentrations of NSE predict poor neurological outcome with 100% specificity at 24 to 72 hours after cardiac arrest, but there is a wide variability of thresholds for 100% specificity across studies. Lack of blinding was a limitation in most of included studies, even if withdrawal of life sustaining therapy based only on NSE was not documented.

Although the risk of self-fulfilling prophecy for S-100B protein is lower than that observed in other predictors, the evidence is limited by the few available studies and the wide variability of thresholds for 100% specificity across studies.

The supporting evidence about the use of neurofilament light chain, glial fibrillary acidic protein, and serum tau protein for prognostication after cardiac arrest is limited to very few studies. Consistent thresholds for 100% specificity need to be identified before any of these biomarkers can be recommended for prognostication in the clinical setting. These biomarker tests are not widely available. The methods used for measuring these biomarkers need to be more widely available, standardized, and studied.

Knowledge Gaps

- Large cohort studies are desirable to identify consistent NSE and S-100B thresholds for predicting poor neurological outcome after cardiac arrest. There is very little evidence concerning the predictive value of these biomarkers when measured later than 72 hours after ROSC.
- Further studies on glial fibrillary acidic protein, serum tau protein, and neurofilament light chain are needed to confirm their predictive value after cardiac arrest, to assess their reproducibility, and to identify consistent thresholds for 100% specificity.
- The potential impact of TTM on prognostication remains to be determined.

Imaging for Prognostication (ALS 450, 713, 458: SysRev)

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults who are comatose after resuscitation from cardiac arrest in any setting (in-hospital or out-of-hospital) and regardless of target temperature
- Intervention: Imaging studies assessed within 1 week after cardiac arrest
- Comparator: None
- Outcome: Unfavorable neurological outcome defined as CPC 3 to 5 or mRS 4 to 6 at hospital discharge, 1 month, or later
- Study design: Prognostic accuracy studies where the 2×2 contingency table (ie, the number of true/false negatives and positives for prediction of poor outcome) was reported, or where those variables could be calculated from reported data, are eligible for inclusion. Unpublished studies, reviews, case reports, case series, studies including fewer than 10 patients, letters, editorials, conference abstracts, and studies published in abstract form were excluded.
- Time frame: In 2015,[1,7] an ILCOR evidence review identified 4 categories of predictors of neurological outcome after cardiac arrest, namely clinical examination, biomarkers, electrophysiology, and imaging. In the last 4 years, several studies have been published and new predictors have been identified, therefore the topic needs an update.
- The most recent search of the previous SysRevs on neuroprognostication was launched on May 31, 2013. We searched studies published from January 1, 2013, to December 31, 2019.
- PROSPERO Registration: CRD42019141169

Consensus on Science

Gray Matter–to–White Matter Ratio

Gray Matter–to–White Matter Ratio: Average. The prognostic value of the gray matter–to–white matter ratio (GWR) average was investigated in 7 observational studies.[203,214,258–262] In 4 studies,[214,260,261,263] a GWR

Table 3a. Sensitivity and Specificity of GWR at 50 (IQR, 26–107) Minutes From ROSC by Brain Location in Patients With Cardiac Arrest of Cardiac Etiology

Study, Year	GWR	Location or Type	Sensitivity	Specificity	Certainty of Evidence
Poor Neurological Outcome at Discharge					
Lee, 2015[266]	≤1.13	Average	3.5%	100%	Very low
	≤1.11	Basal ganglia	3.5%	100%	Very low
	≤1.107	Putamen/corpus callosum	5.6%	100%	Very low
	≤1.06	Simplified	3.5%	100%	Very low
	≤1.094	Caudate nucleus/posterior limb of the internal capsule	3.5%	100%	Very low
	≤1.15	Cerebrum	4.2%	100%	Very low

GWR indicates gray matter–to–white matter ratio; and IQR, interquartile range.

average 1.23 or less within 6 hours after ROSC predicted poor neurological outcome from hospital discharge to 6 months with 100% specificity and sensitivity ranging from 13.3% to 83.8% (certainty of evidence from low to very low).

In 1 study,[203] a GWR average 1.13 or less at 124.5±59.9 minutes from ROSC predicted poor neurological outcome at 1 month with 85% specificity and 29.8% sensitivity (very low-certainty evidence).

In 1 study,[259] a GWR average 1.077 or less within 24 hours after ROSC predicted poor neurological outcome at hospital discharge with 100% specificity and 15.6% sensitivity (very low-certainty evidence).

In 1 study,[258] a GWR average 1.14 or less within 72 hours after ROSC predicted poor neurological outcome at hospital discharge with 100% specificity and 38.1% sensitivity (very low-certainty evidence).

Gray Matter–to–White Matter Ratio: Basal Ganglia. The prognostic value of the GWR in the basal ganglia was investigated in 4 observational studies.[199,258,261,264] In 1 study,[261] GWR-basal ganglia 1.12 or less within 1 hour after ROSC predicted poor neurological outcome at hospital discharge with 100% specificity and 3.3% sensitivity (very low-certainty evidence).

In 2 studies,[199,264] GWR-basal ganglia 1.21 or less within 24 hours after ROSC predicted poor neurological outcome at 6 months with 100% specificity and sensitivity ranging from 41.8% to 42.1% (certainty of evidence from moderate to very low).

In 1 study,[258] GWR-basal ganglia 1.12 or less within 72 hours after ROSC predicted poor neurological outcome at hospital discharge with 100% specificity and 28.6% sensitivity (very low-certainty evidence).

Gray Matter–to–White Matter Ratio: Putamen/Corpus Callosum. The prognostic value of the GWR putamen/corpus callosum was investigated in 3 observational studies.[247,260,265]

In 2 studies,[247,260] the GWR putamen/corpus callosum 1.17 or less within 6 hours after ROSC predicted poor neurological outcome from hospital discharge to 6 months with 100% specificity and sensitivity ranging from 31.3% to 52.9% (very low-certainty evidence).

In 1 study,[265] of 258 patients, the GWR putamen/corpus callosum 0.91 or less within 24 hours after ROSC predicted poor neurological outcome at 6 months with 100% specificity and 1.7% sensitivity (very low-certainty evidence).

Gray Matter–to–White Matter Ratio: Simplified (Putamen/Posterior Limb of Internal Capsule). In 1 observational study, GWR-simplified[258] a ratio 1.1 or less

Table 3b. Sensitivity and Specificity of GWR at 67 (IQR, 29–115) Minutes From ROSC by Brain Location in Patients With Cardiac Arrest of Noncardiac Etiology

Study	GWR	Location or Type	Sensitivity	Specificity	Certainty of Evidence
Poor Neurological Outcome at Discharge					
Lee, 2016[267]	≤1.22	Average	28.3%	100%	Very low
	≤1.17	Basal ganglia	26.2%	100%	Very low
	≤1.2	Putamen/corpus callosum	43.4%	100%	Very low
	≤1.12	Simplified	9.7%	100%	Very low
	≤1.138	Caudate nucleus/posterior limb of the internal capsule	20%	100%	Very low
	≤1.2	Cerebrum	11%	100%	Very low

GWR indicates gray matter–to–white matter ratio; and IQR, interquartile range.

within 72 hours after ROSC predicted poor neurological outcome at hospital discharge with 100% specificity and 28.6% sensitivity (very low-certainty evidence).

Gray Matter–to–White Matter Ratio: Caudate Nucleus/Posterior Limb of Internal Capsule. In 2 observational studies,[247,260] a GWR in the caudate nucleus/posterior limb of the internal capsule 1.15 or less within 6 hours after ROSC predicted poor neurological outcome from hospital discharge to 6 months with 100% specificity and sensitivity ranging from 19.8% to 40.6% (very low-certainty evidence).

Gray Matter–to–White Matter Ratio: Cerebrum. The prognostic value of the GWR in the cerebrum was investigated in 2 observational studies.[258,261] In 1 study,[261] a GWR in the cerebrum 1.12 or less within 1 hour after ROSC predicted poor neurological outcome at hospital discharge with 100% specificity and 20% sensitivity (very low-certainty evidence).

In 1 study,[258] a GWR in the cerebrum 1.09 or less within 72 hours after ROSC predicted poor neurological outcome at hospital discharge with 100% specificity and 28.6% sensitivity (very low-certainty evidence).

Gray Matter–to–White Matter Ratio: Thalamus/Corpus Callosum. In 1 observational study,[260] a GWR in the cerebrum thalamus/corpus callosum 1.13 or less at a median time of 90 (IQR, 52–150) minutes after ROSC predicted poor neurological outcome at 6 months with 100% specificity and 50% sensitivity (very low-certainty evidence).

Gray Matter–to–White Matter Ratio: Caudate Nucleus/Corpus Callosum. In 1 observational study,[260] the GWR in the caudate nucleus/corpus callosum 1.15 or less at median time of 90 (IQR, 52–150) minutes after ROSC predicted poor neurological outcome at 6 months with 100% specificity and 46.9% sensitivity (very low-certainty evidence).

Gray Matter–to–White Matter Ratio in Cardiac Versus Noncardiac Etiology. One study assessed the predictive value of GWR specifically in patients with cardiac arrest of cardiac etiology, and one other focused exclusively on cardiac arrest with noncardiac etiology.[266,267] Both of these studies reported GWRs that had 100% specificity for poor neurological outcome, and sensitivity was low in all cases. Results are presented in detail in Tables 3a and 3b.

Diffusion-Weighted MRI

The prognostic value of diffusion-weighted magnetic resonance imaging (MRI) was investigated in 5 observational studies.[198,214,260,268,269]

In 1 study,[260] high signal intensity on diffusion-weighted MRI within 6 hours after ROSC predicted poor neurological outcome at 6 months with 100% specificity and 81.3% sensitivity (very low-certainty evidence).

In 4 studies,[198,214,268,269] positive findings on diffusion-weighted MRI within 5 days after ROSC predicted poor neurological outcome from hospital discharge to 6 months with specificity ranging from 55.7% to 100% and sensitivity ranging from 26.9% to 92.6% (very low-certainty evidence).

Apparent Diffusion Coefficient

The prognostic value of apparent diffusion coefficient (ADC) was investigated in 2 studies.[261,269a]

In 1 study,[270] a mean ADC 726×10–6 mm^2/s or less at less than 48 hours after ROSC predicted poor neurological outcome at 6 months with 100% specificity and 44% sensitivity (very low-certainty evidence).

In the same study,[270] a mean ADC 627×10–6 mm^2/s or less at 48 hours to 7 days after ROSC predicted poor neurological outcome at 6 months with 100% specificity and 20.8% sensitivity (very low-certainty evidence).

In the same study,[270] an ADC volume proportion (400×10–6 mm^2/s) greater than 2.5% at less than 48 hours after ROSC predicted poor neurological outcome at 6 months with 100% specificity and 64% sensitivity (very low-certainty evidence).

In the same study,[270] an ADC volume proportion (400×10–6 mm^2/s) greater than 1.66% at 48 hours to 7 days after ROSC predicted poor neurological outcome at 6 months with 100% specificity and 79.2% sensitivity (very low-certainty evidence).

In another study,[269a] maximum cluster size in different cerebral regions on MRI 151.7×10–6 mm^2/s or less at 46 (IQR, 37–52) hours after ROSC predicted poor neurological outcome at 6 months with 100% specificity and sensitivity ranging from 62.5% to 90% (very low-certainty evidence).

In that same same study,[269a] the lowest mean ADC in different cerebral regions on MRI 555.7×10–6 mm^2/s or less at 46 (IQR, 37–52) hours after ROSC predicted poor neurological outcome at 6 months with 100% specificity and sensitivity ranging from 50% to 72.5% (very low-certainty evidence).

In the same study,[269a] the lowest minimum ADC in different cerebral regions MRI 466.8×10–6 mm^2/s or less at 46 (IQR, 37–52) hours after ROSC predicted poor neurological outcome at 6 months with 100% specificity and sensitivity ranging from 42.5% to 82.5% (very low-certainty evidence).

Treatment Recommendations

We recommend that neuroprognostication always be undertaken by using a multimodal approach because no single test has sufficient specificity to eliminate false positives (strong recommendation, very low-certainty evidence).

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).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision tables are included Supplement Appendixes A-21, 22, and 23. As noted in the 2015 CoSTR on this topic,[1,7] the task force consensus is that a multimodal approach should be used in all cases with all supplementary tests considered in the context of prognostication.

In patients who are comatose after cardiac arrest, severe brain edema predicts poor outcome with high specificity. Calculation of GWR allows a quantitative evaluation of brain edema. However, there is a wide heterogeneity of measurement techniques (sites and calculation methods) for GWR. This may partly explain the wide variability of thresholds for 100% specificity across the identified studies. The evidence supporting use of the GWR for prognostication has very low certainty.

Assessing diffusion-weighted imaging has potential for predicting poor neurological outcome after cardiac arrest. The definition of a positive diffusion weighted magnetic resonance image after cardiac arrest was inconsistent or even absent in the identified studies. The supporting evidence had very low certainty.

Assessing ADC has a potential for predicting poor neurological outcome after cardiac arrest with high sensitivity. There is a wide heterogeneity of measurement techniques (sites and calculation methods) for ADC across studies. The supporting evidence for ADC had very low certainty.

Knowledge Gaps

- A consistent GWR threshold for predicting poor neurological outcome after cardiac arrest should be identified.
- A standardization of the methods for GWR calculation is warranted.
- The optimal timing for prognostication using brain computed tomography after cardiac arrest is still unknown. Studies assessing serial brain computed tomography after cardiac arrest are desirable.
- The criteria for defining a positive diffusion-weighted MRI after cardiac arrest need to be standardized.
- A consistent ADC threshold for predicting poor neurological outcome after cardiac arrest should be identified.
- Standardization of the methods for ADC calculation is needed.
- The potential impact of TTM on prognostication remains to be determined.

ALS COSTR TOPICS NOT REVIEWED IN 2020

Post-ROSC Percutaneous Coronary Intervention

Updates to 2015 CoSTRs for acute coronary syndromes (ACS) are now part of ALS postresuscitation care because there is no longer an ACS Task Force.[271,272] The topics of percutaneous coronary intervention after ROSC in patients with and without ST-segment elevation (ACS 340, ACS 885) will be addressed in the 2021 CoSTR after publication of an ongoing SysRev.

Organ Donation After Cardiac Arrest

The 2015 treatment recommendations[1,7] have not been updated for 2020. An ILCOR scientific statement on organ donation after OHCA will provide a narrative summary of the world literature on the incidence and outcomes of organ donation after OHCA as well as an estimation of potential donors and published implementation strategies with or without extracorporeal resuscitation. The statement includes a review of the international ethical issues and provides cost effectiveness estimates. It will make summary suggestions for implementation as well as identify key knowledge gaps that need to be addressed by future research.

Manual Defibrillation Topics Not Reviewed in 2020

- Algorithm for transition from shockable to nonshockable rhythm and vice versa (ALS 444)
- Biphasic waveforms (ALS 470)
- Pulsed biphasic waveforms (ALS 470)
- First shock energy (ALS 470)
- Single shocks versus stacked shocks (ALS 470)
- Fixed versus escalating defibrillation energy (ALS 470)
- Cardioversion strategies with implantable cardioverter-defibrillators or pacemakers (ALS 475)

Circulatory Support Topics Not Reviewed in 2020

- IABP versus manual CPR (ALS 724)
- Open-chest CPR (ALS 574)

- Impedance threshold device (ALS 579)
- Mechanical CPR devices (ALS 782)

Drugs During CPR Topics Not Reviewed in 2020

- IV fluids during cardiac arrest (ALS 578)
- Drugs for atrial fibrillation (ALS 466)
- Drugs for narrow complex tachycardia (ALS 463)
- Drugs for monomorphic wide complex tachycardia (ALS 464)
- Drugs for undifferentiated stable wide complex tachycardia (ALS 583)
- Drugs for bradycardia (ALS 465)
- Atropine for cardiac arrest (ALS 491)
- Calcium for cardiac arrest (ALS 482)

Intra-arrest Monitoring Topics Not Reviewed in 2020

- Point-of-care echocardiography for diagnosis during CPR (ALS 658)

Special Circumstances Topics Not Reviewed in 2020

- Cardiac tamponade (ALS 478)
- Cardiac arrest during coronary catheterization (ALS 479)
- Cardiac arrest in operating room (ALS 812)
- Post-op cardiothoracic surgery cardiac arrest (ALS 572)
- Electrolyte disturbances (ALS 456)
- Digoxin toxicity (ALS 468)
- Tricyclic antidepressant toxicity (ALS 429)
- Cyanide toxicity (ALS 471)
- Cocaine toxicity (ALS 474)
- Carbon monoxide toxicity (ALS 480)
- Calcium channel blocker toxicity (ALS 481)
- Beta blocker toxicity (ALS 485)
- Benzodiazepine toxicity (ALS 486)
- Lipid therapy for cardiac arrest secondary to drug toxicity (ALS 834)
- Avalanche victims (ALS 489)
- Morbid obesity (ALS 452)
- Asthma and cardiac arrest (ALS 492)
- Cardiac arrest caused by anaphylaxis (ALS 494)

Postresuscitation Care Topics Not Reviewed in 2020

- IV fluids after cardiac arrest (ALS 577)
- Mechanical circulatory support postresuscitation (ALS 447)
- Glucose control after resuscitation (ALS 580)
- Hemofiltration postresuscitation (ALS 453)
- Percutaneous coronary intervention after ROSC with ST-segment elevation (ACS 340)
- Percutaneous coronary intervention after ROSC without ST-segment elevation (ACS 885)
- Organ donation (ALS 449)

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*Modest.

†Significant.

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Circulation

Pediatric Life Support

2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

ABSTRACT: This *2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations* (CoSTR) for pediatric life support is based on the most extensive evidence evaluation ever performed by the Pediatric Life Support Task Force. Three types of evidence evaluation were used in this review: systematic reviews, scoping reviews, and evidence updates. Per agreement with the evidence evaluation recommendations of the International Liaison Committee on Resuscitation, only systematic reviews could result in a new or revised treatment recommendation.

Systematic reviews performed for this 2020 CoSTR for pediatric life support included the topics of sequencing of airway-breaths-compressions versus compressions-airway-breaths in the delivery of pediatric basic life support, the initial timing and dose intervals for epinephrine administration during resuscitation, and the targets for oxygen and carbon dioxide levels in pediatric patients after return of spontaneous circulation. The most controversial topics included the initial timing and dose intervals of epinephrine administration (new treatment recommendations were made) and the administration of fluid for infants and children with septic shock (this latter topic was evaluated by evidence update). All evidence reviews identified the paucity of pediatric data and the need for more research involving resuscitation of infants and children.

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CONTENTS

The *2020 International Consensus on Cardiopulmonary Resuscitation* (CPR) *and Emergency Cardiovascular Care* (ECC) *Science With Treatment Recommendations* (CoSTR) is the fourth in a series of annual publications from the International Liaison Committee on Resuscitation (ILCOR). This 2020 CoSTR summary for pediatric life support (PLS) includes new topics addressed by Systematic Reviews (SysRevs) performed within the past 12 months. It also includes updates of the PLS CoSTR statements published from 2010 through 2019 as needed, based on additional evidence evaluations. As a result, this 2020 CoSTR summary for PLS is the most comprehensive update since 2010. The 3 major types of evidence evaluation supporting this 2020 publication are the SysRev, the Scoping Review (ScopRev), and the Evidence Update (EvUp).

Topics and types of reviews were prioritized by the PLS Task Force over the past 12 months on the basis of task force consensus that the answers to the review questions were critical, task force expert awareness of recent studies on the topics that could change treatment recommendations, and input and requests from the ILCOR member councils. SysRevs were performed on topics if deemed critical on the basis of the questions involved or if publication of studies suggested the need to consider new or modified treatment recommendations. ScopRevs and EvUps were performed if the task force or member councils identified a topic as important or if it had not been reviewed in several years; ScopRevs and EvUps were intended to determine if sufficient published evidence existed to suggest the need for a SysRev.

The SysRev is a rigorous process following strict methodology to answer a specific question, and each of these ultimately resulted in the generation of a task force CoSTR included in this summary. The SysRevs were performed by a knowledge synthesis unit, an expert systematic reviewer, or the PLS Task Force, and many resulted in separate SysRevs publications.

To begin the SysRev, the question to be answered was phrased in terms of the PICOST (population, intervention, comparator, outcome, study design, time frame) format. The methodology used to *identify* the evidence was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[1] The approach used to *evaluate* the evidence was based on that proposed by the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) working group.[2] Using this approach, the PLS Task Force rated as high, moderate, low, or very low the certainty/confidence in the estimates of effect of an intervention or assessment across a body of evidence for each of the predefined outcomes. Randomized controlled trials (RCTs) generally began the analysis as high-certainty evidence, and observational studies generally began the analysis as low-certainty evidence; examination of the evidence using the GRADE approach could result in downgrading or upgrading the certainty of evidence. For additional information, refer to "Evidence Evaluation Process and Management of Potential Conflicts of Interest."[3,3a]

When a pre-2015 CoSTR treatment recommendation was not updated, the language used in the recommendation differed from that used in the GRADE approach because GRADE was not used before 2015.[4–6]

Draft 2020 (ie, new) CoSTRs for PLS were posted on the ILCOR website[7] for public comment between March 26, 2018, and January 10, 2020. The draft CoSTR statements were viewed 31 468 times with 16 comments received. All comments were discussed by the PLS Task

Force and modifications made as needed to the content or to the recommendations for future search strategies.

This summary contains the final wording of the CoSTR statements as approved by the ILCOR PLS Task Force and the ILCOR member councils after review and consideration of comments posted online in response to the draft CoSTRs. In this publication, each topic includes the PICOST as well as the CoSTR, an expanded Justification and Evidence to Decision Framework Highlights section, and a list of knowledge gaps requiring future research studies. An evidence-to-decision table is included for each CoSTR in Appendix A in the Supplemental Materials.

The second major type of evidence evaluation performed to support this 2020 CoSTR summary for PLS is a ScopRev. ScopRevs are designed to identify the extent, range, and nature of evidence on a topic or question, and they were performed by topic experts in consultation with the PLS Task Force. The task force analyzed the identified evidence and determined its value and implications for resuscitation practice or research. The rationale for the ScopRev, the summary of evidence, and task force insights—all are highlighted in the body of this publication. Any previous treatment recommendations are reiterated. The task force noted whether the ScopRev identified substantive evidence that could result in a change in the ILCOR treatment recommendations. If sufficient evidence was identified, the task force suggested consideration of a (future) SysRev to support the development of an updated CoSTR. All ScopRevs are included in their entirety in Appendix B in the Supplemental Materials.

The third type of evidence evaluation supporting this 2020 CoSTR for PLS is an EvUp. EvUps were generally performed to identify new studies published after the most recent ILCOR evidence evaluation, typically by using search terms and methodologies from previous reviews. These EvUps were performed by task force members, collaborating experts, or members of council writing groups. The EvUps are cited in the body of this publication with a note as to whether the evidence suggested the need to consider a SysRev; the most recent ILCOR treatment recommendation was reiterated.

In this publication, no change in an ILCOR treatment recommendation resulted from a ScopRev or an EvUp; if substantial new evidence was identified, the task force recommended consideration of a SysRev. All EvUps are included in Appendix C in the Supplemental Materials, as they were drafted by the reviewers.

Note: The reviews and treatment recommendations apply to infants (28 days to 12 months) and children (the age definitions varied in the cited studies). Evidence evaluation of studies of resuscitation of newborns (especially at birth) can be found in "Neonatal Life Support: 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations"[7a,7b] in this supplement.

TOPICS REVIEWED IN THIS 2020 PLS CoSTR

Note: As indicated above, the PLS CoSTR evidence reviews were all completed by January 10, 2020. As a result, this document does not address the topic of potential influence of coronavirus disease 2019 (COVID-19) on resuscitation practice. In the spring of 2020, an ILCOR writing group was assembled to identify and evaluate the published evidence regarding risks of aerosol generation and infection transmission during attempted resuscitation of adults, children, and infants. This group developed a consensus on science with treatment recommendations and task force insights. This statement is published as a separate document.[8] As new evidence emerges, the ILCOR task forces will review and update this statement, so the reader is referred to the ILCOR website[7] for the most up-to-date recommendations.

Pediatric Basic Life Support (PBLS): CPR and CPR Quality

- Sequence of compression and ventilation (BLS 661: Shared SysRev)
- Pulse check accuracy (PLS 393: EvUp)
- Chest compression–only versus conventional CPR (2017 CoSTR)
- Pediatric compression depth (PLS 314: ScopRev)
- 1-hand versus 2-hand compressions for children (PLS 375: EvUp) combined with circumferential compressions for infants (PLS 416: EvUp)

PBLS: Automated External Defibrillation

- Use of automated external defibrillators (AEDs) for infants with out-of-hospital cardiac arrest (OHCA) (PLS 425: EvUp)

PBLS: Prevention of Cardiac Arrest

- Pediatric early-warning scores (PEWS) (PLS 818: ScopRev)
- Pediatric medical emergency/rapid response teams (PLS 397: EvUp)

Pediatric Advanced Life Support (PALS): Recognition and Treatment of Septic Shock

- Fluid administration for the child with septic shock (PLS 1534: EvUp)
- Vasoactive drugs for septic shock (PLS 1604: ScopRev)
- Corticosteroids for pediatric septic shock (PLS 413: EvUp)

PALS: Recognition and Prearrest Treatments for Shock

- Graded volume resuscitation for traumatic/hemorrhagic shock (PLS 400: ScopRev)
- Timing of intubation for shock (PLS 399: EvUp)
- Prearrest care of the infant or child with dilated cardiomyopathy or myocarditis (PLS 819: EvUp)
- Cardiogenic shock and inotropes (PLS 418: EvUp)

PALS: Management of Deterioration With Pulmonary Hypertension

- Prevention and management of pulmonary hypertensive crises in infants and children (PLS 391: EvUp)
- Opioids, sedatives, and neuromuscular blocking drugs for pulmonary hypertension (PLS New: EvUp)
- Therapy with inhaled nitric oxide or prostaglandin I_2 for pulmonary hypertensive crisis and right heart failure (PLS New: EvUp)

PALS: Recognition and Treatment of Nonarrest Arrhythmias

- Drugs for supraventricular tachycardia (PLS 379: EvUp)
- Treatment for unstable ventricular tachycardia (PLS 409: EvUp)
- CPR for heart rate of less than 60/min (PLS 1535: EvUp)
- Drugs for the treatment of bradycardia: Atropine versus no atropine and atropine versus epinephrine (PLS New: EvUp)
- Emergency transcutaneous pacing for bradycardia (PLS New: EvUp)
- Channelopathies (PLS 417: EvUp)

PALS: Manual Defibrillation

- Pad size, type, and placement for pediatric defibrillation (PLS 378 and PLS 043: EvUp)
- Energy doses for defibrillation (PLS 405: ScopRev)
- Single or stacked shocks for pediatric defibrillation (PLS 389: EvUp)

PALS: Airways, Oxygenation, and Ventilation

- Ventilation rate when a perfusing rhythm is present (PLS 3103A and PLS 382: EvUp)
- Oxygen concentration during cardiac arrest (PLS 396: ScopRev)
- Ventilation during CPR with bag and mask compared with an advanced airway (2019 CoSTR)
- Use of cuffed or uncuffed tracheal tubes (PLS 412: EvUp)
- Atropine for emergency intubation (PLS 821: EvUp)
- Cricoid pressure during intubation (PLS 376: EvUp)
- Use of devices to verify advanced airway placement (PLS 385: EvUp)
- Ventilation rate with advanced airway during cardiac arrest (PLS 3103A and PLS 382: EvUp)

PALS: Circulatory Support During CPR

- Extracorporeal CPR for in-hospital cardiac arrest (2019 CoSTR)

PALS: Physiological Monitoring During Arrest to Guide Therapy and/or Intra-arrest Prognostication

- Invasive blood pressure monitoring during CPR (PLS 826: ScopRev)
- Use of near-infrared spectroscopy (NIRS) during cardiac arrest (PLS New: ScopRev)
- Bedside ultrasound to identify perfusing rhythm (PLS 408: ScopRev)
- End-tidal CO_2 monitoring during CPR (PLS 827: ScopRev)

PALS: Resuscitation Drug Administration and Timing

- Methods of calculating pediatric drug doses (PLS 420: EvUp)
- Intraosseous (IO) versus intravenous (IV) route of drug administration (PLS, neonatal life support [NLS], and advanced life support [ALS]: SysRev)
- Epinephrine time of initial dose and dose interval during CPR (PLS 1541: SysRev)
- Amiodarone versus lidocaine for shock-resistant ventricular fibrillation or pulseless ventricular tachycardia (2018 CoSTR)
- Sodium bicarbonate administration for children in cardiac arrest (PLS 388: EvUp)
- Calcium administration in children (PLS 421: EvUp)

PALS: Special Resuscitation Situations—Septic Shock, Congenital Heart Disease, and Trauma

- Resuscitation of the child with septic shock (PLS 1534: EvUp)
- Resuscitation of the patient with a single ventricle (PLS 390: EvUp)
- Resuscitation of the patient with hemi-Fontan or Fontan circulation (PLS 392: EvUp)
- Resuscitation after traumatic arrest (PLS 498: EvUp)

PALS: Post–Cardiac Arrest Care, Including Postarrest Prognostication

- Targeted temperature management (2019 CoSTR)
- Oxygen and carbon dioxide targets in pediatric patients with return of spontaneous circulation (ROSC) after cardiac arrest (PLS 815: SysRev)
- Post-ROSC blood pressure control (PLS 820: EvUp)
- Post-ROSC neuro-prognostication and use of electroencephalogram (PLS 813 and PLS 822: EvUp)

PBLS: CPR AND CPR QUALITY

The PBLS topics in this section include the optimal sequence of compressions and ventilation, pulse check accuracy, compression-only compared with conventional CPR, the optimal depth of chest compressions, and 1-hand versus 2-hand chest compressions for children and circumferential chest compressions for infants.

Sequence of Compression and Ventilation (BLS 661: Shared SysRev)

The PLS Task Force last reviewed the sequence of pediatric BLS in 2015.[9,10] In 2020, the BLS Task Force performed a SysRev on the topic (see the Starting CPR section [BLS 661: SysRev] of the BLS publication in this supplement). This SysRev search included adults and children in all settings. Refer to the BLS publication

for details of the evidence summary and task force considerations.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with OHCA
- Intervention: Commencing CPR beginning with compressions first (30:2)
- Comparator: CPR beginning with ventilation first (2:30)
- Outcome: Survival with favorable neurological / functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival only at discharge, 30 days, 60 days, 180 days, and/or 1 year; and ROSC
- Study design: RCTs and nonrandomized studies (nonrandomized controlled trials [non-RCTs], interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All languages were included if there was an English abstract. The literature search was updated in September 2019.

Summary of Evidence

The 2020 PLS ScopRev did not identify any new human pediatric evidence about sequencing for initiating CPR published after the 2015 CoSTR.[11,12]

As a result, the recommendations for sequencing of BLS steps for infants and children in cardiac arrest remain unchanged from those published in 2015 (see Treatment Recommendations), with insufficient evidence to make a recommendation. To review the entire SysRev for adult data, see the Starting CPR section [BLS 661: SysRev] of the BLS publication in this supplement.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[11,12]

The confidence in effect estimates is so low that the panel decided that a recommendation was too speculative.

Pulse Check Accuracy (PLS 393: EvUp)

This EvUp was performed to identify studies after the review about pulse check accuracy in 2010.[9,10] Studies about the accuracy of pulse check versus assessment of signs of life were insufficient to identify cardiac arrest, and the task force agreed that there is no need to suggest consideration of a SysRev. As a result, the 2010 treatment recommendation is unchanged.[9,10] To review the EvUp, see Supplement Appendix C-1.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in cardiac arrest
- Intervention: Use of pulse check
- Comparator: Assessment of signs of life
- Outcome: Improve accuracy of diagnosis of pediatric cardiopulmonary arrest
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and all languages were included if there was an English abstract. Literature was updated in December 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

Palpation of a pulse (or its absence) is not reliable as the sole determinant of cardiac arrest and need for chest compressions. If the victim is unresponsive, and not breathing normally, and there are no signs of life, lay rescuers should begin CPR.

In infants and children with no signs of life, healthcare providers should begin CPR unless they can definitely palpate a pulse within 10 seconds.

Chest Compression–Only Versus Conventional CPR (2017 CoSTR)

In 2017, a SysRev[13] and an ILCOR Pediatric CoSTR[14,15] were published on the topic of compression-only CPR compared with conventional CPR for infants and children. Refer to those publications for details of the evidence summary and task force considerations.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Patients of all ages (ie, neonates, children, adults) with cardiac arrest from any cause and across all settings (in-hospital and out-of-hospital); studies that included animals not eligible
- Intervention: All manual CPR methods including compression-only CPR, continuous compression CPR, and CPR with different compression-to-ventilation ratios. Compression-only CPR included continuous delivery of compressions with no ventilation; continuous chest compression CPR included compression with asynchronous ventilation or minimally interrupted cardiac resuscitation. Studies that mentioned the use of a mechanical device during CPR were considered only if the same device was used across all relevant intervention arms and would therefore not confound the observed effect.
- Comparator: Studies had to compare at least 2 different CPR methods from the eligible interventions; studies without a comparator were excluded
- Outcome: The primary outcome was favorable neurological outcomes, evaluated by cerebral performance scale or a modified Rankin Scale score; secondary outcomes were survival, ROSC, and quality of life

- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion; study designs without a comparator group (eg, case series, cross-sectional studies), reviews, and pooled analyses excluded
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated in December 2019.

Treatment Recommendations

These treatment recommendations are unchanged from 2017.[14,15]

We suggest that bystanders provide CPR with ventilation for infants and children younger than 18 years with OHCA (weak recommendation, very low-quality evidence).

We recommend that if bystanders cannot provide rescue breaths as part of CPR for infants and children younger than 18 years with OHCA, they should at least provide chest compressions (good practice statement).

Pediatric Compression Depth (PLS 314: ScopRev)

Rationale for Review

The most recent (2015) PLS review[11,12] about pediatric chest compression depth was based on a SysRev that identified 2 observational pediatric studies.[16,17] There is now greater availability of CPR feedback devices providing real-time data about the specific targets for components of CPR, including depth of compression; studies in adults[18,19] demonstrated that overcompression can cause harm. The ScopRev was undertaken to determine the extent of current available evidence about the effectiveness of various compression depths used during resuscitation of infants and children. For details of the ScopRev, see Supplement Appendix B-1.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children who had received chest compressions after out-of-hospital or in-hospital cardiac arrest (excluding newborn children)
- Intervention: Any specific chest compression depth
- Comparator: Depth specified in 2017 CoSTR publication[14,15]
  - At least one third the AP [anteroposterior] chest depth
  - Approximately 1½ inches (4 cm) in infants, 2 inches (5 cm) in children
- Outcome:
  - Short-term survival and neurological outcomes (eg, ROSC, hospital discharge, 28 days, 30 days, and 1 month)
  - Long-term survival and neurological outcomes (eg, 3 months, 6 months, and 1 year)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The search was updated to October 2019.

Summary of Evidence

No new published evidence was identified with this ScopRev. The PLS Task Force did identify an ongoing large prospective observational international multicenter study on CPR quality using dual-sensor CPR feedback devices.[20] The results of this study, once published, may help address the impact of chest compression depth on CPR outcomes. The task force concluded that there is no need to recommend a new SysRev at this time, and the decision will be reconsidered following the publication of any relevant studies. For this 2020 CoSTR update, the 2015 treatment recommendations[11,12] are unchanged.

Task Force Insights

The PLS Task Force recognized the paucity of pediatric studies and substantial identified gaps in the pediatric literature about chest compression depth (eg, the absence of data on the impact of overcompression). Previous studies used feedback devices with a single displacement sensor/accelerometer; these are notably unreliable because the compression depth they measure can be affected by the type of surface on which the compressions are performed; overestimation of compression depth occurs if the surface on which the patient rests (eg, bed or trolley mattress) enables movement even if a CPR board is used. Chest compression depth studies using feedback devices with dual displacement sensors/accelerometers may improve the accuracy of measurement of compression depth.

Treatment Recommendations

These treatment recommendations are unchanged from 2015.[11,12]

We suggest that rescuers compress an infant's chest by at least one third the anteroposterior dimension, or approximately 1½ inches (4 cm). We suggest that rescuers compress a child's chest by at least one third the anteroposterior dimension, or approximately 2 inches (5 cm) (weak recommendation, very low-quality evidence).

One-Hand Versus 2-Hand Compressions for Children (PLS 375: EvUp) Combined With Circumferential Compressions for Infants (PLS 416: EvUp)

An EvUp was performed to identify the available evidence about different techniques for chest compressions for infants and children. The previous review was published in 2010.[9,10] The EvUp did identify several studies published after 2010, and the task force

agreed that these studies suggest the need to consider requesting a SysRev. Until a new SysRev is completed and analyzed by the PLS Task Force, the 2010 treatment recommendation remains in effect. To review the EvUp, see Supplement Appendix C-2.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in cardiac arrest in any setting
- Intervention: 2 hands, 1 hand, circumferential, 2 fingers, a specific other method, a specific location
- Comparator: Another method or location
- Outcome: Any
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. Literature was searched to December 2019.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[9,10]

Either a 1-hand or a 2-hand technique can be used for performing chest compressions on children.

There are insufficient data to make a recommendation for or against the need for a circumferential squeeze of the chest when performing the 2 thumb–encircling hands technique of external chest compression for infants.

PBLS: AUTOMATED EXTERNAL DEFIBRILLATION

Use of Automated External Defibrillators for Infants With Out-of-Hospital Cardiac Arrest (PLS 425: EvUp)

An EvUp was performed to determine if there were any published studies about the use of AEDs for infants with OHCA. The EvUp identified insufficient evidence to justify a SysRev or suggest the need for a change to the 2010 treatment recommendation; as a result, the 2010 treatment recommendation is unchanged.[9,10] To review the EvUp, see Supplement Appendix C-3.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in cardiac arrest in any setting
- Intervention: Use of an automated external defibrillators at a certain moment in the algorithm
- Comparator: At another moment in the algorithm or not using an automated external defibrillator or using an automated external defibrillator with a dose attenuator
- Outcome: Any
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. Literature was searched to December 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

For treatment of out-of-hospital ventricular fibrillation (VF)/pulseless ventricular tachycardia (pVT) in infants, the recommended method of shock delivery by device is listed in order of preference below. If there is any delay in the availability of the preferred device, the device that is available should be used. The AED algorithm should have demonstrated high specificity and sensitivity for detecting shockable rhythms in infants. The order of preference is as follows:

1. Manual defibrillator
2. AED with dose attenuator
3. AED without dose attenuator

PBLS: PREVENTION OF CARDIAC ARREST

Pediatric Early-Warning Scores (PLS 818: ScopRev)

Rationale for Review

The topic was selected for review because the task force was aware of several recent relevant publications, including SysRevs, a ScopRev, and a large-scale RCT published after the most recent (2015) CoSTR on the topic.[11,12]

PEWS are tools that evaluate clinical presentation risk of clinical deterioration.

See Supplement Appendix B-2.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in a hospital setting
- Intervention: PEWS with or without rapid response teams/medical emergency teams
- Comparator: No PEWS with or without rapid response teams or medical emergency teams
- Outcome: In-hospital deterioration, including mortality
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were

excluded. The literature search was updated to September 15, 2019.

Summary of Evidence

We identified 3 SysRevs[21–23] and 1 ScopRev[24] published after 2015; all noted the limited evidence for the usefulness of PEWS for preventing physiological deterioration and improving clinical outcomes.

The Evaluating Processes of Care and the Outcomes of Children in Hospital (EPOCH) study was published in 2018. This was an international cluster RCT of 21 hospitals enrolling patients from birth (gestational age 37 weeks or more) up to 18 years of age.[25] This study included all-cause mortality as a primary outcome and as a secondary outcome a composite outcome reflecting late critical care admission. Ten hospitals implemented a bedside PEWS system compared with usual care (ie, did not use a severity early-warning score) in 11 hospitals. This was one of the largest studies of its kind, involving 144 539 patient discharges with 559 443 patient days and 144 539 patients in total completing the trial.

There was no significant reduction in all-cause mortality when the use of bedside PEWS was compared with standard care (1.93 per 1000 patient discharges compared with 1.56 per 1000 patient discharges; adjusted odds ratio [OR], 1.01; 95% CI, 0.61–1.69). The prevalence of significant clinical deterioration events was lower (0.5 per 1000 patient days compared with 0.84 per 1000 patient days) at hospitals using bedside PEWS compared with usual care hospitals (adjusted rate ratio 0.77 [95% CI, 0.61–0.97]).

The EPOCH authors concluded that their findings did not support the use of PEWS to reduce mortality.[25]

The PLS draft ScopRev was posted on the ILCOR website and was viewed 345 times without any comments that addressed the need for a SysRev on this topic. To review the ScopRev, see Supplement Appendix B-2.

Task Force Insights

The PLS Task Force concluded that the implementation of PEWS should be part of an overall clinical response system, with the task force placing a higher value on improving healthcare provider ability to recognize and intervene for patients with deteriorating illness over the expense incurred by a healthcare system committing significant resources to implement PEWS. The task force also noted that the complex process of optimizing patient care is likely to include both the implementation of PEWS and ongoing healthcare provider education. The PLS Task Force agreed that the decision to use PEWS should be balanced between use of existing resources and capabilities of the healthcare setting to adapt to its use and the consequences of its use.

In the PEWS studies, mortality is a common outcome marker. However, the incidence of cardiac arrest is low (especially outside the critical care setting), so the incidence of significant clinical deterioration is an additional important outcome in determining sample sizes for such studies.

The PLS Task Force agreed that there is a need to request a SysRev. Until completion of the SysRev, the 2015 treatment recommendations remain in effect.[11,12]

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[11,12]

The confidence in the estimate of predictive value is so low that the panel decided that a recommendation is too speculative.

Pediatric Medical Emergency/Rapid Response Teams (PLS 397: EvUp)

Rapid response teams (RRTs) are hospital teams that are activated to evaluate and respond to patients at risk for clinical deterioration. The topic of medical emergency teams (METs)/RRTs was last reviewed in 2015.[11,12] This EvUp was requested to identify relevant evidence on the topic published after that date. Two preintervention/postintervention studies demonstrated a decrease in the number of resuscitation events, although there was no clear decrease in mortality. One observational registry study demonstrated no change in the mortality rate beyond that which was already expected from the preimplementation trends. This finding is not significantly different from the 2015 review. To review the EvUp, see Supplement Appendix C-4. There is no indication to change the 2015 CoSTR recommendation.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[11,12]

We suggest the use of pediatric MET/RRT systems in hospitals that care for children (weak recommendation, very low-quality evidence). In making this recommendation, we place a higher value on the potential to recognize and intervene for patients with deteriorating illness over the expense incurred by a healthcare system committing significant resources to implement a MET/RRT system. We recognize that the decision to use a MET/RRT system should be balanced by the existing resources and capabilities of the institution.

PALS: RECOGNITION AND TREATMENT OF SEPTIC SHOCK

Fluid Administration for the Child With Septic Shock (PLS 1534: EvUp)

Note: This topic was prioritized for review because the approach to the management of fluid resuscitation in infants and children with septic shock is changing as

a result of recent published evidence. The summary of this EvUp is more detailed than for other EvUps owing to the critical nature of these new findings and in acknowledgment of the 2020 publication of new guidelines for the management of infants and children with septic shock.[26]

This topic was last reviewed in 2015,[11,12] when the evidence evaluation included fluid administration for shock associated with dengue fever and malaria. This EvUp looked specifically at the impact of different fluid regimens in infants and children with septic shock but excluded studies of shock associated with dengue or malaria because the pathophysiology of shock with those conditions is atypical when compared with septic shock associated with other causes. The role of fluid administration in shock associated with dengue or malaria will be considered in future reviews.

This draft EvUp can be viewed in Supplement Appendix C-5 because it is only outlined here in the main body of text. Among the 12 studies in the final evidence review were 3 RCTs[27–29] and 3 SysRevs.[30–32] In addition, the EvUp identified 1 RCT[33] that did not directly address the PICO (population, intervention, comparator, outcome) question but provided information about the effect of a fluid bolus on pediatric cardiac index. The EvUp also analyzed the results of 4 nonrandomized studies[34–37] and 1 study protocol.[38]

The Society of Critical Care Medicine's Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children was published in February 2020,[26] immediately before the submission of this publication. In these 2020 surviving sepsis guidelines, recommendations for fluid administration differ based on the availability of intensive care within the system caring for the infant or child. For systems *with* the availability of intensive care, the authors suggest the administration of 10 to 20 mL/kg boluses, up to a total of 40 to 60 mL/kg in the first hour, to be titrated to the patient's response and to be discontinued if the signs of fluid overload develop. If hypotension is present in systems *without* the availability of intensive care, the authors suggest the administration of 10 to 20 mL/kg boluses, up to a total of 40 mL/kg in the first hour (also titrated to response and discontinued if signs of fluid overload develop). If the infant or child is *not* hypotensive and is in a system *without* the availability of intensive care, the authors recommend *against* bolus fluid administration but to start maintenance fluids.[26]

The PLS Task Force agreed that a new SysRev is needed to reevaluate the evidence and modify the 2015 PLS treatment recommendations as needed. Until the SysRev is completed and analyzed by the task force, the 2015 treatment recommendations remain in effect.[11,12]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children who are in septic shock in any setting
- Intervention 1: Use of restrictive volume of resuscitation fluid (less than 20 mL/kg)
- Comparator 1: Nonrestrictive volume (20 mL/kg or greater) or the use of noncrystalloid fluids
- Intervention 2: Use of noncrystalloid fluids
- Comparator 2: Use of crystalloid fluids
- Intervention 3: Use of balanced crystalloid solution (eg, Ringer's lactate)
- Comparator 3: Use of unbalanced isotonic crystalloid solution (normal saline)
- Outcome: Survival to hospital discharge, need for mechanical ventilation, need for vasopressor support, complications, time to resolution of shock, hospital length of stay, ventilator-free days, or total IV fluids administered
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and all languages were included if there was an English abstract. The literature search was from January 2015 to January 2020.

Treatment Recommendations

These treatment recommendations are unchanged from 2015.[11,12]

We suggest using an initial fluid bolus of 20 mL/kg for infants and children with shock, with subsequent patient reassessment, for patients with the following disease states:

- Severe sepsis (weak recommendation, low-quality evidence)
- Severe malaria (weak recommendation, low-quality evidence)*
- Dengue shock syndrome (weak recommendation, low-quality evidence)*

We suggest against the routine use of bolus intravenous fluids (crystalloids or colloids) for infants and children with a "severe febrile illness" who are not in shock (weak recommendation, low-quality evidence).*

Reassessment, regardless of therapy administered, should be emphasized so that deterioration is detected at an early stage.

Vasoactive Drugs for Septic Shock (PLS 1604: ScopRev)

Rationale for Review

Although pediatric septic shock is associated with significant mortality/morbidity, substantial progress has

*These populations were included in the 2015 CoSTR but not the 2020 EvUp.

been made in improving the recognition of septic shock and the development of bundles of care aimed at bettering patient outcomes. The most recent review of vasoactive drugs (labeled "inotropes and vasopressors") for septic shock was published in 2010.[9,10] That CoSTR considered all forms of distributive shock, whereas this ScopRev looked specifically at the use of vasoactive drugs in pediatric septic shock, excluding other forms of distributive shock. This ScopRev looked at comparative studies of 1 vasoactive drug with another. To review the ScopRev, see Supplement Appendix B-3.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with septic shock, with and without myocardial dysfunction
- Intervention: Use of any specific vasoactive drug
- Comparator: Standard care
- Outcome: Improved patient outcomes (hemodynamics, survival)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was from 1946 to November 2019.

Summary of Evidence

The ScopRev identified 2 relevant RCTs. The first[39] included 60 children with septic shock in emergency departments or critical care units and compared the effects of dopamine with those of epinephrine. The primary outcome was resolution of shock in the first hour, which was more likely to occur among those receiving epinephrine rather than dopamine (OR, 4.8; 95% CI, 1.3–17.2; *P*=0.019). On day 3, there were lower sequential organ failure assessment scores (ie, less derangement) in the epinephrine group (8 versus 12, *P*=0.05). There was no difference in the adverse event rate (16.1% versus 13.8%, *P*=0.8) and no difference in mortality, although this study was not powered for mortality.

The second study[40] was a double-blind RCT that evaluated 120 children with refractory septic shock (despite the administration of 40 mL/kg of fluid). Randomization was to either dopamine or epinephrine, with the primary outcome of 28-day mortality and the secondary outcome of healthcare-associated infection. Dopamine administration was linked with an increased risk of death and healthcare-associated infection in comparison with epinephrine administration. The PLS Task Force members were concerned that the doses of epinephrine would have produced a disproportionately greater physiological effect than the matched doses of dopamine. To review the ScopRev, see Supplement Appendix B-3.

Of note, the 2020 surviving sepsis guidelines[26] suggest the use of epinephrine or norepinephrine compared with dopamine based on very-low-quality evidence. The authors state that they could not make a recommendation for a first-line vasoactive infusion for septic shock, noting that in their practices they use epinephrine or norepinephrine.

Task Force Insights

The studies identified by the ScopRev did not evaluate vasoactive agents other than dopamine and epinephrine and did not include other drugs such as norepinephrine that are commonly used to treat fluid-resistant septic shock. The 2 RCTs were single-center studies in low- and middle-income healthcare systems, so questions about their generalizability to other healthcare settings arose. The task force agreed that the adult findings could not be extrapolated to the pediatric population because infants and children have different physiological responses to vasoactive drugs (varying according to age even within the age range of infants and children), particularly when compared with adult physiological responses.

The task force agreed that the current evidence does not support the need for a SysRev and the 2010 treatment recommendations remain in effect.[9,10]

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

There is insufficient evidence to recommend a specific inotrope or vasopressor to improve mortality in pediatric distributive shock. The selection of an inotrope or vasopressor to improve hemodynamics should be tailored to each patient's physiology and adjusted to the individual's clinical responses.

Corticosteroids for Pediatric Septic Shock (PLS 413: EvUp)

The PLS Task Force sought an EvUp on this topic because it was last reviewed in 2010.[9,10] The evidence for or against the use of corticosteroids in pediatric septic shock is of very low certainty. There is limited evidence that a specific subpopulation may benefit from the administration of corticosteroids, but these patients are not easily identifiable at the bedside. As a result, the current (2010) treatment recommendation continues unmodified. To review the EvUp, see Supplement Appendix C-6.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children being treated for septic shock and circulatory failure in any setting, during the first hours of treatment
- Intervention: Early administration of corticosteroids
- Comparator: No corticosteroid or postponed administration
- Outcome: All

- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was conducted to December 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

There is insufficient evidence to support or refute the routine use of stress-dose or low-dose hydrocortisone and/or other corticosteroids in infants and children with septic shock. Stress-dose corticosteroids may be considered in children with septic shock unresponsive to fluids and requiring vasoactive support.

PALS: RECOGNITION AND PREARREST TREATMENTS FOR SHOCK

Graded Volume Resuscitation for Traumatic/Hemorrhagic Shock (PLS 400: ScopRev)

Rationale for Review

The PLS Task Force reevaluated this topic because the previous review was published in 2010.[9,10] This 2020 ScopRev sought to identify available evidence about the effectiveness of graded volume resuscitation compared with standard care for traumatic hemorrhagic shock. To review the ScopRev, see Supplement Appendix B-3.

The term *graded volume resuscitation* includes *restrictive volume resuscitation* and *permissive hypotension*, with volume administered to resuscitate a hypovolemic trauma victim with relatively small volumes, repeated to restore perfusion to a specific target.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in hemorrhagic shock following trauma in any setting
- Intervention: Graded volume resuscitation (now restrictive volume resuscitation)
- Comparator: Standard care
- Outcome: Any clinical outcome
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was from March 2009 to November 2019.

Summary of Evidence

Seven retrospective pediatric studies were identified.[41–47] All were derived from trauma registries. Only 1 study assessed the volume of fluid given to children with traumatic injuries in the prehospital setting.[41] Four studies compared the total crystalloid volume given in 24 hours,[42,44–46] and 1 study assessed the volume of crystalloid given to patients needing transfusion.[43] The study that reported the critical outcome of survival to 24 hours[41] found no benefit to survival associated with graded/"limited" volume compared with standard care for trauma resuscitation. None reported on survival at 30 days with good neurological outcome. For the critical outcome of survival to discharge, 4 studies found no benefit associated with graded/limited volume administration compared with standard care.[41,44,46,47] One study reported lower survival to hospital discharge associated with high-volume crystalloid administration (greater than 60 mL/kg per 24 hours) compared with low- and moderate-volume crystalloid administration (ie, 0–40 mL/kg per 24 hours or 40–60 mL/kg per 24 hours),[42] and 1 reported lower survival rates associated with higher administered crystalloid volumes (ie, greater than 150 mL/kg per 24 hours compared with 150 mL/kg or less per 24 hours) among those receiving massive transfusions.[43] Five studies reported an increased hospital or intensive care length of stay associated with higher crystalloid volume administration in the first 24 hours.[42–44,46,47] All studies were retrospective, and they reported different interventions on differing patient populations and differing associated outcomes. Although it is difficult to compare results, there is a suggestion of a possible advantage of using limited volume resuscitation. To review the ScopRev, see Supplement Appendix B-4.

Task Force Insights

The task force discussed the term *graded resuscitation* used in the 2010 CoSTR evidence evaluation; this term was infrequently found in the trauma literature published in the past decade. The task force discussed the definition of *hypotensive resuscitation* in children and infants with trauma (because it was agreed that this is unclear in the literature), as well as other terms used in trauma resuscitation, such as *restrictive resuscitation* and *delayed versus early resuscitation.*

Adult data favor restrictive volume resuscitation, and the recommendations for this population have been to promote damage control resuscitation. The National Institute for Health and Care Excellence trauma guidelines[48] and the American College of Surgeons Advanced Trauma Life Support guidelines[49] follow these principles for adult practice because both suggest restrictive volume resuscitation with early use of blood components in hemorrhagic shock.

The task force discussed the ILCOR mandate and whether it includes the review and analysis of trauma resuscitation topics. Because trauma remains a major cause of death in children worldwide and there is still a lack of evidence-based guidelines, most task force

members agreed that this is an important issue for ILCOR to address.

RCTs or, in their absence, studies from large trauma registries are required to address the effects of different volume resuscitation strategies on mortality and morbidity outcomes. Optimal timing for the administration of fluid resuscitation in pediatric trauma was not addressed in this review but will be considered for a future SysRev.

The task force agreed that more data are needed, but this ScopRev did not identify sufficient new evidence to prompt a new SysRev, so the 2010 treatment recommendation (noting insufficient evidence to make a recommendation) remains in place.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

There is insufficient evidence about the best timing or quantity for volume resuscitation in infants and children with hemorrhagic shock following trauma.

Timing of Intubation for Shock (PLS 399: EvUp)

The evidence to support specific timing of intubation for infants and children in shock (ie, all types of shock) was most recently evaluated in 2010.[9,10] At that time, the PLS Task Force noted the paucity of published evidence. This EvUp was undertaken to identify any relevant evidence published thereafter. Once again, insufficient evidence was found to warrant the suggestion of a pediatric SysRev. Only 5 animal studies, one 1 adult study and the 2020 Society of Critical Care Medicine Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children[26] were identified. The 2020 surviving sepsis guidelines authors noted they were "unable to make a recommendation about whether to intubate children with fluid-refractory-catecholamine-resistant septic shock. However, in our practice, we commonly intubate children [with] fluid-refractory-catecholamine-resistant septic shock without respiratory failure."[26] To review the EvUp, see Supplement Appendix C-7.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in shock
- Intervention: Early intubation and assisted ventilation
- Comparator: The use of these interventions only for respiratory failure
- Outcome: Improved patient outcomes (hemodynamics, survival)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to December 2019.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[9,10]

There is insufficient evidence to support or refute the use of endotracheal intubation of infants and children in shock before the onset of respiratory failure.

Prearrest Care of the Infant or Child With Dilated Cardiomyopathy or Myocarditis (PLS 819: EvUp)

This EvUp was performed because the most recent PLS CoSTR on the topic of prearrest care for a child with dilated cardiomyopathy or myocarditis was in 2015.[11,12] The management of these patients has continued to evolve since then, noting that the EvUp identified an additional 5 studies not captured in the 2015 CoSTR.

The task force agreed to consider a request for a SysRev to assess those studies and any others identified pertaining to the prearrest care of an infant or child with myocarditis. Until a new SysRev is completed and analyzed by the PLS Task Force, the 2015 treatment recommendation (noting insufficient evidence to make a recommendation) remains in effect. To review the EvUp, see Supplement Appendix C-8.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with myocarditis or dilated cardiomyopathy and impending cardiac arrest
- Intervention: A specific approach
- Comparator: The usual management of shock or cardiac arrest
- Outcome: Survival with favorable neurological/functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; cardiac arrest frequency; ROSC
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was completed in September 2019.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[11,12]

The confidence in effect estimates is so low that the panel decided that a specific recommendation was too speculative.

Cardiogenic Shock and Inotropes (PLS 418: EvUp)

This EvUp was undertaken because the most recent CoSTR on the topic was published in 2010,[9,10] and the task force sought to identify any studies published after that review. The task force agreed that there is insufficient evidence identified in the EvUp to consider a request for a SysRev. As a result, the 2010 treatment recommendations[9,10] remain in place. To review the EvUp, see Supplement Appendix C-9.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children who are being treated for cardiogenic shock in any setting, during the first hours of treatment
- Intervention: The early addition of certain vasoactive drugs
- Comparator: Postponed administration and/or a specific vasoactive drug versus another
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to December 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

The catecholamine dose for inotropic support in cardiogenic shock must be titrated for each individual because there is wide variability in the clinical response to vasoactive drugs. It is reasonable to use epinephrine, levosimendan, dopamine, or dobutamine for inotropic support in infants and children with cardiogenic shock. Milrinone may be beneficial for the prevention and treatment of low cardiac output following cardiac surgery. There are insufficient data to support or refute the use of norepinephrine in pediatric cardiogenic shock.

PALS: MANAGEMENT OF DETERIORATION WITH PULMONARY HYPERTENSION

This section includes 3 topics about the management and prevention of critical pulmonary hypertension crises in the infant or child. All were evaluated by EvUps to identify the availability of evidence published after the most recent review of the management of infants and children with pulmonary hypertension (appeared in the literature in 2010).[9,10]

Prevention and Management of Postoperative Pulmonary Hypertensive Crises in Infants and Children (PLS 391: EvUp)

Although the general topic of pulmonary hypertension was reviewed in the 2010 CoSTR,[9,10] the focus was on treatment of cardiac arrest in patients with pulmonary hypertension. This EvUp was performed to identify any evidence about the postoperative care of infants and children with pulmonary hypertension at high risk of pulmonary hypertensive crisis. The EvUp identified several RCTs. In addition, the PLS Task Force is aware of 3 scientific publications—2 from the American Heart Association (AHA)[50,51] and 1 from the European Pediatric Pulmonary Vascular Disease Network[51a]—each group having completed a SysRev in 2015. The task force agreed that the EvUp identified sufficient published evidence to indicate the need to consider a SysRev. Until such time as a new SysRev is completed and analyzed by the PLS Task Force, the 2010 treatment recommendation remains in effect for treatment of children with pulmonary hypertension and cardiac arrest. To review the EvUp, see Supplement Appendix C-10.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with pulmonary hypertension at high risk of postoperative pulmonary hypertensive crises
- Intervention: Postoperative care such as careful respiratory management and monitoring to avoid hypoxia and acidosis
- Comparator: Standard postoperative care
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to November 2019.

Treatment Recommendations

This treatment recommendation for the care of children with pulmonary hypertension and cardiac arrest (below) is unchanged from 2010.[9,10]

Rescuers should provide conventional PALS, including oxygenation and ventilation, for cardiac arrest

associated with pulmonary hypertension. It may be beneficial to attempt to correct hypercarbia. If the administration of medications (IV or inhaled) to decrease pulmonary artery pressure has been interrupted, it may be advisable to reinstitute it.

Inhaled nitric oxide or aerosolized prostacyclin or analogues to reduce pulmonary vascular resistance should be considered. If these are unavailable, an IV bolus of prostacyclin may be considered.

Note: A SysRev will be needed to generate treatment recommendations for *postoperative* care of children with pulmonary hypertension at risk for pulmonary hypertensive crisis.

Opioids, Sedatives, and Neuromuscular Blocking Drugs for Pulmonary Hypertension (PLS New: EvUp)

Although the general topic of pulmonary hypertension was reviewed in the 2010 CoSTR,[9,10] the focus was on treatment during cardiac arrest; there were no specific PICOST questions and no treatment recommendations about the use of opioids, sedatives, and neuromuscular blocking drugs for an infant or a child with pulmonary hypertension who is not in cardiac arrest. The PLS Task Force is aware of 3 scientific publications—2 from the AHA[50,51] and 1 from the European Pediatric Pulmonary Vascular Disease Network[51a]—each group having completed a SysRev in 2015. To review the EvUp, see Supplement Appendix C-11. The PLS Task Force agreed to consider the need for a SysRev to evaluate the available evidence and see if treatment recommendations were required after review of the literature.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children at high risk of pulmonary hypertensive crises
- Intervention: Provision of adequate opiates, sedatives, and neuromuscular blocking drugs
- Comparator: Standard care without opiates
- Outcome: All, especially pulmonary hypertensive crises
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to November 2019.

Treatment Recommendations

There are no previous treatment recommendations.

Therapy With Inhaled Nitric Oxide or Prostaglandin I_2 for Pulmonary Hypertensive Crisis and Right Heart Failure (PLS New: EvUp)

Although the general topic of pulmonary hypertension was reviewed in the 2010 CoSTR,[9,10] the focus was on the treatment of cardiac arrest; this 2020 EvUp focused on the evidence supporting inhaled nitric oxide or prostaglandin I_2 to manage pulmonary hypertensive crises and right heart failure in infants and children with or without cardiac arrest. This EvUp identified 3 scientific publications—2 from the AHA[50,51] and 1 from the European Pediatric Pulmonary Vascular Disease Network[51a]—each group having completed a SysRev in 2015. In addition, a previous EvUp (see Supplement Appendix C-12) identified a SysRev[52] that reported the results of an RCT on inhaled nitric oxide for the postoperative treatment of pulmonary hypertension.[53]

The EvUp and the PLS Task Force member group identified sufficient published data about the use of inhaled nitric oxide and prostaglandin I_2 to consider recommending a SysRev to evaluate the available evidence and, if required, make new treatment recommendations. Until a new SysRev is completed and analyzed, the 2010 treatment recommendations remain in effect for the general management of pulmonary hypertension and not specifically to address this PICOST because that will require further analysis of the literature.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children at high risk of pulmonary hypertensive crises
- Intervention: Provision of pulmonary vasodilators such as inhaled nitric oxide or prostaglandin I_2
- Comparator: Standard therapy with no provision of therapy such as inhaled nitric oxide or prostaglandin I_2
- Outcome: Alter the outcome of pulmonary hypertensive crises or acute right heart failure
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to November 2019.

Treatment Recommendations

The broad treatment recommendations published in 2010, regarding inhaled nitric oxide, remain in effect.[9,10]

Rescuers should provide conventional PALS, including oxygenation and ventilation for cardiac arrests associated with pulmonary hypertension. It may be beneficial to attempt to correct hypercarbia. If the administration

of medications (IV or inhaled) to decrease pulmonary artery pressure has been interrupted, it may be advisable to reinstitute it.

Inhaled nitrous oxide or aerosolized prostacyclin or analogue to reduce pulmonary vascular resistance should be considered. If unavailable, an IV bolus of prostacyclin may be considered.

PALS: RECOGNITION AND TREATMENT OF NONARREST ARRHYTHMIAS

Drugs for Supraventricular Tachycardia (PLS 379: EvUp)

This topic was last reviewed in 2010.[9,10] This EvUp was to identify any evidence about the management of supraventricular tachycardia in infants and children published after 2010. The EvUp identified 6 studies; all were retrospective and observational, and none compared adenosine with other IV drugs for the management and resolution of supraventricular tachycardia. The PLS Task Force concluded that there was insufficient evidence to suggest the need for a SysRev and no need to consider a change in the previous (2010) treatment recommendations.[9,10] To review the EvUp, see Supplement Appendix C-13.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with supraventricular tachycardia with a pulse
- Intervention: Use of any drug or combination of drugs
- Comparator: Adenosine
- Outcome: Termination of abnormal rhythm, survival
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract from ILCOR 2010 guidance. The search was performed in November 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

For infants and children with supraventricular tachycardia with a palpable pulse, adenosine should be considered the preferred medication. Verapamil may be considered an alternative therapy in older children, but it should not be routinely used in infants. Procainamide or amiodarone given by a slow IV infusion with careful hemodynamic monitoring may be considered for refractory supraventricular tachycardia.

Note: The 2020 PLS Task Force wishes to add the caveat that expert consultation is encouraged before the use of procainamide or amiodarone.

Treatment for Unstable Ventricular Tachycardia (PLS 409: EvUp)

The management of unstable VT was last reviewed in 2010.[9,10] This 2020 EvUp was to determine if there was sufficient evidence to consider a SysRev. The task force concluded that there was insufficient published evidence of the management of unstable tachycardia to recommend the consideration of a SysRev, so the 2010 treatment recommendations remain in effect.[9,10] To review the EvUp, see Supplement Appendix C-14.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with unstable ventricular tachycardia (prehospital and in-hospital)
- Intervention: Any drug, combination of drugs, or intervention (eg, cardioversion)
- Comparator: No drugs or intervention
- Outcome: Termination of rhythm, survival
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The search was finished in November 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

It is reasonable to use synchronized electric cardioversion as the preferred first therapy for pediatric VT with hypotension or evidence of poor perfusion. If drug therapy is used to treat unstable VT, amiodarone may be a reasonable choice, with careful hemodynamic monitoring performed during its slow delivery.

CPR for Heart Rate of Less Than 60/min (PLS 1535: EvUp)

PLS council guidelines[54,55] recommend that PLS providers begin chest compressions if an infant or child has a heart rate under 60 beats per minute with signs of poor perfusion despite support of the airway, adequate oxygenation, and ventilation; this recommendation represents expert consensus provided by council guidelines rather than by an ILCOR evidence review. No previous search strategy was identified for this topic. As a result, a new search strategy was developed. The EvUp identified 2 nonrandomized studies that

documented improved outcomes associated with CPR for bradycardia with pulses and poor perfusion when compared with outcomes associated with pulseless electric activity or asystole cardiac arrest without preceding chest compressions.[56,57] Lower survival was associated with longer time intervals between the start of CPR for bradycardia with pulse and poor perfusion, and the loss of the pulse.[56]

Although the evidence base is limited, the task force agreed that the importance of the question when to initiate CPR for bradycardia suggests the need for consideration of a SysRev. To review the EvUp, see Supplement Appendix C-15.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children who are in cardiac arrest
- Intervention: Starting CPR if they have a heart rate of less than 60/min with signs of shock and with a palpable pulse
- Comparator: Starting CPR for patients with a heart rate of less than 60/min and no palpable pulse
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion; unpublished studies (eg, conference abstracts, trial protocols) excluded
- Time frame: All years since 2010 and all languages were included if there was an English abstract until December 2019.

Treatment Recommendations

There is no ILCOR PLS treatment recommendation at this time.

Drugs for the Treatment of Bradycardia: Atropine Versus No Atropine and Atropine Versus Epinephrine (PLS New: EvUps)

The PLS Task Force reviewed this topic in 2010.[9,10] Two EvUps were performed to determine if any studies were published after 2010 about atropine compared with epinephrine (see Supplement Appendix C-16) and atropine compared with no atropine (see Supplement Appendix C-17) for the treatment of bradycardia in infants or children. The EvUps identified no studies published after 2010. After completion of the reviews, however, the task force identified 1 nonrandomized (in-hospital registry) study about epinephrine for children receiving CPR for bradycardia and poor perfusion.[58] The PLS Task Force agreed that there remains insufficient evidence for consideration of a SysRev; as a result, the 2010 treatment recommendation remains in effect.[9,10]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with bradycardia for any reason
- Intervention: Use of atropine at a specific dose
- Comparator: Not using atropine, using another drug, or using it [atropine] at a different dose
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was conducted in November 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

Epinephrine may be administered to infants and children with bradycardia and poor perfusion that is unresponsive to ventilation and oxygenation. It is reasonable to administer atropine for bradycardia caused by increased vagal tone or anti-cholinergic drug toxicity. There is insufficient evidence to support or refute the routine use of atropine for pediatric cardiac arrest.

Emergency Transcutaneous Pacing for Bradycardia (PLS New: EvUp)

This topic was last addressed by the Pediatric Task Force in 2000,[59] when an international consensus on science and international guidelines were published. As a result, the PLS Task Force requested an EvUp to determine if there was relevant evidence to suggest the need to consider a SysRev. After review of the EvUp (see Supplement Appendix C-18), the task force agreed that there is insufficient evidence to suggest the need for a SysRev. As a result, the 2000 treatment recommendation remains in effect.[59]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- There was no previous PICOST for this question. See Supplement Appendix C-18 for details of the search strategy.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2000.[59]

In selected cases of bradycardia caused by complete heart block or abnormal function of the sinus node, emergency transthoracic pacing may be lifesaving. Pacing is not helpful in children with bradycardia secondary to a postarrest hypoxic/ischemic myocardial insult or respiratory failure. Pacing was not shown to be effective in the treatment of asystole in children.

Channelopathies (PLS 417: EvUp)

The topic of channelopathies was last addressed in the PLS 2010 CoSTR.[9,10] That review as well as this 2020 EvUp considered a channelopathy after either sudden, unexplained death in children or after an attempted resuscitation following sudden unexplained cardiac arrest in a previously healthy child or young adult.

One issue identified in both the 2010 and this 2020 evidence evaluation is that there is a role for selective screening for inheritable heart disease and channelopathy where indicated but that expert advice should be sought in this regard. To review the EvUp see Supplement Appendix C-19. The 2010 treatment recommendation remains in effect.[9,10] For clarity, the task force modified the first sentence to begin with "Following attempted resuscitation for" before "sudden cardiac arrest" to make clear that the screening is performed after resuscitation efforts, not during them.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

The following PICOST elements were used in the 2010 review.[9,10]

- Population: Infants and children undergoing resuscitation from cardiac arrest
- Intervention: Consideration of a channelopathy as the etiology of the cardiac arrest
- Comparator: Standard management
- Outcome: ROSC, survival to discharge, survival with favorable neurological outcome
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract in ILCOR. The search was performed in November 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

After attempted resuscitation for sudden unexplained cardiac arrest, providers should obtain a thorough history (including syncopal episodes, seizures, unexplained accidents/ or drownings, or sudden death) and review any available previous electrocardiograms. All infants, children, and young adults with sudden, unexpected death should, if possible, have an unrestricted complete autopsy, preferably performed by pathologists with training and expertise in cardiovascular pathology. Consideration should be given to the reservation and genetic analysis of tissue from the index patient to determine the presence or absence of a channelopathy. It is recommended that families of patients who child's cause of death is not found on autopsy be referred to a healthcare provider or center with expertise in cardiac rhythm disturbances.

PALS: MANUAL DEFIBRILLATION

This section includes several topics on the subject of pediatric manual defibrillation, including pad size and type and pad or paddle placement during defibrillation, the use of stacked shocks, and the evidence about defibrillation energy dose in infants and children.

Pad Size, Type, and Placement for Pediatric Defibrillation (PLS 378 and PLS 043: EvUp)

The topics of pad size and placement and adhesive pads compared with paddles were last reviewed in 2010.[9,10] In the decade after that review, the technological advances were rapid, hence an EvUp was performed to identify any relevant evidence published after 2010. The PLS Task Force agreed to combine these topics into a single EvUp because they expected to identify relatively little evidence. (To review the EvUp, see Supplement Appendix C-20). The task force agreed that the EvUp did not identify sufficient evidence to suggest the need to consider a SysRev, so the 2010 treatment recommendations for both topics remain in effect.[9,10]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in cardiac arrest in any setting
- Intervention: Specific use of self-adhesive pads *or* any specific paddle or pad size, orientation, and position
- Comparator: Use of paddles *or* any other paddle or pad size, orientation, and position
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was from 2010 to December 2019.

Treatment Recommendations

These treatment recommendations (below) are unchanged from 2010.[9,10]

There is insufficient evidence to alter the current recommendations to use the largest size paddles that fit an infant's or child's chest without touching each other or to recommend one paddle or pad position or type over another.

Either self-adhesive defibrillation pads or paddles may be used in infants and children in cardiac arrest.

Energy Doses for Defibrillation (PLS 405: ScopRev)

Rationale for Review

In the 2015 CoSTR,[11,12] the PLS Task Force recommended an initial dose of 2 to 4 J/kg to treat shockable rhythms of cardiac arrest. There are differences in the first shock dose recommended by ILCOR member councils, however, with the European Resuscitation Council recommending 4J/kg for the first and all subsequent shocks[55] and the AHA recommending an initial dose of 2 to 4 J/kg (but for ease of teaching, a dose of 2 J/kg is used in algorithms and training materials). For refractory VF, the AHA guidelines recommend increasing the defibrillation dose to 4 J/kg, suggesting that subsequent energy doses should be at least 4 J/kg and noting that higher levels may be considered, not to exceed 10 J/kg.[60] The task force undertook this review to determine if sufficient evidence exists to recommend consideration of a SysRev that may result in greater consistency in doses recommended for pediatric manual defibrillation. See Supplement Appendix B-5.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children who are in VF or pVT in any setting
- Intervention: Specific energy dose or regimen of energy doses for the initial or subsequent defibrillation attempt(s)
- Comparator: 2 to 4 J/kg
- Outcome: Harm to the patient, ROSC, hospital discharge, long-term survival, survival with good neurological outcome

Summary of Evidence

The review identified a single 2019 SysRev[61] of pediatric human and animal studies that met the search criteria. The SysRev identified no studies linking the initial or cumulative energy delivered to survival to hospital discharge and no link between long-term survival or survival with good neurological outcome. Meta-analysis could not be performed because the component population groups were extremely heterogeneous.

Task Force Insights

Shockable rhythms are less common in infants and children with OHCA (less than 10%[62,63]) compared with in-hospital cardiac arrest (IHCA) (5% to 24%[64,65]) and less common in pediatric than in adult OHCA[66] and in IHCA.[64] The task force acknowledged that the lower frequency of occurrence does affect the sample size for studies to demonstrate statistically significant improvement in survival associated with different defibrillation energy doses.

It may be difficult to determine accurately the precise weight of children with OHCA in the prehospital arena (as may be the case in the emergency department setting for such patients), hence the calculation of defibrillation doses administered in J/kg could be imprecise. In addition, the interval from cardiac arrest to the delivery of first shock and the quality of CPR could each influence the outcomes for VF or pVT survival after shock delivery.

None of the studies identified in the single SysRev[61] found a significant association between the initial defibrillation energy dose and the rate of sustained ROSC or survival. The task force agreed to prioritize this topic for consideration of a SysRev; until it is completed and reviewed, the 2015 treatment recommendation remains in effect.[11,12]

Note: In June 2020, task force members received a PubMed automated alert about the publication of a new study of energy doses for pediatric defibrillation. The task force chair (IM) repeated the original search and verified that the study identified[67] was the only study meeting the search criteria published since the November 2019 search on the topic. The new in-hospital registry study identified 422 infants and children 18 years of age or younger with cardiac arrest and initial VF/pVT. First shock energy doses other than 1.7 to 2.5 J/kg were associated with lower survival to hospital discharge among the 301 patients 12 years of age or younger with initial VF/pVT, and first shock doses more than 2.5 J/kg were associated with lower survival rates in all patients 18 years of age or younger with initial VF.[67] There was insufficient time for the task force to analyze the study or its conclusions before submission of this PLS CoSTR, but the task force did want to acknowledge this additional new publication.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[11,12]

We suggest the routine use of an initial dose of 2 to 4 J/kg of monophasic or biphasic defibrillation waveforms for infants or children in VF or pVT cardiac arrest (weak recommendation, very-low-quality evidence). There is insufficient evidence on which to base a recommendation for second and subsequent defibrillation doses.

Single or Stacked Shocks for Pediatric Defibrillation (PLS 389: EvUp)

The evaluation of the evidence in support of single compared with stacked shocks for pediatric defibrillation was most recently addressed in 2010.[9,10] The task force undertook this EvUp to identify any new evidence published after 2010. The task force agreed that there was no new evidence to suggest the need to consider a request for a SysRev or to change the 2010 treatment recommendation. To review the EvUp, see Supplement Appendix C-21.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in VF or pVT in any setting
- Intervention: More than 1 shock for the initial or subsequent defibrillation attempt(s)
- Comparator: A single shock
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated in December 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

A single-shock strategy followed by immediate CPR (beginning with chest compressions) is recommended for children with out-of-hospital or in-hospital VF or pVT.

PALS: AIRWAYS, OXYGENATION, AND VENTILATION

Central to the management of the critically ill or injured child is to ensure that the airway is patent and that ventilation and oxygenation are effective.

In this section, the evidence evaluations for the following airway and oxygenation and ventilation topics are summarized: ventilation rate when a perfusing rhythm is present, oxygen concentration during cardiac arrest, ventilation during CPR with bag and mask compared with an advanced airway, use of cuffed or uncuffed tracheal tubes, minute ventilation during cardiac arrest, use of cricoid pressure during intubation, use of devices to verify advanced airway placement, and ventilation rate with an advanced airway during cardiac arrest.

Ventilation Rate When a Perfusing Rhythm Is Present (PLS 3103A and PLS 382: EvUp)

This EvUp was undertaken to determine if there was published evidence to support the recommendation to deliver 1 breath every 3 seconds or any other specific ventilation rate for infants and children who require bag-mask ventilation but have a pulse and perfusing rhythm. The 2000 CoSTR on pediatric basic life support noted, "the goal of ventilation with a bag and mask should be to approximate normal ventilation and achieve physiological oxygen and carbon dioxide concentration while minimizing risk of iatrogenic injury."[68] The recommendation was based on expert consensus rather than a formal review of the evidence on the subject. To review the EvUp, see Supplement Appendix C-22.

The PLS Task Force has not made any previous recommendations for specific ventilation rate for the infant or child with respiratory arrest and a perfusing rhythm. Such recommendations have been included in council guidelines rather than in the ILCOR CoSTRs. The search conducted in December 2019 for this EvUp did not reveal any relevant evidence, and the task force concluded that there was no need to consider a recommendation for a SysRev.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with a perfusing rhythm but absent or inadequate respiratory effort
- Intervention: Giving 1 breath every 3 to 5 seconds (12–20 breaths/min)
- Comparator: Alternative ventilation rates
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated in February 2019.

Treatment Recommendations

No treatment recommendations will be made until a future SysRev identifies sufficient evidence to make a recommendation.

Oxygen Concentration During Cardiac Arrest (PLS 396: ScopRev)

Rationale for Review

The published evidence supporting a specific inspired oxygen concentration to use during attempted resuscitation of infants and children was last reviewed in 2010.[9,10] To review the ScopRev, see Supplement Appendix B-6.

The evidence supporting titration of oxygen after ROSC is addressed in a separate review; see Oxygen and Carbon Dioxide Targets in Pediatric Patients With Return of Spontaneous Circulation After Cardiac Arrest.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants (age 28 days to 12 months) and children in cardiac arrest in any setting
- Intervention: Fraction of inspired oxygen (F_{IO_2}) titrated to oxygenation during cardiac arrest
- Comparator: Use of 100% oxygen (F_{IO_2} 1.00)

- Outcome: Any
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to October 2019.

Summary of Evidence

The ScopRev identified no human studies in infants (beyond the neonatal period) and children about oxygen concentration or its titration during cardiopulmonary resuscitation. The ScopRev identified 2 SysRevs[69,70] and a 2019 ILCOR CoSTR summary statement[71,72] about initial resuscitation of newborns, although these were not relevant to this 2020 ScopRev. This is because they pertained to the resuscitation of newborns in the first minutes of life (ie, during the transition from placental to pulmonary oxygenation).

The ScopRev identified 2 studies in immature animal models,[73,74] a SysRev with meta-analysis of neonatal animal models,[75–77] and 2 mature animal studies.[78,79] From this body of work there appeared to be no difference in ROSC rates but greater evidence of metabolic derangement associated with the administration of 100% oxygen during resuscitation of the animals.

Task Force Insights

There were no human studies in infants or children that addressed the topic, and the indirectness of results from animal models were considered insufficient to alter the existing 2010[9,10] treatment recommendation. Also see Oxygen and Carbon Dioxide Targets in Pediatric Patients With Return of Spontaneous Circulation After Cardiac Arrest below.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010. Note that the task force deleted a second recommendation that was included in the 2010 treatment recommendations regarding F_{IO_2} after ROSC because it is addressed in a separate 2020 treatment recommendation.[9,10]

There is insufficient information to recommend a specific inspired oxygen concentration for ventilation during attempted resuscitation after cardiac arrest in infants and children.

Ventilation During CPR With Bag and Mask Compared With an Advanced Airway (2019 CoSTR)

A 2019 SysRev[80] and an ILCOR Pediatric CoSTR statement were published as part of the 2019 CoSTR summary.[71,72] The publications addressed advanced airway interventions for pediatric cardiac arrest, comparing bag-mask ventilation with ventilation through an advanced airway. Refer to those publications for details of the evidence summary and task force considerations.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in any setting (in-hospital or out-of-hospital) who have received chest compressions or a shock and are receiving CPR
- Intervention: Placement of an advanced airway device
- Comparator: Primary—bag-mask ventilation alone or with non–advanced airway interventions; secondary—another advanced airway device
- Outcome: Any clinical outcome
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to January 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2019, with the minor addition of "or insertion of" before "a supraglottic airway."[71,72]

We suggest the use of bag-mask ventilation rather than tracheal intubation or insertion of a supraglottic airway in the management of children with cardiac arrest in the out-of-hospital setting (weak recommendation, very-low–certainty evidence).

There is insufficient evidence to support any recommendation about the use of tracheal intubation or insertion of a supraglottic airway in the management of children with cardiac arrest in the in-hospital setting.

Use of Cuffed or Uncuffed Tracheal Tubes (PLS 412: EvUp)

The PLS Task Force last reviewed the evidence comparing cuffed with uncuffed tracheal tubes in 2010.[9,10] This 2020 EvUp was to identify any evidence on the topic published after 2010. The EvUp identified 3 SysRevs, 2 RCTs, and 3 observational studies published since the previous evidence review. To review the EvUp, see Supplement Appendix C-23. The task force agreed that the evidence identified by the 2020 EvUp supports the consideration of a SysRev about the use of cuffed versus uncuffed tubes in cardiopulmonary resuscitation to ascertain if the treatment recommendation requires modification. Until the completion and analysis of a new SysRev,

the 2010 treatment recommendation remains in effect.[9,10]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with respiratory failure who undergo endotracheal intubation in any setting
- Intervention: Use of cuffed tracheal tubes
- Comparator: Use of uncuffed tracheal tubes
- Outcome: Any
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to December 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

Both cuffed and uncuffed tracheal tubes are acceptable for infants and children undergoing emergency intubation. If tracheal tubes are used, avoid excessive cuff pressures.

Atropine for Emergency Intubation (PLS 821: EvUp)

The PLS Task Force reviewed the evidence about the routine use of atropine as a premedication before emergency intubation in 2015.[11,12] An EvUp was undertaken but found insufficient literature for consideration of a SysRev. To review the EvUp, see Supplement Appendix C-24. The 2015 CoSTR remains in effect.[11,12]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children requiring emergency tracheal intubation
- Intervention: Use of atropine as a premedication before intubation
- Comparator: No use of atropine
- Outcome: Survival with favorable neurological outcome at 180 days, survival to hospital discharge, survival with favorable neurological outcome at 30 days follow-up, survival with favorable neurological outcome at discharge, likelihood of cardiac arrest, likelihood of shock, incidence of arrhythmias
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to September 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[11,12]

The confidence in effect estimates is so low that the panel decided that a recommendation was too speculative.

Cricoid Pressure During Intubation (PLS 376: EvUp)

The PLS Task Force last reviewed the evidence about the use of cricoid pressure during tracheal intubation in 2010.[9,10]

The EvUp identified 2 observational studies suggesting an association between external laryngeal manipulation, such as cricoid pressure, and increased difficulty during tracheal intubation of children in the emergency setting. To review the EvUp, see Supplement Appendix C-25. The PLS Task Force concluded that they should consider the need for a comprehensive SysRev to determine if the 2020 treatment recommendation should be amended. Until a new SysRev is completed and analyzed by the PLS Task Force, the 2010 treatment recommendation remains in effect.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children treated for acute illness or injury in any setting, during first hour of treatment
- Intervention: Use of cricoid pressure or laryngeal manipulation during endotracheal intubation
- Comparator: Any other type of or no laryngeal manipulation
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to December 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

If cricoid pressure is used during emergency intubation in infants and children, it should be discontinued if it impedes ventilation or interferes with the speed or ease of intubation.

Use of Devices to Verify Advanced Airway Placement (PLS 385: EvUp)

This 2020 EvUp was undertaken to determine if there was new evidence to support the use of devices to confirm advanced airway placement published after the most recent review of the topic in 2005.[81,81a] The EvUp identified 1 SysRev,[82] relevant output from national surveys,[83] and 2 RCTs.[84,85] Although these studies chiefly involved adults or preterm infants rather than infants beyond 28 days of age or children, the PLS Task Force agreed that there is sufficient new evidence to suggest the need to consider a SysRev. Until a new SysRev is completed and analyzed by the PLS Task Force, the 2005 treatment recommendation remains in effect. To review the EvUp, see Supplement Appendix C-26.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children who are in respiratory failure who undergo endotracheal intubation in any setting
- Intervention: The use of devices (eg, CO_2 detection device, CO_2 analyzer, or esophageal detector device)
- Comparator: Not using such a device
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to November 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2005.[81] The task force agreed to remove the weight minimum of 20 Kg or greater for capnography. In addition, the task force noted that continuous monitoring of waveform capnography has now become routine in many settings.

Confirmation of tracheal tube position using exhaled CO_2 detection (colorimetric detector or capnography) should be used for intubated infants and children with a perfusing cardiac rhythm in all settings (eg, out-of-hospital, emergency department, intensive care unit, inpatient, operating room). In infants and children with a perfusing rhythm, it may be beneficial to monitor continuous capnography or frequent intermittent detection of exhaled CO_2 during out-of-hospital and intrahospital or interhospital transport.

Ventilation Rate With Advanced Airway During Cardiac Arrest (PLS 3103A and PLS 382: EvUp)

The 2010 CoSTR was the most recent review of the evidence about optimal minute ventilation (product of tidal volume and respiratory rate/min) after the placement of an advanced airway during CPR in infants or children. The minute ventilation recommended in the 2010 CoSTR was based on expert consensus.[9,10]

This 2020 EvUp was to identify any evidence published after 2010 that might indicate the need for a new SysRev and for possible modification of the current treatment recommendations. This EvUp was prioritized for inclusion in this 2020 CoSTR because the task force identified the differences in recommended or proposed minute ventilation and respiratory rates across resuscitation councils and sought to identify any evidence that could assist in the development of a consistent recommended ventilation rate.

The EvUp identified a small single-center observational paper that reported an association of ventilation rates during cardiac arrest higher than 12 to 20/min with improved outcomes.[86] Ongoing studies are anticipated to conclude later in 2020 that may provide further data. As a result, the PLS Task Force will await the publication of more evidence to consider the need for a SysRev and possible revision of the treatment recommendation. To review the EvUp, see Supplement Appendix C-27.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with cardiac arrest and an advanced airway
- Intervention: The use of a higher ventilation rate
- Comparator: The current recommendation of 8 to 10 breaths/min
- Outcome: ROSC, survival to discharge, survival with favorable neurological status

Treatment Recommendations

The treatment recommendations (below) are unchanged from 2010 except for a minor edit to clarify types of arrest as asphyxial or arrhythmic (rather than VF) in origin.[9,10]

After placement of a secure airway, avoid hyperventilation of infants and children during resuscitation from cardiac arrest, whether asphyxial or arrhythmic in origin.

A reduction in minute ventilation to less than baseline for age is reasonable to provide sufficient ventilation to maintain adequate ventilation-to-perfusion ratio during CPR while avoiding the harmful effects of hyperventilation.

There are insufficient data to identify the optimal tidal volume or respiratory rate.

PALS: CIRCULATORY SUPPORT DURING CPR

Extracorporeal CPR for In-Hospital Cardiac Arrest (2019 CoSTR)

A SysRev about extracorporeal CPR (ECPR) for pediatric IHCA was performed in 2018[87] and an ILCOR Pediatric CoSTR was published as part of the 2019 CoSTR summary.[71,72] The summary of the consensus on science can be found in that 2019 CoSTR. Refer to those publications for details of the evidence summary and task force considerations.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults (age 18 years or older) and children (age younger than 18 years) with cardiac arrest in any setting (out-of-hospital or in-hospital)
- Intervention: Extracorporeal CPR (ECPR) including extracorporeal membrane oxygenator therapy or cardiopulmonary bypass during cardiac arrest
- Comparator: Manual or mechanical CPR
- Outcome: Clinical outcomes, including short-term survival and neurological outcomes (eg, hospital discharge, 28 days, 30 days, and 1 month) and long-term survival and neurological outcomes (eg, at 3 months, 6 months, and 1 year)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to January 2019.

Treatment Recommendations

These treatment recommendations (below) are unchanged from 2019.[71,72]

We suggest that ECPR may be considered as an intervention for selected infants and children (eg, pediatric cardiac populations) with IHCA refractory to conventional CPR in settings where resuscitation systems allow ECPR to be well performed and implemented (weak recommendation, very low-quality evidence).

There is insufficient evidence in pediatric OHCA to formulate a treatment recommendation for the use of ECPR.

PALS: PHYSIOLOGICAL MONITORING DURING ARREST TO GUIDE THERAPY AND/OR INTRA-ARREST PROGNOSTICATION

Physiological monitoring and feedback during CPR can facilitate the adjustment of CPR delivery during resuscitation and, as a result, may improve the quality of resuscitation and even resuscitation outcomes. Such monitoring may also allow for "individualized CPR" tailored to the patients' needs and their responses to resuscitation interventions. This section highlights the reviews about the use of invasive blood pressure monitoring, bedside ultrasound, near-infrared spectroscopy, and end-tidal carbon dioxide ($ETCO_2$) to assist with the optimal delivery of CPR.

Invasive Blood Pressure Monitoring During CPR (PLS 826: ScopRev)

Rationale for Review

Maintenance of adequate arterial systolic (compression) and diastolic (relaxation) or mean pressure during CPR is crucial to maintain coronary and cerebral perfusion. Maintaining a sufficient minimum threshold blood pressure should be associated with improved clinical outcomes. It is unknown if CPR directed to meet individualized rather than uniform standard blood pressure targets will improve outcomes from cardiac arrest. This topic was most recently reviewed in 2015,[11,12] and the 2020 ScopRev was performed to identify any evidence on this topic published after 2015.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children undergoing CPR
- Intervention: Use of invasive hemodynamic monitoring to titrate to a specific systolic and diastolic blood pressure
- Comparator: No use of invasive monitoring to a specific systolic and diastolic blood pressure
- Outcome: Change in survival to 180 days with good neurological outcome, survival to 60 days with good neurological outcome, survival to hospital discharge with good neurological outcome, the likelihood of survival to discharge or ROSC
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to November 2019.

Summary of Evidence

There was no association between blood pressures measured during CPR and neurological outcomes in an observational study of survivors of pediatric critical care (including cardiac critical care).[88] In an observational study of a highly selected pediatric critical care population with arterial pressure monitoring in place when cardiac arrest developed, there was a significant association between the mean diastolic blood pressure of 25 mm Hg or greater in infants and 30 mm Hg or greater in children within the first 10 minutes postarrest and their survival as well as with survival with favorable

neurological function.[89] To review the ScopRev, see Supplement Appendix B-7.

Task Force Insights

The information identified in this ScopRev applies only to pediatric patients with intra-arterial access along with continuous monitoring of blood pressure at the time they develop cardiac arrest. The work by Berg and colleagues[89] identified an association between the mean diastolic blood pressure associated with neurologically intact survival and the blood pressure thresholds below which no child survived. The evidence was too limited, however, to consider the diastolic blood pressure threshold by itself sufficient to identify CPR futility.

The PLS Task Force considered that, for children with IHCA and an arterial line already in place, hemodynamic-directed CPR might be considered. The task force agreed, however, that more evidence is required and that there is insufficient evidence currently available to consider a request for a SysRev. The 2015 treatment recommendation remains in effect.[11,12]

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[11,12]

The confidence in effect estimates is so low that the panel decided that a recommendation was too speculative.

Use of Near-Infrared Spectroscopy During Cardiac Arrest (PLS New: ScopRev)

Rationale for Review

NIRS is a noninvasive mode of estimating regional cerebral and renal/mesenteric oxygen saturation ($rSco_2$) and can detect these signals in no blood flow situations as in cardiopulmonary arrest. Cerebral NIRS values can reflect cerebral physiological changes (ie, intracranial tissue oxygenation that can be affected by arterial blood flow, tissue perfusion, and venous drainage) during cardiac arrest, during changes in intracranial pressure, during arrest resolution, and after ROSC. NIRS uses adhesive sensors placed on the forehead (to evaluate regional cerebral oxygen saturation of hemoglobin $rSco_2$ and over the abdomen. Each sensor contains a light source and 2 fiberoptic bundles that can detect the light absorption and reflection at different tissue depths.

This ScopRev addresses the use of NIRS as an intra-arrest variable that may assist in tailoring CPR technique to improve blood flow and oxygen delivery. The PLS Task Force has not previously considered use of NIRS in this manner, hence there are no current treatment recommendations. To review the ScopRev, see Supplement Appendix B-8.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in any setting (in-hospital or out-of-hospital) with cardiac arrest
- Intervention: The presence of variables—images, cut-off values, or trends—during CPR (intra-arrest) that can provide physiological feedback to guide resuscitation efforts, namely NIRS and cerebral oxygen saturation monitoring
- Comparator: The absence of such factors—images, cut-off values, or trends
- Outcome: Any clinical outcome
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to October 2019.

Summary of Evidence

The ScopRev identified no pediatric RCTs but did identify 1 ongoing adult RCT that compared the outcomes of NIRS-guided CPR with current standard CPR practice (this study is anticipated to conclude in 2021) (NCT03911908) and 2 adult SysRevs. Both adult SysRevs concluded that higher $rSco_2$ was associated with higher likelihood of ROSC and survival, whereas lower $rSco_2$ was associated with an increased mortality.[90,91] There was no consensus on the predictive threshold value of $rSco_2$ for any outcomes.[92–94] A trend of rising $rSco_2$ (between 7% and 15% from baseline measurement) may be a more reliable predictive factor for ROSC.[90,95,96]

The ScopRev also identified 2 observational studies of NIRS in children during CPR. One found that cerebral physiological changes were associated with changed NIRS measurements during cardiac arrest, increased intracranial pressure reduction, arrest resolution, and after ROSC.[97]

The second small study found an association between higher minimum $rSco_2$ during CPR and ROSC,[98] but overall survival was too low to detect changes in survival. An adult observational study found $ETCO_2$ to be a more accurate predictor of ROSC in OHCA.[99]

Task Force Insights

Survival after cardiac arrest may increase when resuscitation is tailored to the cause of the arrest and to the patient's responses to treatment. The level of certainty about the use of NIRS is very low, however, and the absence of consensus thresholds reduces its usefulness. The value of monitoring trends in the $rSco_2$ during pediatric resuscitation still requires validation. The PLS Task Force agreed that given the limited evidence available, there was currently insufficient evidence to warrant

consideration of a SysRev. As a result, there will continue to be no treatment recommendation.

Treatment Recommendations

No treatment recommendation has been made.

Bedside Ultrasound to Identify Perfusing Rhythm (PLS 408: ScopRev)

Rationale for Review

This topic was most recently reviewed in the 2010 CoSTR document.[9,10] The PLS Task Force agreed that the increased use of this technology warranted a ScopRev to determine any evidence published after 2010. To review the ScopRev, see Supplement Appendix B-9.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in any setting (in-hospital or out-of-hospital) with cardiac arrest
- Intervention: Point-of-care ultrasound (echocardiography during cardiac arrest)
- Comparator: Absence of point-of-care ultrasound (echocardiography)
- Outcome: Any clinical outcome
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and all languages were included if there was an English abstract. This literature search was updated to May 2019.

Summary of Evidence

The PLS Task Force posed 3 questions for this ScopRev:

1. Can diagnostic images be reliably obtained by noncardiology sonographers?
2. Can reversible causes of death be identified with high sensitivity and specificity?
3. Can the procedure be used to predict outcome?

Echocardiography typically requires pauses in chest compressions,[100–103] although the use of a protocol can reduce the duration of these pauses.[103,104] Practical difficulties in the use of ultrasound in infants and children (that do not occur in adults) include small patient size that may limit access to some views, particularly if other monitoring pads are on the chest. In addition, abnormal cardiac anatomy requires advanced training if noncardiac sonographers are to derive helpful information in this setting.

There is very limited pediatric evidence documenting the use of ultrasonography to identify reversible causes of arrest, for prognostication, or to determine cardiac futility. One small series of high-risk children with ultrasound diagnosis of pulmonary emboli resulted in successful thrombolytic therapy for all, with 80% survival to hospital discharge.[105] Complete cardiac standstill as determined sonographically is unlikely to be used as a sign of futility during pediatric resuscitation in light of case reports demonstrating that use of ECPR resulted in viable cardiac function after cardiac standstill.[106] Finally, significant cost is associated with the purchase of equipment and training of users, which may limit its use in resource-limited settings.

Task Force Insights

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

In addition, there is inadequate pediatric evidence about its intra-arrest prognostic utility, and the task force urges great caution until more literature is available. See Supplement Appendix B-9.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

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

End-Tidal CO_2 Monitoring During CPR (PLS 827: ScopRev)

Rationale for Review

The PLS Task Force initially recommended $ETCO_2$ monitoring to confirm tracheal tube placement in 2000.[59] $ETCO_2$ monitoring can also offer an indirect indication of cardiac output and pulmonary blood flow (noting caveats in relation to pulmonary blood flow and ventilation: perfusion ratio or with, for example, rapid changes caused by deterioration or response to effective treatment). As a result, $ETCO_2$ has been proposed as a method to evaluate the effectiveness of CPR and to identify possible ROSC. A rapid increase in $ETCO_2$ may be associated with improved CPR (or ROSC), and a sustained decline or persistently low $ETCO_2$ may be observed in the absence of ROSC. This 2020 ScopRev was performed to identify the evidence available to support

the use of $ETCO_2$ to provide feedback to guide resuscitation efforts.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in any setting (in-hospital or out-of-hospital) with cardiac arrest
- Intervention: Presence of variables—images, cut-off values, or trends—during CPR (intra-arrest) that can provide physiological feedback to guide resuscitation efforts, namely $ETCO_2$
- Comparator: The absence of such factors—images, cut-off values, or trends
- Outcome: Any clinical outcomes
- Time frame: All years and languages were included if there was an English abstract. This literature search was updated to January 2020.

Summary of Evidence

The ScopRev identified only 2 pediatric observational studies,[107,108] so the search was extended to include adult and animal literature. The latter evidence is indirect, meaning that caution is needed in extrapolating their findings to children. To review the ScopRev, see Supplement Appendix B-10.

Task Force Insights

The PLS Task Force agreed that it is important to identify measures to improve the quality of CPR. Accurate monitoring of $ETCO_2$ during resuscitation, however, requires the insertion of an advanced airway; advanced airway insertion may produce undesirable effects (see Ventilation During CPR With Bag and Mask Compared With an Advanced Airway). The 2 pediatric observational studies identified by the ScopRev included a subset of children in cardiac arrest, namely those who were intubated in the intensive care unit at the time of arrest. This is a very different population from infants and children with OHCA or those who arrest in less specialized settings such as a less well-resourced general pediatric hospital setting or clinic.

The PLS Task Force agreed that the evidence for or against the use of $ETCO_2$ to guide resuscitation efforts and improve pediatric cardiac arrest outcomes is insufficient to recommend consideration of a SysRev. As a result, the 2015 treatment recommendation remains in effect.[11,12]

Treatment Recommendations

This treatment recommendation (below) is unchanged from the 2015.[11,12]

The confidence in effect estimates is so low that the panel decided that a recommendation was too speculative.

PALS: RESUSCITATION DRUG ADMINISTRATION AND TIMING

Drugs are used in resuscitation to support cardiovascular physiology and organ perfusion and to ameliorate underlying pathophysiologic processes to reduce morbidity and mortality. The medication topics that were evaluated for 2020 included the optimal ways to calculate body weight for prescribing medications dosed by weight, amiodarone versus lidocaine for shock-resistant VF or pVT, and the role of sodium bicarbonate and of calcium in the management of cardiopulmonary arrest.

Methods of Calculating Pediatric Drug Doses (PLS 420: EvUp)

The PLS Task Force last considered this topic in 2010.[9,10] The search performed for this EvUp identified multiple publications relating to pediatric weight estimation, considering many different methods of weight estimation. In light of the volume of pediatric publications identified, the PLS Task Force agrees that there is sufficient evidence to consider a request for a SysRev. Until the SysRev is completed and analyzed, the 2010 treatment recommendation remains in effect. To review the EvUp, see Supplement Appendix C-28.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Pediatric patients with cardiac arrest (prehospital [OHCA] or in-hospital [IHCA])
- Intervention: The use of any specific alternative method for calculating drug dosages
- Comparator: Standard weight-based dosing
- Outcome: Achieving expected drug effect, ROSC, survival, avoidance of toxicity
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to October 2019.

Treatment Recommendations

These treatment recommendations (below) are unchanged from 2010.[9,10]

To calculate the dose of resuscitation medications, use the child's weight if known. If the child's weight is unknown, it is reasonable to use a body length tape with precalculated doses.

In nonobese pediatric patients, initial resuscitation drug doses should be based on actual body weight (which closely approximates ideal body weight). If necessary, body weight can be estimated from body length.

In obese patients, the initial doses of resuscitation drugs should be based on ideal body weight that can

be estimated from length. Administration of drug doses based on actual body weight in obese patients may result in drug toxicity.

Subsequent doses of resuscitation drugs in both nonobese and obese patients should take into account the observed clinical effects and toxicities. It is reasonable to titrate the dose to the desired therapeutic effect, but it should not exceed the adult dose.

Intraosseous Versus Intravenous Route of Drug Administration (PLS, NLS, and ALS: SysRev)

Rationale for Review

This topic was last reviewed in 2010.[9,10] A SysRev was requested to identify evidence comparing effects of intraosseous with intravenous drug administration during pediatric cardiac arrest. The PLS Task Force joined with the ALS and NLS Task Forces in requesting the SysRev.

Refer to the ALS and NLS publications in this supplement for details of the evidence summary.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Pediatric patients in any setting (in-hospital or out-of-hospital) with cardiac arrest
- Intervention: Placement of an intraosseous (IO) cannula and drug administration through this IO during cardiac arrest
- Comparator: Placement of an intravenous (IV) cannula and drug administration through this IV during cardiac arrest
- Outcome: Return of spontaneous circulation, survival to hospital discharge, and survival to hospital discharge with a favorable neurological outcome
- Study design: Randomized trials, non-RCTs, and observational studies (cohort studies and case-control studies) comparing IO with IV administration of drugs included; randomized trials assessing the effect of specific drugs (eg, epinephrine, amiodarone/lidocaine) in subgroups related to IO versus IV administration also included
- Time frame: All years and languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. The literature search was updated to September 2019.

Consensus on Science

The SysRev identified no papers involving infants and children in cardiac arrest. To review the adult evidence identified by the SysRev, see the ALS publication in this supplement (ALS 2046: SysRev). To review the neonatal evidence identified by the SysRev, see the intraosseous versus umbilical vein for emergency access discussion in the NLS publication of this supplement (NLS 616: SysRev).

The PLS Task Force agreed that, in the absence of new evidence, the previous (2010) treatment recommendation should remain in effect.[9,10]

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

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

Epinephrine Time of Initial Dose and Dose Interval During CPR (PLS 1541: SysRev)

Rationale for Review

Epinephrine administration for cardiac arrest was previously reviewed in the 2015 CoSTR.[11,12] The task force reported receiving many questions about the effectiveness and timing of epinephrine administration, so they requested a SysRev to identify any evidence published after 2015 that could enable the formulation of a new treatment recommendation. To review the SysRev Evidence-to-Decision Table, see Supplement Appendix A-2.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children in cardiac arrest (in- or out-of-hospital) (excluding resuscitation at birth)
- Intervention: (1) Administration of the initial dose of epinephrine earlier or later than current guideline recommendations. (2) Administration of epinephrine more or less frequently than every 3 to 5 minutes following the initial dose
- Comparator: Timing of administration of epinephrine in line with current guideline recommendations
- Outcome: Clinical outcomes, including short-term survival and neurological outcomes (eg, hospital discharge, 28 days, 30 days, and 1 month), and long-term survival and neurological outcomes (eg, 3 months, 6 months, and 1 year)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion; unpublished studies (eg, conference abstracts, trial protocols) excluded
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to July 2019.
- International Prospective Register of Systematic Reviews (PROSPERO) Registration: Registered November 21, 2019. Final registration number 146531.

Consensus on Science

We identified no pediatric RCTs on this topic. We did, however, identify 1 observational study of pediatric IHCA[109] and 4 observational studies[110-113] of OHCA comparing the administration of the initial dose of epinephrine earlier or later than current guideline recommendations; we also identified 2 observational studies[114,115] of pediatric IHCA on the topic of administration of epinephrine more or less frequently than every 3 to 5 minutes after the initial dose. We identified no observational studies of pediatric OHCA addressing the interval between epinephrine doses.

Time to First Epinephrine Less Than 15 Minutes Compared With 15 Minutes or More After Pediatric IHCA

For the critical outcomes of survival with good neurological outcome, survival to discharge, or ROSC, we identified 1 observational in-hospital registry study of 1558 children younger than 18 years with cardiac arrest.[109] In multivariable analysis, this study provided very low-certainty evidence (downgraded for risk of bias and imprecision) of no benefit associated with first epinephrine dose less than 15 minutes compared with administration 15 minutes or more after cardiac arrest.

Time to First Epinephrine Less Than 10 Minutes Compared With 10 Minutes or More After Pediatric IHCA

For the critical outcome of survival with good neurological outcome, we found an observational study from the same database that identified 1395 pediatric patients younger than 18 years of age with IHCA.[109] In multivariable analysis, the study provided very low-certainty evidence (downgraded for risk of bias) of benefit associated with time to first epinephrine dose of less than 10 minutes compared with 10 minutes or more after cardiac arrest (RR, 3.37; 95% CI, 1.11–10.25; 113 more per 1000; 95% CI, from 5 more to 440 more).

For the critical outcome of survival to discharge, we identified the same observational study reporting outcomes of 1558 children with IHCA.[109] After multivariable analysis, this study provided very low-certainty evidence (downgraded for risk of bias) of a benefit associated with time to first epinephrine dose of less than 10 minutes compared with 10 minutes or more after cardiac arrest (RR, 2.61; 95% CI, 1.36–5.01; 198 more per 1000; 95% CI, from 44 more to 494 more).

For the critical outcome of 24-hour survival, we found the same observational study of 1558 children with IHCA.[109] In multivariable analysis, the study provided very low-certainty evidence (downgraded for risk of bias) of benefit associated with time to first epinephrine dose less than 10 minutes compared with 10 minutes or more after cardiac arrest (RR, 1.58; 95% CI, 1.09–2.28; 178 more per 1000; 95% CI, from 28 more to 394 more).

For the critical outcome of ROSC, we found the same study of 1558 pediatric patients with IHCA.[109] In multivariable analysis, this study provided very low-certainty evidence (downgraded for risk of bias) of benefit associated with time to first epinephrine dose of less than 10 minutes compared with 10 minutes or more after cardiac arrest (RR, 1.56; 95% CI, 1.16–2.08; 233 more per 1000; 95% CI, from 66 more to 449 more).

Time to First Epinephrine Less Than 5 Minutes Compared With 5 Minutes or More After Pediatric IHCA

For the critical outcome of survival with good neurological outcome, we identified the same observational study reporting on outcomes of 1395 children younger than 18 years with IHCA.[109] In multivariable analysis, this study provided very low-certainty evidence (downgraded for risk of bias) of benefit of time to first epinephrine dose less than 5 minutes compared with 5 minutes or more after cardiac arrest (RR, 1.74; 95% CI, 1.13–2.66; 71 more per 1000; 95% CI, from 12 more to 159 more).

For the critical outcome of survival to discharge, we identified the same observational study of reporting on 1558 pediatric patients with IHCA.[109] In multivariable analysis, this study provided very low-certainty evidence (downgraded for risk of bias) of benefit associated with time to first epinephrine dose less than 5 minutes compared with 5 minutes or more after cardiac arrest (RR, 1.57; 95% CI, 1.21–2.04; 120 more per 1000; 95% CI, from 44 more to 219 more).

For the critical outcome of 24-hour survival, we identified the same observational study reporting on outcomes of 1558 children with IHCA.[109] In multivariable analysis, this study provided very low-certainty evidence (downgraded for risk of bias) of benefit associated with time to first epinephrine dose less than 5 minutes compared with 5 minutes or more (RR, 1.44; 95% CI, 1.20–1.73; 153 more per 1000; 95% CI, from 70 more to 254 more).

For the critical outcome of ROSC, we identified the same observational study reporting on outcomes of 1558 pediatric patients with IHCA.[109] In multivariable analysis, this study provided very low-certainty evidence (downgraded for risk of bias) of benefit associated with time to first epinephrine dose less than 5 minutes compared with 5 minutes or more (RR, 1.29; 95% CI, 1.13–1.47; 149 more per 1000; 95% CI; from 67 more to 242 more).

Time to First Epinephrine Less Than 3 Minutes Compared With 3 Minutes or More After Pediatric IHCA

For the critical outcome of survival with good neurological outcome, we identified 1 observational study of

1395 pediatric patients with IHCA.[109] In multivariable analysis, this study provided very low-certainty evidence (downgraded for risk of bias) of benefit from time to first epinephrine dose less than 3 minutes compared with 3 minutes or more (RR, 1.38; 95% CI, 1.05–1.81; 48 more per 1000; 95% CI, from 6 more to 101 more).

For the critical outcome of survival to discharge, we identified the same observational study of 1558 pediatric patients with IHCA.[109] In multivariable analysis, this study provided very low-certainty evidence (downgraded for risk of bias) of benefit associated with time to first epinephrine dose less than 3 minutes compared with 3 minutes or more (RR, 1.38; 95% CI, 1.17–1.63; 95 more per 1000; 95% CI, from 43 more to 158 more).

For the critical outcome of 24-hour survival, we identified the same observational study of 1558 pediatric patients with IHCA.[109] In multivariable analysis, this study provided very-low-certainty evidence (downgraded for risk of bias) of benefit associated with time to first epinephrine dose less than 3 minutes compared with 3 minutes or more (RR, 1.27; 95% CI, 1.13–1.43; 110 more per 1000; 95% CI, from 53 more to 175 more).

For the critical outcome of ROSC, we identified the same observational study of 1558 pediatric patients with IHCA.[109] In multivariable analysis, this study provided very-low-certainty evidence (downgraded for risk of bias) of benefit associated with time to first epinephrine dose less than 3 minutes compared with 3 minutes or more (RR, 1.24; 95% CI, 1.13–1.35; 133 more per 1000; 95% CI, from 72 more to 195 more).

Time to First Epinephrine Less Than 15 Minutes Compared With 15 Minutes or More After Pediatric OHCA

For the critical outcome of survival with good neurological outcome, we identified 2 observational studies of 725 pediatric patients 19 years or younger with traumatic (509 children)[110] and nontraumatic, nonshockable (216 children)[111] OHCA. These studies provided very-low-certainty evidence (downgraded for risk of bias, inconsistency, and imprecision), finding no benefit associated with a first dose of epinephrine less than 15 minutes compared with 15 minutes or more (RR, 3.94; 95% CI, 0.99–15.64; 80 more per 1000; 95% CI, from 0 fewer to 397 more).

For the critical outcome of survival to discharge, we identified 3 observational studies enrolling 27 480 children. These included emergency medical services–treated children younger than 18 years with nonshockable arrest who did not experience ROSC within 10 minutes (26 755 children)[112] and children 19 years or younger with traumatic (509 children)[110] and nontraumatic, nonshockable (216 children)[111] OHCA. These studies provided very-low-certainty evidence (downgraded for risk of bias, inconsistency, and other considerations of large effect) of benefit associated with time to first epinephrine dose less than 15 minutes compared with 15 minutes or more (RR, 2.49; 95% CI, 1.30–4.77; 28 more per 1000; 95% CI, from 6 more to 70 more).

For the critical outcome of 30-day survival, we identified 1 observational registry study of 225 children between 1 and 17 years with OHCA.[113] This study provided very-low-certainty evidence (downgraded for risk of bias, imprecision, and other considerations of very large effect) of benefit associated with time to first epinephrine dose less than 15 minutes compared with 15 minutes or more (RR, 5.78; 95% CI, 2.82–11.86; 348 more per 1000; 95% CI, from 133 more to 791 more).

For the critical outcome of survival to intensive care unit admission, we identified 1 observational study of 225 children 19 years or younger with nontraumatic, nonshockable OHCA.[111] This study provided very-low-certainty evidence (downgraded for risk of bias and imprecision) of benefit associated with time to first epinephrine dose less than 15 minutes compared with 15 minutes or more (RR, 1.96; 95% CI, 1.37–2.81; 274 more per 1000; 95% CI, from 106 more to 517 more).

For the critical outcome of ROSC, we identified 2 observational studies of 725 pediatric patients with traumatic[110] and nontraumatic, nonshockable[111] OHCA. These studies provided very-low-certainty evidence (downgraded for risk of bias and imprecision) of benefit associated with time to first epinephrine dose less than 15 minutes compared with 15 minutes or more (RR, 1.61; 95% CI, 1.37–1.90; 226 more per 1000; 95% CI, from 137 more to 334 more).

Time to First Epinephrine Less Than 10 Minutes Compared With 10 Minutes or More After Pediatric OHCA

For the critical outcome of 30-day survival, we identified 1 observational study of 225 children between 1 and 17 years with OHCA.[113] This study provided very-low-certainty evidence (downgraded for risk of bias, imprecision, and other considerations of very large effect) of benefit associated with time to first epinephrine dose less than 10 minutes compared with 10 minutes or more (RR, 5.07; 95% CI, 1.20–21.42; 402 more per 1000; 95% CI, from 20 more to 1000 more).

For the critical outcome of survival to discharge, we identified 1 observational study of 26 755 emergency medical service–treated children younger than 18 years with nonshockable OHCA arrest who did not experience ROSC within 10 minutes.[112] This study provided very-low-certainty evidence (downgraded for risk of bias) of benefit with time to first epinephrine dose less than 10 minutes compared with 10 minutes or more (RR, 1.55; 95% CI, 1.31–1.83; 9 more per 1000; 95% CI, from 5 more to 14 more).

Time to First Epinephrine Less Than 5 Minutes Compared With 5 Minutes or More After Pediatric OHCA

For the critical outcome of survival to discharge, we identified 1 observational study of 26 755 emergency medical services–treated children younger than 18 years with nonshockable OHCA arrest who did not experience ROSC within 10 minutes.[112] This study provided very-low-certainty evidence (downgraded for risk of bias) of benefit associated with time to first epinephrine dose less than 5 minutes compared with 5 minutes or more (RR, 1.81; 95% CI, 1.43–2.30; 16 more per 1000; 95% CI, from 9 more to 26 more).

Time to First Epinephrine Less Than 3 Minutes Compared With 3 Minutes or More After Pediatric OHCA

For the critical outcome of survival to discharge, we identified 1 observational study of 26 755 emergency medical services–treated children younger than 18 years with nonshockable OHCA arrest who did not experience ROSC within 10 minutes.[112] This study provided very-low-certainty evidence (downgraded for risk of bias) of benefit associated with time to first epinephrine dose less than 3 minutes compared with 3 minutes or more (RR, 1.74; 95% CI, 1.14–2.67; 16 more per 1000; 95% CI, from 3 more to 35 more).

Epinephrine Dose Interval of Less Than 5 Minutes Compared With 5 Minutes or More for Pediatric IHCA

For the critical outcome of 12-month survival, we identified 1 observational study of 235 pediatric patients with IHCA who received 2 minutes or more of chest compressions.[114]

This study represented a subset of all patients with IHCA because it enrolled only patients who were eligible for the Therapeutic Hypothermia After Pediatric Cardiac Arrest in-hospital (THAPCA-IH) trial; the enrollees were all comatose and mechanically ventilated after cardiac arrest, and the parents consented to enroll the children in the trial. This study provided very low-certainty evidence (downgraded for risk of bias, imprecision, and plausible confounding reducing demonstrated effect) of lower 12-month survival associated with an epinephrine dose interval of less than 3 minutes (adjusted OR 0.50; 95% CI, 0.24–1.06), 5 to less than 8 minutes (adjusted OR 0.42; 95% CI, 0.20–0.89), or more than 8 minutes (adjusted OR 0.35; 95% CI, 0.16–0.75) compared with a 3 to less than 5-minute dose interval.

For the critical outcome of survival to discharge, we identified 1 observational in-hospital registry study of 1630 children with cardiac arrest.[115] This study provided very-low-certainty evidence (downgraded for risk of bias, imprecision, and plausible confounding suggesting spurious effect) of benefit associated with more than 5-minute to less than 8-minute dose intervals (adjusted OR [AOR], 1.81; 95% CI, 1.26–2.59) and 8 to less than 10-minute intervals (AOR, 2.64; 95% CI, 1.53–4.55) compared with dose intervals of 1 to 5 minutes.

For the critical outcome of ROSC (survival of the IHCA event), we identified the same observational study of 1630 children with IHCA.[115] This study provided very-low-certainty evidence (downgraded for risk of bias, imprecision, and plausible confounding suggesting spurious effect) of benefit associated with more than 5 to less than 8 minute dose intervals (AOR, 1.71; 95% CI, 1.27–2.31) and 8 to less than 10-minute intervals (AOR, 1.93; 95% CI, 1.23–3.03) compared with dose intervals of 1 to 5 minutes.

The same observational study of 1630 pediatric patients with IHCA included a subset analysis of 1183 children who were not receiving vasoactive infusions at the time of arrest.[115] We identified very-low-certainty evidence (downgraded for risk of bias, imprecision, and plausible confounding suggesting spurious effect) of benefit associated with more than 5 to less than 8 minute dose intervals (AOR, 1.99; 95% CI, 1.29–3.06) and 8 to less than 10-minute dose intervals (AOR, 2.67; 95% CI, 1.41–5.04) compared with dose intervals of 1 to 5 minutes.

The same observational study of 1630 pediatric patients with IHCA included a subset analysis of 447 children who were receiving vasoactive infusions at the time of arrest.[115] We identified very-low-certainty evidence (downgraded for risk of bias, imprecision, and plausible confounding suggesting spurious effect) of benefit associated with more than 5 to less than 8 minute dose intervals (AOR, 1.52; 95% CI, 0.77–3.02) and 8 to less than 10-minute intervals (AOR, 2.62; 95% CI, 0.85–8.07) compared with dose intervals of 1 to 5 minutes.

Epinephrine Dose Interval of Less Than 3 Minutes Compared With 3 Minutes or More for Pediatric IHCA

For the critical outcome of 12-month survival, we identified 1 observational study of 161 pediatric patients with IHCA who were enrolled in the THAPCA-IH trial.[114] This study provided very-low-certainty evidence (downgraded for risk of bias, imprecision, and plausible confounding reducing demonstrated effect) of harm associated with a dose interval of less than 3 minutes (AOR, 0.50; 95% CI, 0.24–1.06) as well as 5 to less than 8 minutes (AOR, 0.42; 95% CI, 0.20–0.89) as well as 8 minutes or more (AOR, 0.5; 95% CI, 0.16–0.75) compared with a dose interval of 3 to less than 5 minutes.

Treatment Recommendations

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

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

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

Justification and Evidence to Decision Framework Highlights

Time to the Initial Dose of Epinephrine

In general, observational studies can be associated with many potential biases. Resuscitation time bias often occurs in intracardiac arrest studies such as epinephrine administration studies because the longer the duration of the resuscitation, the lower the rate of survival. As a result, patients who received the epinephrine earlier rather than later may have a lower mortality for reasons other than the time of the epinephrine administration.[115a] This bias can contribute to a trend toward appearance of a harmful effect of later initial epinephrine doses. Therefore, when interpreting studies of time to the initial dose of epinephrine, the task force considered the role of potential resuscitation time bias.

Epinephrine Interval

Hoyme et al[115] demonstrated that an increased epinephrine interval was associated with a decreased probability of survival, with an unadjusted odds ratio for survival of 0.60 for 5 to 8 minutes between epinephrine doses and 0.62 for 8 to 10 minutes between epinephrine doses compared with 1 to 5 minutes between epinephrine dose. However, in the adjusted statistical model, conversely, an increased epinephrine interval was associated with an increased probability of survival. The task force considered the fact that in the current meta-analysis, the unadjusted results, rather than the adjusted results, were incorporated. In addition, both Hoyme et al[115] and Meert et al[114] calculated the average interval of epinephrine doses by averaging all doses within the total arrest time; this differs from the actual interval between any 2 doses. For these reasons, the task force felt that confidence in the estimates of effect was too low to support a treatment recommendation regarding epinephrine dose interval. For further information, please refer to Supplement Appendix A-2.

Knowledge Gaps

Current knowledge gaps include but are not limited to

- There is clinical equipoise and the need for pediatric randomized trials addressing the optimal timing of initial epinephrine dose and the optimal interval of epinephrine doses.
- Researchers must establish a consistent method to accurately calculate/report the interval between epinephrine doses.
- There is a need to minimize the effects of resuscitation time bias in resuscitation clinical trials.

Amiodarone Versus Lidocaine for Shock-Resistant Ventricular Fibrillation or Pulseless Ventricular Tachycardia (2018 CoSTR)

The topic of amiodarone versus lidocaine for shock-resistant VF or pVT was evaluated by the PLS Task Force in the 2018 CoSTR Update.[115b,115c] Refer to those publications for details of the evidence summary and task force considerations.

The task force agreed that a multicenter trial comparing different anti-arrhythmic agents would be helpful. Until further data are available, the 2018 treatment recommendation remains in effect.[115b,115c]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Patients of all ages (neonates, children, adolescents younger than 18 years) in any setting with cardiac arrest and a shockable rhythm at any time during CPR or immediately after ROSC
- Intervention: Administration (IV or IO) of an anti-arrhythmic drug
- Comparator: Another anti-arrhythmic or placebo
- Outcome: Survival to hospital discharge with good neurological outcome, survival to hospital discharge, ROSC, and rearrest after ROSC
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to August 2017.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2018.[115b,115c]

We suggest that amiodarone or lidocaine may be used for the treatment of pediatric shock-resistant VF or pVT (weak recommendation, very low-quality evidence).

Sodium Bicarbonate Administration for Children in Cardiac Arrest (PLS 388: EvUp)

The most recent PLS Task Force review of the evidence about sodium bicarbonate administration during cardiac arrest was in 2010.[9,10] An EvUp was performed and found insufficient evidence to consider a SysRev of this topic, so the recommendations of 2010 remain in effect. To review the EvUp, see Supplement Appendix C-29.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children who are in cardiac arrest in any setting
- Intervention: Buffering agent administration
- Comparator: No use of buffering agents
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to November 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

Routine administration of sodium bicarbonate is not recommended in the management of pediatric cardiac arrest.

Calcium Administration in Children (PLS 421: EvUp)

This EvUp was performed to identify any evidence published after the most recent PLS Task Force review of this topic in 2010.[9,10]

The PLS Task Force agreed that there is insufficient evidence to suggest the need for a SysRev or alter the 2010 treatment recommendation, which remains in effect. To review the EvUp, see Supplement Appendix C-30.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children who are in cardiac arrest in any setting
- Intervention: Calcium administration
- Comparator: No calcium administration
- Outcome: All clinical outcomes
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was updated to November 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

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

PALS: SPECIAL RESUSCITATION SITUATIONS—SEPTIC SHOCK, CONGENITAL HEART DISEASE, AND TRAUMA

This section summarizes the evidence reviews about resuscitation of children with cardiac arrest and septic shock, congenital heart disease such as single-ventricle physiology, or Fontan circulation. The PLS Task Force also reviewed the evidence about unique aspects of resuscitation after traumatic arrest.

Resuscitation of the Child With Septic Shock (PLS 1534: EvUp)

The management of children with septic shock–associated cardiac arrest has not been previously reviewed by the PLS Task Force. This EvUp was requested to determine the available evidence about this topic. The EvUp identified several studies involving prevention of cardiac arrest, but there was insufficient evidence of unique management approaches to the children with septic shock–associated cardiac arrest. As a result, the task force agreed that there was no indication of a need to consider a SysRev, and no treatment recommendation could be made at this time. To review the EvUp, see Supplement Appendix C-31.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with sepsis in cardiac arrest
- Intervention: Specific alteration in treatment algorithm
- Comparator: Standard care (according to 2010 treatment algorithm)
- Outcome: All

Treatment Recommendation

There is no treatment recommendation at this time.

Resuscitation of the Patient With a Single Ventricle (PLS 390: EvUp)

This EvUp was performed to identify any evidence published after the most recent PLS Task Force review in 2010.[9,10] The EvUp identified nonrandomized studies reporting the impact of modification to standard cardiac arrest care on outcomes in postsurgical infants. The PLS Task Force agreed that this and additional evidence[50,115d] may warrant consideration for a SysRev. Until a new SysRev is performed and analyzed by the PLS Task Force, the 2010 treatment recommendations remain in effect. To review the EvUp, see Supplement Appendix C-32.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with single-ventricle, status/post–stage I repair who require resuscitation from cardiac arrest or prearrest states
- Intervention: Any specific modification to standard practice
- Comparator: Standard resuscitation practice
- Outcome: ROSC, survival to discharge, survival with good neurological outcome
- Study design: Included only observational studies and RCTs from the time of the previous search review
- Time frame: All years and languages were included if there was an English abstract. The literature search was from January 2008 to October 2019.

Treatment Recommendations

These treatment recommendations are unchanged from 2010.[9,10]

Standard resuscitation (prearrest and arrest) procedures should be followed for infants and children with single-ventricle anatomy after stage I repair. Neonates with a single ventricle before stage I repair who demonstrate shock caused by elevated pulmonary to systemic flow ratio might benefit from inducing mild hypercarbia ($Paco_2$ 50–60 mm Hg); this can be achieved during mechanical ventilation by reducing minute ventilation, adding CO_2 to inspired air, or administering opioids with or without chemical paralysis.

Resuscitation of the Patient With Hemi-Fontan or Fontan Circulation (PLS 392: EvUp)

This EvUp was performed to identify any evidence about this topic published after the PLS Task Force's most recent review in 2010.[9,10] The EvUp identified 1 registry-based study that reported outcomes of infants and children with Fontan/ or bidirectional Glenn who had circulatory support initiated during a peri-arrest phase.[115d] The PLS Task Force agreed that there is insufficient evidence[50,115d] to recommend a new SysRev, and the 2010 treatment recommendation remains in effect,[9,10] with the addition of a brief explanatory phrase within brackets. To review the EvUp, see Supplement Appendix C-33.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with Fontan or hemi-Fontan or bidirectional Glenn circulation who require resuscitation from cardiac arrest or prearrest states (prehospital or in-hospital)
- Intervention: Specific modification to standard resuscitation practice
- Comparator: Standard resuscitation practice
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract. The literature search was from January 2013 to September 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010 with the exception of limiting the recommendation to children with hemi-Fontan[9,10] or bidirectional Glenn physiology who are in a prearrest state; hypercarbia achieved by hypoventilation may be beneficial to increase oxygenation and cardiac output.

Negative-pressure ventilation, if available, may be beneficial for children with either hemi-Fontan or bidirectional Glenn or Fontan physiology by increasing cardiac output.

During cardiopulmonary arrest, it is reasonable to consider ECPR for patients with Fontan physiology.

There is insufficient evidence to support or refute the use of ECPR in patients with hemi-Fontan or bidirectional Glenn physiology.

Resuscitation After Traumatic Arrest (PLS 498: EvUp)

An EvUp was performed to identify any relevant studies published in the decade after the 2010 PLS Task Force review of the topic.[9,10] The PLS Task Force agreed that the evidence warrants consideration of a SysRev, preferably one including not only adults but also infants and children in the study population, to determine the evidence to support specific recommendations about resuscitation for traumatic cardiac arrest. To review the EvUp, see Supplement Appendix C-34.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children with major (blunt or penetrating) injury in cardiac arrest in any setting
- Intervention: Any specific alteration in treatment algorithm
- Comparator: Standard care (according to 2010 treatment algorithm)
- Outcome: All
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages included if there was an English abstract; literature search was updated to December 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[9,10]

There is insufficient evidence to make a recommendation for modification of standard resuscitation for infants and children experiencing cardiac arrest due to major trauma, although consideration should be given to selectively performing a resuscitative thoracotomy in children with penetrating injuries who arrive at the hospital with a perfusing rhythm.

PALS: POST–CARDIAC ARREST CARE, INCLUDING POSTARREST PROGNOSTICATION

Targeted Temperature Management (2019 CoSTR)

A SysRev addressing targeted temperature management (TTM) was published in 2019,[116] and an ILCOR Pediatric CoSTR was published as part of the 2019 CoSTR summary.[71,72] Refer to those publications for details of the evidence summary and task force considerations.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Pediatric patients (more than 24 hours to 18 years of age) who achieved ROSC after OHCA or IHCA
- Intervention: TTM with a target temperature of 32°C to 36°C
- Comparator: No TTM or TTM at an alternative target temperature range
- Outcome:
  - Primary outcome: Good neurobehavioral survival long term
  - Secondary outcomes:
    - Good neurobehavioral survival short term and intermediate term
    - Survival short term, intermediate term, and long term
    - Neurobehavioral score changes from prearrest, intermediate term, and long term
    - Health-related quality of life score intermediate term and long term
    - Health-related quality of life score change from prearrest, intermediate term, and long term
  - Additional in-hospital adverse outcomes:
    - Infection (culture proven)
    - Recurrent cardiac arrest (not leading to death)
    - Serious bleeding (red blood cell transfusion)
    - Arrhythmias (any)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages included if there was an English abstract; literature search was updated to December 2018.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2019 (with the exception of the addition of text to clarify that recommendations apply to children who remain comatose after OHCA or IHCA and to clarify that the temperature should be maintained 37.5°C or less).

We suggest that for infants and children who remain comatose following ROSC from OHCA and IHCA, TTM be used to maintain a central temperature of 37.5°C or less (weak recommendation, moderate-certainty evidence).

On the basis of 2 randomized trials and 8 retrospective observational cohort studies that provided comparative data on favorable neurological outcome, survival, and in-hospital adverse events, there is inconclusive evidence to support or refute the use of TTM 32°C to 34°C compared with TTM 36°C to 37.5°C (or an alternative temperature) for children who achieve ROSC but remain comatose after OHCA or IHCA.

Oxygen and Carbon Dioxide Targets in Pediatric Patients With Return of Spontaneous Circulation After Cardiac Arrest (PLS 815: SysRev)

A SysRev of arterial oxygen and carbon dioxide targets in adults and children with ROSC after cardiac arrest,[116a] was conducted with involvement of clinical content experts from the ALS and PLS Task Forces. Evidence from adult and pediatric literature was sought and considered by the ALS and PLS Task Forces, respectively. This CoSTR focuses on evidence derived from infants and children. See Supplement Appendix A-3 for more details.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Unresponsive children with sustained return of spontaneous circulation (ROSC) after cardiac arrest in any setting
- Intervention: A ventilation strategy targeting specific Spo_2 [oxygen saturation], Pao_2 [partial pressure of oxygen], and/or $Paco_2$ [partial pressure of carbon dioxide] targets
- Comparator: Treatment without specific targets or with an alternate target to the intervention
- Outcome: Clinical outcome including survival/survival with a favorable neurological outcome at hospital discharge/30 days, and survival/survival

with a favorable neurological outcome after hospital discharge/30 days (eg, 90 days, 180 days, 1 year)
- Study design: Randomized trials, non-RCTs, and observational studies (cohort studies and case-control studies) with a control group (ie, patients treated with no specific Spo_2, Pao_2, and/or $Paco_2$ targets or an alternative target to the intervention) included
- Time frame: All years and languages included; literature search was updated to August 2019.

Consensus on Science

Oxygen Targets

We identified no pediatric RCTs on this topic but did identify 2 observational studies published in the 5 years after the previous (2015[11,12]) review.[117,118] One of these[118] was deemed at critical risk of bias for lack of adjustment for cardiac arrest characteristics; for this reason, interpretation of these results is severely limited. Within these limitations, this study included 253 patients and found no association between hyperoxemia and clinical outcomes in adjusted analyses (numeric adjusted results not reported). Of all studies identified (including those reviewed in 2015[11,12]), only 3 pediatric studies,[117,119,120] including a total of 618 patients, were deemed to have only serious risk of bias, and in all of these studies only adjusted results were reported.

For the critical outcome of survival to hospital discharge with good neurological outcome, we identified 1 observational study of 153 pediatric patients with ROSC after cardiac arrest.[120] This study provided very-low-certainty evidence (downgraded for indirectness, imprecision, and risk of bias), finding no benefit of hyperoxemia compared with no hyperoxemia (OR, 1.02; 95% CI, 0.46–2.27; 5 more per 1000; 95% CI, from 170 fewer to 202 more).

For the critical outcome of survival to hospital discharge, we identified 1 observational study of 164 pediatric patients with ROSC after IHCA[119] providing very low-certainty evidence (downgraded for indirectness, imprecision, and very serious risk of bias) comparing hyperoxemia with normoxemia and finding no benefit to hyperoxemia, although numeric results of adjusted analyses were not reported. We identified a second study of 200 pediatric patients with ROSC after cardiac arrest[117] that provided very low-certainty evidence (downgraded for indirectness, imprecision, and serious risk of bias) and that showed no association of post-ROSC Pao_2 greater than 200 mm Hg with outcome (OR 0.81; 95% CI, 0.41–1.59; absolute risk difference not calculable because the number of survivors in the normoxemia group was not reported).

One large registry-based study[121] found that hyperoxemia was associated with higher mortality when compared with normoxemia. Although this study was much larger than the others, it was deemed at critical risk of bias as a result of lack of adjustment for cardiac arrest characteristics (increasing the risk of confounding) and the exclusion of the 31% of all eligible patients who lacked an arterial blood gas analysis within 1 hour of ROSC. The task force thought that this exclusion increased risk of selection bias because patients who did not have an arterial blood gas analysis within 1 hour of ROSC are likely disproportionally normoxemic or hyperoxemic rather than hypoxemic.

Carbon Dioxide Targets

We identified no pediatric RCTs on this topic. Two observational studies were identified,[118,119] 1 of which[118] was published in the interval after the search was completed for the 2015 CoSTR. Only adjusted results from these studies were reported. One study[119] including 223 patients provided very-low-certainty evidence (downgraded for risk of bias and indirectness) of an increase in hospital mortality associated with both hypocapnia (OR, 2.71; 95% CI, 1.04–7.05; 242 more per 1000; 95% CI, from 9 more to 446 more) and hypercapnia after ROSC (OR, 3.27; 95% CI, 1.62–6.61; 286 more per 1000; 95% CI, from 114 more to 423 more). The 1 study published after the 2015 review[118] was deemed at critical risk of bias for lack of adjustment for cardiac arrest characteristics. Within these limitations, this study included 253 patients and found an increase in hospital mortality associated with both hypocapnia compared with normocapnia (OR, 2.62; 95% CI, 1.08–6.4; 233 more per 1000; 95% CI, from 17 more to 429 more) and hypercapnia compared with normocapnia (OR, 2.0; 95% CI, 1.01–3.97; 166 more per 1000; 95% CI, from 2 more to 332 more) 1 hour after ROSC.

The available evidence on the effect of hypercapnia or hypocapnia in adults is inconsistent, with the randomized trials done to date showing no effect.

Treatment Recommendations

We suggest that rescuers measure Pao_2 after ROSC and target a value appropriate to the specific patient condition. In the absence of specific patient data, we suggest rescuers target normoxemia after ROSC (weak recommendation, very low-quality evidence).*

Given the availability of continuous pulse oximetry, targeting an oxygen saturation of 94% to 99% may be a reasonable alternative to measuring Pao_2 for titrating oxygen when feasible to achieve normoxia (based on expert opinion).

We suggest that rescuers measure $Paco_2$ after ROSC and target normocapnia (weak recommendation, very low-certainty evidence).

*Note: This treatment recommendation applies to infants 28 days to 12 months and children in cardiac arrest. For recommendations applying to newborns resuscitated at birth, refer to "Neonatal Life Support: 2020 International Consensus on CPR and ECC Science With Treatment Recommendations"[7a,7b] in this supplement.

Consider adjustments to the target $Paco_2$ for specific patient populations where normocapnia may not be desirable (eg, chronic lung disease with chronic hypercapnia, congenital heart disease with single-ventricle physiology, increased intracranial pressure with impending herniation).

Justification and Evidence to Decision Framework Highlights

Measurement of the arterial Pao_2 and $Paco_2$ is much easier to perform in the hospital than in the out-of-hospital setting. Yet without such monitoring in the out-of-hospital setting, it will be difficult for providers to judge within tolerable ranges the balance between hypoxemia and hyperoxemia and between overventilation and underventilation. These ranges of appropriate Pao_2 and $Paco_2$ will also differ for some patients, such as those with cyanotic congenital heart disease.

In steady state situations (eg, steady temperature, $Paco_2$, and pH), providers may be able to correlate the $Paco_2$ with the $ETCO_2$ to determine trends that may provide information about ongoing ventilatory responses to support ventilation.

The PLS Task Force recognized the paucity of data available to make recommendations about target values for Pao_2 and $Paco_2$ in infants and children after ROSC.

Oxygen Targets

Accurate targeting of post-ROSC normoxemia might be achievable and acceptable being guided by pulse oximetry in the hospital setting, but the use of pulse oximetry to titrate oxygen administration to target normoxemia in the out-of-hospital setting has not been studied and is not without risk of inadvertent patient hypoxemia. Given the known risks of hypoxemia and the uncertain risks of hyperoxia, any titration of oxygen delivery to children after ROSC must be balanced against the risk of inadvertent hypoxemia stemming from overzealous weaning of Fio_2. Further challenges include identifying the appropriate targets for specific pediatric patient subpopulations (eg, infants and children with cyanotic heart disease).

Carbon Dioxide Targets

Accurate targeting of post-ROSC normocapnia might be achievable and acceptable in the in-hospital critical care setting. Serial assessment of ventilation through arterial blood gas analysis is facilitated by arterial catherization, which may also be beneficial for targeting post-ROSC blood pressure targets. Correlation of $Paco_2$ and $ETCO_2$ may allow ongoing monitoring of ventilation when continuous capnography is available. Further challenges include identifying any modified $Paco_2$ targets needed for specific pediatric patient subpopulations (eg, infants and children with suspected increased intracranial pressure).

For further information about task force development of treatment recommendations from the published evidence on this topic, see the evidence-to-decision table in Supplement Appendix A-3.

Knowledge Gaps

The PLS Task Force identified the following knowledge gaps:

- There are no pediatric randomized trials comparing oxygen or carbon dioxide management strategies in post–cardiac arrest care.
- We found no published evidence to determine how $Paco_2$ targets should be adjusted in infants and children with chronic CO_2 retention.
- We found no published evidence to determine whether adjusting arterial blood gas analysis to 37°C or to a patient's current temperature is beneficial.

Post-ROSC Blood Pressure Control (PLS 820: EvUp)

This topic was most recently reviewed in 2015.[11,12]

This EvUp was performed to identify new evidence published in the most recent 5 years. The EvUp identified evidence to suggest that post–cardiac arrest hypotension below the fifth percentile for age is associated with poorer outcomes when compared with post–cardiac arrest normotension, and those patients requiring higher inotropic drug support have lower rates of survival to hospital discharge. The task force agreed that the EvUp identified sufficient new evidence to suggest the need for a SysRev. Until such time as a SysRev is completed and evaluated, the 2015 treatment recommendations remain in effect.[11,12] To review the EvUps, see Supplement Appendix C-35 and Supplement Appendix C-36.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children after ROSC
- Intervention: Use of parenteral fluids and inotropes and/or vasopressors to maintain targeted measures of perfusion such as blood pressure
- Comparator: No use of these interventions
- Outcome: Patient satisfaction; survival with favorable neurological and functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival with favorable neurological and functional outcome at discharge, 30 days, 60 days, 180 days, and/or 1 year; survival to hospital discharge; harm to patient
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion

- Time frame: All years and languages included if there was an English abstract; literature search was updated to September 2019.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[11,12]

We recommend that for infants and children after ROSC, parenteral fluids and/or inotropes or vasopressors should be used to maintain a systolic blood pressure of at least greater than the fifth percentile for age (strong recommendation, very low-quality evidence).

Post-ROSC Neuroprognostication and Use of Electroencephalogram (PLS 813 and PLS 822: EvUp)

The most recent PLS Task Force review of post-ROSC predictive factors was published in the 2015 CoSTR but was focused only on the use of electroencephalography.[11,12] This EvUp was performed to determine if sufficient evidence exists to suggest the need for a SysRev. The EvUp identified 8 studies reporting associations of several factors in addition to electroencephalography with outcomes after cardiac arrest.

The PLS Task Force agreed that this topic is of such interest that they support the suggestion of a SysRev, with a broader search strategy to include studies of additional potential prognostic indicators beyond the electroencephalography. Until the SysRev is completed, the 2015 treatment recommendation remains in effect.[11,12] To review the EvUp, see Supplement Appendix C-37.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Infants and children who have had cardiac arrests in the hospital or out-of-hospital setting
- Intervention: Use of neuro-electrophysiology information (electroencephalography). Note: the PLS Task Force agreed that the list of possible interventions or diagnostic tools must expand for the next search.
- Comparator: None
- Outcome: Survival to 1 year with good neurological outcome, survival to 180 days with good neurological outcome, survival to 60 days with good neurological outcome, survival to 6 months, survival to 30 days with good neurological outcome, survival to 30 days with good neurological outcome, survival to hospital discharge with good neurological outcome, survival with favorable neurological outcome, survival to hospital discharge
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) eligible for inclusion
- Time frame: All years and languages included if there was an English abstract; literature search from January 2013 to August 2019

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[11,12]

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

TOPICS NOT REVIEWED IN 2020

- Etomidate and pediatric septic shock (PLS 402)
- Compression-only CPR for intubated neonates outside delivery room (PLS 380)
- Formulas for peds endotracheal tube size (PLS 401)
- Endotracheal tube versus IV drugs (PLS 403)

FUTURE TASKS

The following PICOSTs were prioritized by the task force for performing a SysRev. The PLS Task Force will determine the time-tabling for this body of work.

Fluid administration for septic shock (PLS New)

Fluid administration in shock associated with dengue

Fluid administration in malaria with shock

Optimal timing for the administration of fluid resuscitation in pediatric trauma

Prearrest care of the infant or child with dilated cardiomyopathy or myocarditis (PLS 819: EvUp)

Prevention and management of pulmonary hypertensive crisis in infants and children (PLS 391: EvUp)

Opioids, sedatives, and muscle relaxants for pulmonary hypertension (PLS 056: EvUp)

Therapy with inhaled nitric oxide or prostaglandin I_2 for pulmonary hypertensive crisis and right heart failure (2020 New EvUp)

CPR for heart rate of less than 60/min (PLS 1535: EvUp)

Energy doses for defibrillation (PLS 405: ScopRev)

Advanced airways: Cuffed versus uncuffed tubes (PLS 412: EvUp)

Resuscitation of the patient with a single ventricle (PLS 390: EvUp)

Resuscitation after traumatic arrest (PLS 498: EvUp)

Post-ROSC blood pressure control (PLS 820: EvUp)

Further work will be undertaken to look at diagnostic tests (PLS 411)

Effect of identification and preventive management of genetically related family members of those with channelopathies on incidence of cardiac arrest (PLS 417)

ARTICLE INFORMATION

The American Heart Association requests that this document be cited as follows: Maconochie IK, Aickin R, Hazinski MF, Atkins DL, Bingham R, Couto TB, Guerguerian A-M, Nadkarni VM, Ng K-C, Nuthall GA, Ong GYK, Reis AG, Schexnayder SM, Scholefield BR, Tijssen JA, Nolan JP, Morley PT, Van de Voorde P, Zaritsky AL, de Caen AR; on behalf of the Pediatric Life Support Collaborators. Pediatric life support: 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation*. 2020;142(suppl 1):S140–S184. doi: 10.1161/CIR.0000000000000894

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Janice A. Tijssen	London Health Sciences Center (Canada)	MedEvac Foundation Grant (Transport study)*; Heart and Stroke Foundation of Canada (Grant-in-Aid)*	None	None	None	None	None	None
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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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*Modest.

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Circulation

Neonatal Life Support

2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

ABSTRACT: This *2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations* (CoSTR) for neonatal life support includes evidence from 7 systematic reviews, 3 scoping reviews, and 12 evidence updates. The Neonatal Life Support Task Force generally determined by consensus the type of evidence evaluation to perform; the topics for the evidence updates followed consultation with International Liaison Committee on Resuscitation member resuscitation councils. The 2020 CoSTRs for neonatal life support are published either as new statements or, if appropriate, reiterations of existing statements when the task force found they remained valid.

Evidence review topics of particular interest include the use of suction in the presence of both clear and meconium-stained amniotic fluid, sustained inflations for initiation of positive-pressure ventilation, initial oxygen concentrations for initiation of resuscitation in both preterm and term infants, use of epinephrine (adrenaline) when ventilation and compressions fail to stabilize the newborn infant, appropriate routes of drug delivery during resuscitation, and consideration of when it is appropriate to redirect resuscitation efforts after significant efforts have failed.

All sections of the Neonatal Resuscitation Algorithm are addressed, from preparation through to postresuscitation care. This document now forms the basis for ongoing evidence evaluation and reevaluation, which will be triggered as further evidence is published.

Over 140 million babies are born annually worldwide (https://ourworldindata.org/grapher/births-and-deaths-projected-to-2100). If up to 5% receive positive-pressure ventilation, this evidence evaluation is relevant to more than 7 million newborn infants every year. However, in terms of early care of the newborn infant, some of the topics addressed are relevant to every single baby born.

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On behalf of the Neonatal Life Support Collaborators

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Key Words: AHA Scientific Statements ■ cardiopulmonary resuscitation ■ neonatal resuscitation ■ neonate

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Transition from intrauterine to extrauterine life at birth requires several critical interdependent physiological events to occur rapidly to allow successful conversion from placental to pulmonary gas exchange.[1] Air breathing leads to significant reductions in pulmonary vascular resistance, which increases pulmonary blood flow and thereby maintains left ventricular filling and output (vital for coronary and cerebral perfusion) when the umbilical cord is clamped.[2] When the low-resistance placental circulation is removed, systemic vascular resistance and blood pressure increase and right-to-left shunting across the ductus arteriosus decreases.

The majority (approximately 85%) of babies born at term will initiate breathing within 10 to 30 seconds of birth.[3] An additional 10% will do so in response to stimulation and drying.[4] Nevertheless, approximately 5% of term infants receive positive-pressure ventilation (PPV) to successfully transition, 2% are intubated, 0.1% receive cardiac compressions, and 0.05% receive compressions with epinephrine.[5–8] Although most infants successfully transition without assistance, the large number of births worldwide means that availability of appropriate, timely intervention can prevent morbidity and save millions of newborn lives each year.

Newborn infants who are breathing or crying and have good tone and an adequate heart rate may undergo delayed cord clamping and should be dried and placed skin to skin with their mothers to prevent hypothermia. This does not preclude the need for clinical assessment of the newborn as secondary apnea, persistent cyanosis, or breathing difficulties can still occur. For the approximately 5% of newborn infants who do not initiate adequate respiratory effort after stimulation by drying and warming, providers must deliver effective ventilation with a face mask. This is effective in most cases. If it is not effective, providers should take measures to eliminate mask leaks, check for airway patency, and ensure that adequate inflation pressures are used; if ventilation is still not effective, an alternative airway (endotracheal tube or supraglottic airway) must be considered. Providers must optimize ventilation because it is the most important step for successful transition. If, despite efforts to optimize ventilation, the newborn has a persistent heart rate less than 60/min or asystole, then chest compressions are needed. Epinephrine and administration of fluids for circulatory volume expansion may also be required. The neonatal resuscitation algorithm is shown in Figure 1 and is unchanged from 2015.[1,9,10]

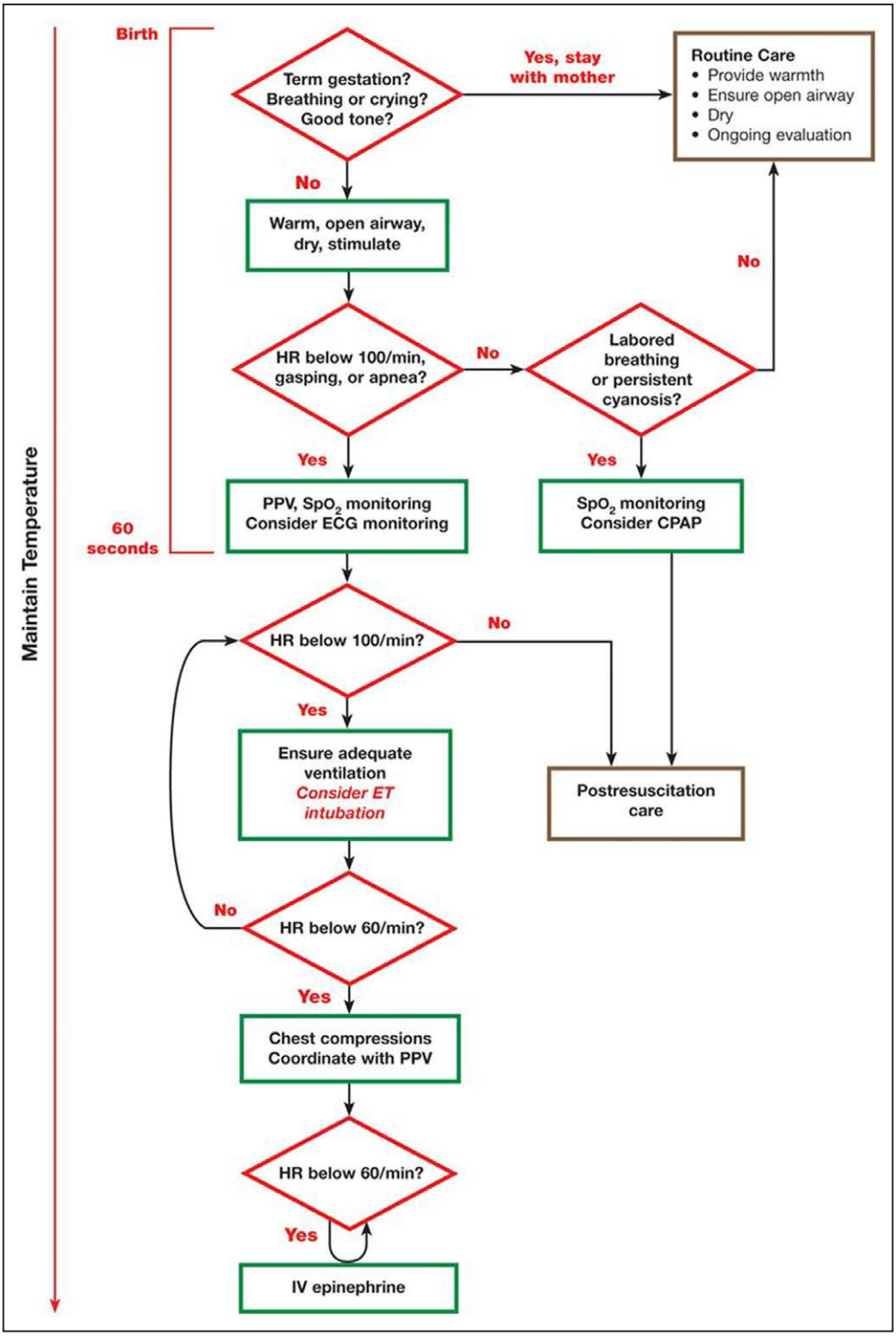

Figure 1. Neonatal Resuscitation Algorithm.
CPAP indicates continuous positive airway pressure; ECG, electrocardiographic; ET, endotracheal; HR, heart rate; IV, intravenous; and PPV, positive-pressure ventilation.

EVIDENCE EVALUATION PROCESS

The *2020 International Consensus on Cardiopulmonary Resuscitation* (CPR) *and Emergency Cardiovascular Care* (ECC) *Science With Treatment Recommendations* (CoSTR) is the fourth in a series of annual publications from the International Liaison Committee on Resuscitation (ILCOR) for neonatal life support (NLS). This 2020 CoSTR for NLS includes new topics addressed by systematic reviews performed within the past 12 months. It also includes updates of NLS treatment recommendations published from 2010 through 2019, based on additional evidence evaluations. The 3 types of evidence evaluation supporting this 2020 document

are the systematic review (SysRev), the scoping review (ScopRev) and the evidence update (EvUp). The choice of the type of evidence evaluation to perform was determined by consensus of the task force and, in the case of EvUps, recommendations of ILCOR member resuscitation councils.

The SysRev is a rigorous process following strict methodology to answer a specific question. The SysRevs informed NLS Task Force deliberations that are summarized in the NLS Task Force CoSTRs included in this document. The SysRevs were performed by a knowledge synthesis unit, an expert systematic reviewer, or by the NLS Task Force, and many resulted in separately published SysRevs.

To begin the SysRev, the question to be answered was developed using the PICOST (population, intervention, comparator, outcome, study design, time frame) format. The methodology used to identify the evidence was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA: http://www.prisma-statement.org). The approach used to evaluate the evidence was based on that proposed by the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) working group (https://gdt.gradepro.org/app/handbook/handbook.html). By using this approach for each of the predefined outcomes, the task force rated as high, moderate, low, or very low the certainty/confidence in the estimates of effect of an intervention or assessment across a body of evidence. Randomized controlled trials (RCTs) generally began the analysis as high-certainty evidence, and observational studies generally began the analysis as low-certainty evidence; examination of the evidence using the GRADE approach could result in downgrading or upgrading the certainty of evidence. For additional information, refer to this supplement's "Evidence Evaluation Process and Management of Potential Conflicts of Interest" section.[11,11a] Disclosure information for writing group members is listed in Appendix 1. Disclosure information for peer reviewers is listed in Appendix 2.

Draft 2020 CoSTRs for NLS were posted on the ILCOR website (www.ilcor.org) for public comment between January 15, 2019, and February 20, 2020, with comments accepted through March 4 for the last NLS CoSTR posted. All of the NLS draft CoSTRs were viewed a total of 45 032 times, with 279 comments posted. When online viewing statistics were available for individual CoSTRs, these are included in the topic information.

This summary statement contains the final wording of the CoSTRs as approved by the ILCOR task forces and by the ILCOR member councils after review and consideration of comments posted online in response to the draft CoSTRs. Within this manuscript, each topic includes the PICOST as well as the CoSTR, an expanded "Justification and Evidence-to-Decision Framework Highlights" section, and a list of knowledge gaps requiring future research studies. In Appendix A in the Supplemental Materials, an evidence-to-decision table is included for each CoSTR and is based on a new SysRev.

The second type of evidence evaluation performed to support this 2020 CoSTR for NLS is the ScopRev. ScopRevs are designed to identify the extent, range, and nature of evidence on a topic or a question, and they were performed by topic experts in consultation with the NLS Task Force. The task force analyzed the identified evidence and determined its value and implications for resuscitation practice or research. The rationale for the ScopRev, the summary of evidence, and task force insights are all highlighted in the body of this manuscript. The most recent treatment recommendations are included. The NLS Task Force notes whether the ScopRev identified substantive evidence suggesting the need for a future SysRev to support the development of an updated CoSTR. Meanwhile, the current treatment recommendation is reiterated. All ScopRevs are included in their entirety in Appendix B in the Supplemental Materials.

The third type of evidence evaluation supporting this 2020 CoSTR for NLS is an EvUp. EvUps are generally performed to identify new studies published after the most recent NLS evidence evaluation, typically through use of similar search terms and methodologies used in previous reviews. These EvUps were performed by task force members, collaborating experts, or members of ILCOR member resuscitation council writing groups. The EvUps are cited in the body of this document with a note as to whether the evidence identified suggested the need to consider a SysRev; the existing ILCOR treatment recommendation is reiterated. In this document, no change in ILCOR treatment recommendations resulted from an EvUp. If substantial new evidence was identified, the task force recommended consideration of a SysRev. All draft EvUps are included in Appendix C in the Supplemental Materials.

GENERATION OF TOPICS

After publication of the *2015 International Consensus on CPR and ECC Science With Treatment Recommendations*,[1,9,10] the NLS Task Force, together with additional neonatal resuscitation content experts (approximately 50 neonatal medicine and nursing professionals, from 17 countries, with expertise in neonatal resuscitation research, education, and implementation), reviewed the list of prior neonatal resuscitation clinical questions to divide them into 3 categories: those that could be retired, those that remained relevant but required additional clinical studies to better address the PICOST question, and those with sufficient evidence to justify a SysRev in the near future. New questions were also proposed and categorized. The list was posted for public comment in June 2017, and as a result, some amendments were made. Using the new ILCOR process of continuous evidence evaluation (see "Evidence Evaluation Process and Management

of Potential Conflicts of Interest"[11] in this supplement), the active questions were prioritized for SysRevs as ILCOR resources became available. Other topics were slated for ScopRevs or EvUps as noted above. The task force met via webinar at least monthly and in person annually; in addition, the task force met with the larger content expert group semiannually to present the science and debate and discuss treatment recommendations. The task force and larger group of content experts identified and reviewed the published literature and reached consensus to review the topics included in this manuscript.

2020 TOPICS REVIEWED

Anticipation and Preparation
- Prediction of need of respiratory support in the delivery room (NLS 611: EvUp)
- Effect of briefing/debriefing following neonatal resuscitation (NLS 1562: ScopRev)

Initial Assessment and Intervention
- Warming adjuncts (NLS 599: EvUp)
- Suctioning of clear fluid (NLS 596: ScopRev)
- Tracheal intubation and suction of nonvigorous meconium-stained newborns (NLS 865: SysRev)

Physiological Monitoring and Feedback Devices
- Heart rate monitoring during neonatal resuscitation (NLS 898: EvUp)

Ventilation and Oxygenation
- Sustained inflation (NLS 809: SysRev)
- Positive end-expiratory pressure (PEEP) versus no PEEP (NLS 897: EvUp)
- Continuous positive airway pressure (CPAP) versus intermittent PPV (NLS 590: EvUp)
- T-piece resuscitator versus self-inflating bag for ventilation (NLS 870: ScopRev)
- Oxygen for preterm resuscitation (NLS 864: 2019 CoSTR publication)
- Oxygen for term resuscitation (NLS 1554: 2019 CoSTR publication)

Circulatory Support
- CPR ratios for neonatal resuscitation (NLS 895: EvUp)
- 2-thumb versus 2-finger compressions for neonatal resuscitation (NLS 605: EvUp)

Drug and Fluid Administration
- Epinephrine (adrenaline) for neonatal resuscitation (NLS 593: SysRev)
- Intraosseous versus umbilical vein for emergency access (NLS 616: SysRev)
- Volume infusion during neonatal resuscitation (NLS 598: EvUp)
- Sodium bicarbonate during neonatal resuscitation (NLS 606: EvUp)

Prognostication During CPR
- Impact of duration of intensive resuscitation (NLS 896: SysRev)

Postresuscitation Care
- Rewarming of hypothermic newborns (NLS 858: EvUp)
- Induced hypothermia in settings with limited resources (NLS 734: EvUp)
- Postresuscitation glucose management (NLS 607: EvUp)

ANTICIPATION AND PREPARATION

The keys to successful neonatal resuscitation include assessment of perinatal risk and a system to rapidly assemble team members with skills that are appropriate to the anticipated need for resuscitation on the basis of that risk. Other critical components of successful resuscitation include an organized resuscitation area that ensures immediate access to all needed supplies and equipment and the standardization of behavioral skills that foster optimal teamwork and communication.

Prediction of Need of Respiratory Support in the Delivery Room (NLS 611: EvUp)

One important aspect of anticipating risk (determining if operative delivery conferred increased risk of need for intubation) was reviewed by the NLS Task Force most recently in 2010.[12–14] In 2020, The NLS Task Force undertook an EvUp to identify additional evidence published after 2010 that warranted consideration of a new SysRev.

An EvUp (see Supplement Appendix C-1) did not identify any evidence that would suggest the need for a new SysRev or a change in the 2010 treatment recommendation.[12–14] Most of the new studies confirmed previously identified risk factors for the need for PPV in the delivery room.

Population, Prognostic Factors, Outcome

Population: Newborn infants who are to be delivered

Prognostic factors: Maternal, perinatal, or delivery risk factors beyond age of gestation

Outcome: Prediction of need for PPV in the delivery room/operating suite

Treatment Recommendation

These treatment recommendations (below) are unchanged from 2010.[12–14]

When an infant without antenatally identified risk factors is delivered at term by cesarean delivery under regional anesthesia, a provider capable of performing assisted ventilation should be present at the delivery. It is not necessary for a provider skilled in neonatal intubation to be present at that delivery.

Effect of Briefing/Debriefing Following Neonatal Resuscitation (NLS 1562: ScopRev)

Rationale for Review

Although a prior review examined the utility of debriefing after simulation training, the NLS Task Force chose this topic for ScopRev because there is emerging evidence in many fields that briefing before and debriefing after clinical events may lead to improvement in practice and outcomes. There was no previous NLS Task Force treatment recommendation on this application of briefing and debriefing.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Among healthcare professionals involved in the resuscitation or simulated resuscitation of a neonate
- Intervention: Does briefing/debriefing
- Comparator: In comparison with no briefing/debriefing
- Outcome: Improve outcomes for infants, families, or clinicians
- 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 eligible for inclusion; animal studies were excluded. Conference abstracts were included; unpublished studies (eg, trial protocols) were excluded.
- Time frame: All years and all languages were included if there was an English abstract.

Summary of Evidence

The ScopRev[14a] identified 1 RCT[15] and 3 observational studies of preintervention and postintervention design.[16–18] One study considered video debriefing,[16] 1 considered the use of a checklist combined with video debriefing,[18] and 1 considered the use of a checklist with a team prebrief/debrief as the key element in a quality improvement bundle.[17] The RCT determined whether there was benefit to rapid cycle deliberate practice compared with standard simulation debriefing.[15] This entire ScopRev[14a] can be found in Supplement Appendix B-1.

Task Force Insights

Because this is a new PICOST question for the NLS Task Force, the task force elected to perform a ScopRev to assess the extent and type of available studies. Although briefing and debriefing in resuscitation has been previously reviewed by the NLS Task Force[12–14] and the Education, Implementation, and Teams Task Force,[19,20] clinical outcomes specific to neonates or neonatal resuscitation were not included in those recommendations.

The evidence identified in this ScopRev is primarily from quality-improvement studies with preintervention and postintervention comparisons. There were no RCTs comparing briefing or debriefing with no briefing or no debriefing. In addition, many investigators studied briefing or debriefing in the context of bundles of interventions; these studies were not included in this evidence review because it was not possible to isolate the effects of briefing or debriefing alone on outcomes.

A small number of studies were identified that included adjuncts to briefing and debriefing (eg, the review of video recordings to assist debriefing, the use of checklists); these studies compared the use of adjuncts with no briefing or no debriefing. There is limited evidence that use of video-assisted debriefing may improve the process of care and adherence to resuscitation guidelines, but none of the included studies evaluated the effect on clinical outcomes. The use of checklists during briefings and debriefings may help improve team communication and process, but the evidence did not report changes in clinical outcomes, and the reported effects on the delivery of care were inconsistent.

We identified limited evidence that rapid-cycle deliberate practice may improve short term performance in a resuscitation simulation but not provider confidence in or retention of skills. These findings were similar to a recent SysRev completed by the ILCOR Education, Implementation, and Teams Task Force (see "Education, Implementation, and Teams: Spaced Versus Massed Learning," in this supplement [EIT 601: SysRev]), which included neonatal studies and also identified limited evidence that rapid-cycle deliberate practice may improve short-term performance in a resuscitation simulation but not provider confidence in or retention of skills.

We conclude that briefing or debriefing may improve short-term clinical and performance outcomes for infants and staff. The effects of briefing or debriefing on long-term clinical and performance outcomes are uncertain.

This scoping review did not identify sufficient evidence to prompt a SysRev.

Treatment Recommendation

There was no previous treatment recommendation on the topic.

INITIAL ASSESSMENT AND INTERVENTION

Warming Adjuncts (NLS 599: EvUp)

Maintenance of normal temperature is a key initial step in stabilization of the newborn at birth. There are multiple strategies to prevent hypothermia of the

newborn. The NLS Task Force published the most recent CoSTR summarizing the evidence supporting warming adjuncts in 2015.[1,9,10] In 2020, the NLS Task Force undertook an EvUp to identify any additional studies that would warrant consideration of a new SysRev.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Preterm neonates less than 32 weeks' gestational age who are under radiant warmers in the hospital delivery room
- Intervention: Increased room temperature, thermal mattress, or another warming adjunct
- Comparator: Compared with plastic wraps alone
- Outcome[21]:
  - Primary: Hypothermia (less than 36.0°C) on admission to neonatal intensive care unit (NICU)
  - Secondary:
    - Survival (critical)
    - Morbidities associated with hypothermia (important)
    - Hyperthermia and associated morbidities (important)

The EvUp (see Supplement Appendix C-2) identified 13 studies (5 SysRevs and 8 RCTs) supporting the 2015 CoSTR.[1,9,10] Although the 2015 treatment recommendations were limited to very preterm babies born at less than 33 weeks' gestational age, the recommendations remain relevant. The task force agreed to suggest the need for a SysRev on the topic of warming adjuncts in the near future. The task force also suggests division of the target populations to separately analyze effects and pertinent outcomes for term versus preterm infants.

Treatment Recommendation

These treatment recommendations (below) are unchanged from 2015.[1,9,10]

Among newborn preterm infants of less than 32 weeks' gestation under radiant warmers in the hospital delivery room, we suggest using a combination of interventions that may include environmental temperature 23°C to 25°C, warm blankets, plastic wrapping without drying, cap, and thermal mattress to reduce hypothermia (temperature less than 36.0°C) on admission to NICU (weak recommendation, very low-certainty evidence).

We suggest that hyperthermia (greater than 38.0°C) be avoided because it introduces potential associated risks (weak recommendation, very low-certainty evidence).

Suctioning of Clear Fluid (NLS 596: ScopRev)

Rationale for Review

Transition from an intrauterine (fetal) to an extrauterine (newborn) physiology involves the replacement of lung liquid in the airways with air. To support liquid clearance, oropharyngeal/nasopharyngeal suctioning at birth was traditionally used to remove oral and nasal secretions in vigorous infants at birth. The 2010 CoSTR for NLS suggested against this routine practice for the first time.[12–14] Similarly, the *2015 American Heart Association Guidelines Update for CPR and ECC* for neonatal resuscitation emphasized that "suctioning immediately after birth, whether with a bulb syringe or suction catheter, may be considered only if the airway appears obstructed or if PPV is required."[22] The balance of risks and benefits associated with routine suctioning remain controversial. Because this literature has not been systematically reviewed in over a decade, the task force agreed that a ScopRev would determine if there is sufficient evidence published after 2010 to warrant a new SysRev in the near future.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Newborns delivered through clear amniotic fluid
- Intervention: Immediate routine suctioning (oropharyngeal or nasopharyngeal)
- Comparator: No suctioning or wiping
- Outcome[21]:
  - Survival (critical)
  - Need for delivery room resuscitation and stabilization interventions (important)
  - Oxygen supplementation, use of PPV, intubation, CPR/medications, Apgar scores, time to reach heart rate greater than 100/min (important)
  - Complications following procedure (desaturation, delay in initiation of PPV, tissue injury, infection)
  - Respiratory complications (respiratory distress, tachypnea) (important)
  - Other inpatient morbidities (important)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted times series, controlled before-and-after studies, cohort studies) were eligible for inclusion
- Time frame: All years and languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. Literature search was updated to November 30, 2019.

Summary of Evidence

Evidence supporting potential benefits of oropharyngeal/nasopharyngeal suctioning is limited and the practice remains controversial. Oropharyngeal suctioning does not impact liquid removal from the lung. The procedure can have serious side effects.

- It is possible that nasopharyngeal suctioning may result in vagal-induced bradycardia as well as increased risk of infection.[23]
- The procedure may take significant time to complete.[24]

- Suctioning may delay initiation of ventilation in nonbreathing infants.[3]
- Newborns who received suctioning compared with a control group had significantly lower oxygen saturation through the first 6 minutes of life and took longer to reach a normal saturation range.[24,25]
- There is a concern that suctioning may have serious additional consequences, such as irritation to mucous membranes and increased risk of iatrogenic infection,[26,27] bradycardia,[26,28] apnea,[28] hypoxemia and arterial oxygen desaturation,[25,27,29] hypercapnia,[30] impaired cerebral blood flow regulation,[31,32] increased intracranial pressure,[33] and development of subsequent neonatal brain injury.[34]

The entire ScopRev can be found in Supplement Appendix B-2.

Task Force Insights

The NLS Task Force noted several strengths and limitations of the evidence identified by the ScopRev:

- The identified studies were from diverse geographical areas, but the results were similar.
- The literature identified by this ScopRev allowed comparisons in 2 types of subgroups (vaginal versus cesarean delivery and preterm versus term infants).
- Most new studies appear to be consistent with the current recommendation of "no routine suctioning" of the newborns in the delivery room.
- Because of the large number of patients (greater than 1500) reported in studies published since 2015, a new SysRev including these patients is likely to increase the certainty of the evidence through GRADE evaluation.

The NLS Task Force suggests consideration of an updated SysRev for this PICO question: "Among vigorous infants delivered through clear amniotic fluid (P), does immediate routine suctioning (oropharyngeal or nasopharyngeal) (I) compared with no suctioning or wiping C) change outcome (O)?" Until such a SysRev is completed and analyzed, the current 2010 treatment recommendation remains.[12–14]

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[12–14]

Routine intrapartum oropharyngeal and nasopharyngeal suctioning for newborn infants with clear or meconium-stained amniotic fluid is no longer recommended.

Tracheal Intubation and Suction of Nonvigorous Meconium-Stained Newborns (NLS 865: SysRev)

Meconium-stained amniotic fluid is present in 5% to 15% of all deliveries and is more common in neonates who are nonvigorous at birth.[35,36] Approximately 3% to 5% of neonates born through meconium-stained amniotic fluid develop meconium aspiration syndrome (MAS), which remains a significant cause of neonatal morbidity and mortality, particularly in developing countries.[37] Optimal management of neonates born through meconium-stained amniotic fluid remains a topic of debate. For decades, routine intubation and endotracheal suctioning for nonvigorous, meconium-exposed neonates was suggested on the basis of extremely low-certainty evidence. In 2015, after publication and analysis of new (although limited) randomized trial data, the NLS Task Force changed the treatment recommendation to eliminate routine tracheal intubation and suctioning for nonvigorous meconium-stained infants.[1,9,10]

Additional studies have been published since 2015, prompting the NLS Task Force to complete a new SysRev with meta-analysis.[37]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Nonvigorous infants born at 34 weeks' or greater gestation delivered through meconium-stained amniotic fluid (of any consistency) at the start of resuscitation (nonvigorous defined as heart rate less than 100/min, decreased muscle tone, and/or depressed breathing at delivery)
- Intervention: Immediate laryngoscopy with or without intubation and suctioning
- Comparator: Immediate resuscitation without direct laryngoscopy at the start of resuscitation
- Outcome[21]:
  - Primary
    - Survival to hospital discharge (critical)
  - Secondary
    - Neurodevelopmental impairment (critical)
    - MAS (critical)
    - Other respiratory outcomes (continuous positive airway pressure or mechanical ventilation, treatment of pulmonary hypertension with inhaled nitric oxide, oral medications or extracorporeal membrane oxygenation) (important)
    - Delivery room interventions (CPR/medications, intubation for PPV) (important)
    - Length of hospitalization (important)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, and cohort studies) were included in the review.
- Time frame: All years and languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) and animal studies were excluded. The literature search was updated to May 2019.

A Priori Subgroups to Be Examined

Consistency of meconium (thin versus thick), gestational age categories (late preterm [34 weeks to 36 weeks and 6 days], term [37 weeks to 41 weeks and 6 days], postterm [42 weeks or greater]), presence or absence

of fetal bradycardia, route of delivery (spontaneous vaginal, instrumented vaginal, cesarean delivery), direct laryngoscopy with versus without suctioning.

International Prospective Register of Systematic Reviews (PROSPERO) Registration: CRD42019122778

Consensus on Science

The SysRev identified 4 eligible studies that included 680 newborn infants.[37] Data from 3 RCTs involving 449 newborns[38–40] and 1 observational study involving 231 newborn infants[41] were included.

A draft CoSTR document based on the SysRev was posted on the ilcor.org website for a 2-week public commenting period. During this period, the draft CoSTR was viewed over 5600 times and 65 comments were provided; most comments were very positive. However, there were concerns about clarity, which the task force subsequently addressed. Suggestions made were used to modify the wording of the treatment recommendations, justification and evidence-to-decision framework highlights, and the knowledge gaps to improve clarity. Although these treatment recommendations do not preclude the use of carefully considered clinical judgment for individual cases, the NLS Task Force cannot use unpublished, personal observations to inform an international consensus on science or to guide treatment recommendations.

For the critical primary outcome of survival to discharge, we identified low-certainty evidence (downgraded for inconsistency and imprecision) from 3 RCTs[38–40] involving 449 nonvigorous newborns delivered through meconium-stained amniotic fluid which showed no benefit from the use of immediate laryngoscopy with or without tracheal suctioning when compared with immediate resuscitation without laryngoscopy (relative risk [RR], 0.99; 95% CI, 0.93–1.06; *P*=0.87); absolute risk reduction, –0.9%; (95% CI, –6.4% to 5.5%), or 9 fewer patients/1000 survived to discharge with the intervention (95% CI, 64 fewer to 55 more patients per 1000 survived to discharge with the intervention). For complete data, see Table 1.

For the remainder of the outcomes of interest (eg, neurodevelopmental impairment (NDI), hypoxic-ischemic encephalopathy (HIE), MAS, use of mechanical ventilation, use of respiratory support excluding mechanical ventilation, endotracheal intubation for PPV in the delivery room, chest compressions in the delivery room, use of epinephrine in the delivery room, treatment of pulmonary hypertension, and length of hospitalization), evidence of very low certainty (downgraded for risk of bias, indirectness, and imprecision) showed no benefit from the use of immediate laryngoscopy with or without tracheal suctioning compared with immediate resuscitation without laryngoscopy for nonvigorous newborns delivered through meconium-stained amniotic fluid (Table 1). The neurodevelopmental assessment from the single study that reported this outcome was performed at an early and nonstandard time, hence the results are poorly predictive of longer-term outcomes. Therefore, the task force concluded that the effect on NDI of immediate laryngoscopy with or without suctioning remains uncertain.

In 2015, the treatment recommendation indicated that there was insufficient human evidence to continue to suggest routine suctioning of meconium in nonvigorous babies born through meconium-stained amniotic fluid.[1,9,10] This new 2020 recommendation is more direct in its suggestion against this practice.

Treatment Recommendations

For nonvigorous newborn infants delivered through meconium-stained amniotic fluid, we suggest against routine immediate direct laryngoscopy with or without tracheal suctioning compared with immediate resuscitation without direct laryngoscopy (weak recommendation, low-certainty evidence).

Meconium-stained amniotic fluid remains a significant risk factor for receiving advanced resuscitation in the delivery room. Rarely, an infant may require intubation and tracheal suctioning to relieve airway obstruction.

Justification and Evidence-to-Decision Framework Highlights

The task force recognizes that, although the direction of the treatment recommendation has not changed, several studies published after 2015 provide additional evidence to support the recommendation. These studies contributed new evidence, but the certainty of the findings remains low or very low because it is difficult to perform unbiased studies of this clinical question. Finally, even combining the data from all studies does not provide sufficient power for certainty as the optimal information size is still not achieved.

The NLS Task Force considered that the procedure of laryngoscopy and suctioning with or without tracheal intubation is invasive and has potential to harm, particularly if initiation of ventilation is delayed. This, together with the evidence of no benefit of routine tracheal suctioning, led the task force to suggest against routine practice of these interventions. It is possible that the infant born through meconium-stained fluid will require intubation for resuscitation. Therefore, trained personnel and equipment for intubation should be readily available for births where meconium-stained amniotic fluid is present. If meconium is obstructing the trachea, suctioning by using an endotracheal tube with a meconium aspirator may be effective in relieving the obstruction.[42,43]

See Supplement Appendix A-1 for the evidence-to-decision table for this SysRev.

Table 1. Meta-analysis of RCTs of Immediate Laryngoscopy With or Without Tracheal Suctioning Versus Immediate Resuscitation Without Laryngoscopy for Nonvigorous Infants Born at 34 Weeks' or Greater Gestation and Delivered Through Meconium-Stained Amniotic Fluid

Outcome	Article With Outcome of Interest	Total, n	Certainty of Evidence	RR (95% CI); I^2	Absolute Difference (95% CI)
Survival at discharge	Chettri, 2015[38]; Nangia, 2016[39]; Singh, 2018[40]	449	Low	0.99 (0.93–1.06); 29%	9/1000 fewer survived to discharge when laryngoscopy ± suction was used (64 fewer to 55 more per 1000)
Cognitive NDI	Chettri, 2015[38]	86	Very low	0.75 (0.37–1.50); NA	80/1000 fewer with cognitive NDI when laryngoscopy ± suction was used (200 fewer to 159 more per 1000)
Motor NDI	Chettri, 2015[38]	86	Very low	0.91 (0.49–1.67); NA	31/1000 fewer with motor NDI when laryngoscopy ± suction was used (174 fewer to 228 more per 1000)
HIE	Nangia, 2016[39]; Singh, 2018[40]	327	Very low	0.85 (0.56–1.30); 0%	52/1000 fewer with HIE when laryngoscopy ± suction was used (152 fewer to 104 more per 1000)
MAS	Chettri, 2015[38]; Nangia, 2016[39]; Singh, 2018[40]	449	Very low	0.94 (0.67–1.33); 49%	23/1000 fewer with MAS when laryngoscopy ± suction was used (126 fewer to 126 more per 1000)
Use of mechanical ventilation	Chettri, 2015[38]; Nangia, 2016[39]; Singh, 2018[40]	449	Very low	1.00 (0.66–1.53); 0%	0/1000 fewer were mechanically ventilated when laryngoscopy ± suction was used (54 fewer to 84 more per 1000)
Use of respiratory support excluding mechanical ventilation	Nangia 2016[39]; Singh 2018[40]	327	Very low	0.99 (0.81–1.20); 0%	4/1000 fewer received respiratory support excluding mechanical ventilation when laryngoscopy ± suction was used (73 fewer to 76 more per 1000)
Endotracheal intubation for PPV in the DR	Chettri, 2015[38]; Nangia, 2016[39]	297	Very low	1.15 (0.83–1.59); 0%	41/1000 more were intubated for PPV in the DR when laryngoscopy ± suction was used (47 fewer to 162 more per 1000)
Chest compressions in the DR	Chettri, 2015[38]; Nangia, 2016[39]; Singh, 2018[40]	449	Very low	1.13 (0.40–3.20); 0%	4/1000 more received chest compressions in the DR when laryngoscopy ± suction was used (19 fewer to 68 more per 1000)
Epinephrine in the DR	Chettri, 2015[38]; Nangia, 2016[39]; Singh, 2018[40]	449	Very low	1.62 (0.37–7.05); 0%	8/1000 more received epinephrine in the DR when laryngoscopy ± suction was used (from 8 fewer to 80 more per 1000)
Treatment of pulmonary hypertension (iNO, medications, ECMO)	Chiruvolu, 2018[41]	231	Very low	0.52 (0.15–1.79); NA	29/1000 fewer received treatment of pulmonary hypertension when laryngoscopy ± suction was used (50 fewer to 47 more per 1000)
Length of hospitalization, days	Nangia, 2016[39]; Singh, 2018[40]	327	Very low	–0.5 days (–1.76 to 0.75); 80%	

DR indicates delivery room; ECMO, extracorporeal membrane oxygenation; HIE, hypoxic-ischemic encephalopathy; iNO, inhaled nitric oxide; MAS, meconium aspiration syndrome; NA, not applicable; NDI, neurodevelopmental impairment; PPV, positive-pressure ventilation; RCT, randomized controlled trial; and RR, relative risk.

Knowledge Gaps

Priorities for research include the following:

- Additional RCTs are needed that focus on nonvigorous infants in a variety of populations, such as where the incidence of MAS is low, and in settings with various levels of healthcare resources.
- Do risks or benefits of intubation with tracheal suctioning vary with any subgroup (gestational age, thickness of meconium, operator experience)?
- Long-term outcomes are needed in future studies. These include neurodevelopmental, behavioral, or educational assessment, which for future studies should be at or beyond 18 months of age and completed with a validated tool.

PHYSIOLOGICAL MONITORING AND FEEDBACK DEVICES

Heart Rate Monitoring During Neonatal Resuscitation (NLS 898: EvUp)

After birth, the newborn's heart rate is used to assess the effectiveness of spontaneous breathing and the need for interventions such as PPV, and it's used as the marker

of response to resuscitation interventions. Therefore, a rapid and reliable method of measuring the newborn's heart rate is a critical adjunct for neonatal resuscitation. The most recent review of this topic was included in the 2015 CoSTR for NLS.[1,9,10] The NLS Task Force undertook an EvUp to identify additional evidence published after 2015 that would warrant consideration of a new SysRev.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Newborns requiring resuscitation
- Intervention: ECG monitoring
- Comparator: Oximetry or auscultation
- Outcome: Measurement of heart rate (speed and reliability) (important)[21]

The EvUp (Supplement Appendix C-3) identified 7 additional studies published after the 2015 CoSTR SysRev,[1,9,10] including 2 SysRevs,[44,45]2 RCTs,[46,47] and 3 observational studies.[48–50] All 7 studies supported the 2015 treatment recommendation.[1,9,10] Thus, the NLS Task Force agreed that no new ILCOR SysRev is warranted at this time, and the current recommendation continues.

Of note, there is a need to develop an additional interventional PICOST to determine if routine use of ECG monitoring during neonatal resuscitation improves clinical outcomes. Also, improved tools and methods to enable detection and measurement of heart rate have been reported in the literature or are under development; as a result, the current PICOST question may be too limited in scope. Such methods include new heart rate monitors, digital stethoscopes, photoplethysmography methods in addition to pulse oximetry, and Doppler ultrasonography methods with auditory or visual displays. New interfaces for ECG monitoring include dry electrode technology. Future SysRevs will need to compare these technologies to the current "gold standard" of ECG monitoring with gel electrodes. Until such evidence is available, the NLS Task Force agreed that there is no justification to seek a new SysRev or alter the current (2015) treatment recommendations.

Treatment Recommendation

This recommendation (below) has not changed from 2015.[1,9,10]

In babies requiring resuscitation, we suggest the ECG can be used to provide a rapid and accurate estimation of heart rate (weak recommendation, very low-certainty evidence).

VENTILATION AND OXYGENATION

Sustained Inflation (NRP 809: SysRev)

When a newborn does not breathe spontaneously, establishing functional residual capacity requires clearing the lung fluid and replacing it with air. Debate continues about the most effective method to achieve this. Animal studies suggest that a longer sustained inflation may be beneficial for short term respiratory outcomes, but most such studies were performed in intubated animal models.[51] It is unknown whether the same is true in newborn infants.[52,53] In 2015, the NLS Task Force evaluated the evidence supporting use of sustained inflation for initiation of PPV in the delivery room and suggested against its routine use.[1,9,10] Multiple clinical trials of sustained inflation have been published after that 2015 recommendation, prompting the NLS Task Force to request a 2020 SysRev.[53a]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Newborn infants who receive PPV due to bradycardia or ineffective respirations at birth
- Intervention: Initiation of PPV with sustained inflation(s) more than 1 second
- Comparator: Initiation of PPV with intermittent inflations, lasting 1 second or less per breath
- Outcome[21]:
  - Primary: Death before discharge (critical)
  - Secondary:
    - Death in the delivery room (critical)
    - Death within first 48 hours (critical)
    - Need for mechanical ventilation during hospitalization (critical)
    - Air leaks (pneumothorax, pneumomediastinum, pneumopericardium, pulmonary interstitial emphysema) reported individually or as a composite outcome at any time during initial hospitalization and also within first 48 hours (critical)
    - Bronchopulmonary dysplasia, any grade,[54] defined as need for supplemental oxygen at 28 days of life; need for supplemental oxygen at 36 weeks' gestational age for infants born at or before 32 weeks of gestation (critical)
    - Intraventricular hemorrhage: Of any grade[55] and Grade 3 or above (critical)
    - Retinopathy of prematurity: Of any stage[56] and Stage 3 or above (critical)
    - Death by time of latest follow-up (critical)
    - Long-term neurodevelopmental or behavioral or education outcomes (greater than18 months of corrected age; test used to assess neurodevelopmental outcome should be of adequate quality and validated) (critical)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion.
- Time frame: All years and languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. Literature search was updated to October 25, 2019.

PROSPERO Registration: CRD 42020155639

A Priori Subgroup Analyses

Preterm infants at 28+0 weeks or less, 28 weeks and 1 day to 31 weeks and 6 days, 32 weeks to 36 weeks and 6 days, 37 weeks or more (term)

Duration of first sustained inflation: 1 to 5 seconds, 6 to 15 seconds, greater than 15 seconds

Inflation pressure used during first sustained inflation: 20 cm H_2O or less, greater than 20 cm H_2O

Interface or device used to generate sustained inflation: Nasopharyngeal tube, endotracheal tube, face mask, or T-piece device versus other device

A Priori Sensitivity Analyses

Effects of whether or not studies allowed multiple sustained inflations

Effects of the methodological quality of trials (to ascertain whether studies with high risk of bias overestimated treatment effects)

Consensus on Science

The SysRev identified 10 eligible RCTs including 1502 newborn infants. From analysis of this evidence, the NLS Task Force developed a draft CoSTR that was posted on the ILCOR website for a 2-week public commenting period beginning February 17, 2020. The Justification section was revised to address the public comments.

For the primary outcome of death before discharge, evidence of low certainty (downgraded for risk of bias and inconsistency) from 10 RCTs[57–66] enrolling 1502 preterm newborns who received PPV for bradycardia or ineffective respirations at birth showed no significant benefit or harm from initiating PPV with sustained inflation greater than 1 second compared with initiating PPV with intermittent inflations lasting 1 second or less. See Table 2.

For the secondary critical long-term neurodevelopmental outcomes and death at latest follow-up, no studies were identified. The remainder of the secondary outcomes are reported in Table 2.

Subgroup Analysis for Primary Outcome

Subgroup Newborns Less Than 28+0 Weeks. For the critical outcome of death before discharge, low-certainty evidence (downgraded for risk of bias and imprecision) from 5 RCTs[57,58,61,62,65] enrolling 862 preterm newborns who received PPV for bradycardia or ineffective respirations at birth showed evidence of potential harm from initiating PPV with sustained inflation(s) greater than 1 second compared with initiating PPV with intermittent inflations lasting 1 second or less per breath (RR, 1.38; 95% CI, 1.00–1.91; I^2, 0%; 46 more patients/1000 died before hospital discharge with sustained inflation(s) [0 fewer to 110 more per 1000]). The number needed to harm is 22 (95% CI, 9–1000 or greater).

Subgroup Newborns 28+1 Weeks to 31+6 Weeks of Age. For the critical outcome of death before discharge, very low-certainty evidence (downgraded for risk of bias and very serious imprecision) from 4 RCTs[57,61,62,66] enrolling 175 preterm newborns who received PPV for bradycardia or ineffective respirations at birth showed no significant benefit or harm from initiating PPV with sustained inflation(s) greater than 1 second when compared with initiating PPV with intermittent inflations lasting 1 second or less per breath (RR, 1.33; 95% CI, 0.22–8.20; I^2, 5%; 4 more patients/1000 died before hospital discharge with sustained inflation(s) [9 fewer to 86 more per 1000]).

Subgroup Newborns 32+0 to 36+6 Weeks. No published data for this gestational age group were available.

Subgroup Newborns 37+0 Weeks or More (Term). No published data for this gestational age group were available.

Subgroup Analyses: by Duration of First Sustained Inflation or Inflation Pressure of the Sustained Inflation. For the critical outcome of death before discharge, subgroup analyses were conducted for the duration of the first sustained inflation (6–15 seconds versus greater than 15 seconds) and for the inspiratory pressure of the first sustained inflation with inspiratory pressure greater than 20 mm Hg versus 20 mm Hg or less). For each of these subgroup analyses, the evidence was of very low certainty (downgraded for risk of bias in all cases and variously for imprecision, very serious imprecision, and inconsistency). None of the subgroup analyses showed any significant benefit or harm of sustained inflation when compared with initiating PPV with intermittent inflations lasting 1 second or less per breath.

These conclusions were based on 9 RCTs[57–61,63–66] enrolling 1300 preterm newborns (sustained inflation 6–15 seconds), 2 RCTs[62,64] enrolling 222 preterm newborns (sustained inflation of greater than 15 seconds), 6 RCTs[58–62,66] enrolling 803 preterm newborns (inspiratory pressure greater than 20 mm Hg), and 4 RCTs[57,63–65] enrolling 699 preterm newborns (inspiratory pressure 20 mm Hg or less).

Sensitivity Analysis for Primary Outcome

Excluding Studies With High Risk of Bias. For the critical outcome of death before discharge, low-certainty evidence (downgraded for risk of bias and imprecision) from 9 RCTs[57–62,64–66] enrolling 1390 preterm newborns who received PPV for bradycardia or ineffective respirations at birth showed no significant benefit or harm from initiating PPV with sustained inflation(s) greater than 1 second compared with initiating PPV with intermittent inflations lasting 1 second or less per breath. (RR, 1.24; 95% CI, 0.92–1.68; I^2, 24%; 21 more patients/1000 died before hospital discharge with sustained inflation(s) [95% CI, 7 fewer to 61 more per 1000]).

Table 2. Meta-analysis of RCTs Comparing Initiation of PPV With Sustained Inflation(s) Greater Than 1 Second Versus Initiation of PPV With Intermittent Inflations, Last 1 Second or Less per Breath

Outcome	Article With Outcome of Interest	Total, n	Certainty of Evidence	RR (95% CI); I^2	Absolute Difference (95% CI)
Death before discharge	Lindner, 2005[57]; Lista, 2015[58]; Schwaberger, 2015[59]; Mercadante, 2016[60]; Jiravisitkul, 2017[61]; Ngan, 2017[62]; El-Chimi, 2017[63]; El-Fattah, 2017[64]; Kirpalani, 2019[65]; La Verde, 2019[66]	1502	Low	1.09 (0.83–1.43); 42%	10/1000 more patients died before discharge when PPV was initiated with sustained inflation(s) >1 s compared with initiating PPV with intermittent inflations lasting ≤1 s per breath (18 fewer to 47 more per 1000)
Death in the DR	Linder, 2005[57]; Lista, 2015[58]; Schwaberger, 2015[59]; Mercadante, 2016[60]; Jiravisitkul, 2017[61]; Ngan, 2017[62]; El-Chimi, 2017[63]; El-Fattah, 2017[64]; LaVerde, 2019[66]	1076	Very low	2.82 (0.45–17.66); 0%	4/1000 more patients died in the DR when PPV was initiated with sustained inflation(s) >1 s compared with initiating PPV with intermittent inflations lasting ≤1 s per breath (1 fewer to 33 more per 1000)
Death within 48 h	Linder, 2005[57]; Lista, 2015[58]; Schwaberger, 2015[59]; Mercadante, 2016[60]; Jiravisitkul, 2017[61]; Ngan, 2017[62]; El-Chimi, 2017[63]; El-Fattah, 2017[64]; Kirpalani, 2019[65]; La Verde, 2019[66]	1502	Low	2.42 (1.15–5.09); 8%	18/1000 more patients died within 48 h after birth when PPV was initiated with sustained inflation(s) >1 s compared with initiating PPV with intermittent inflations lasting ≤1 s per breath (2 more to 51 more per 1000). The number needed to harm is 55 (95% CI, 20–500).
Bronchopulmonary dysplasia	Linder, 2005[57]; Lista, 2015[58]; Schwaberger, 2015[59]; Mercadante, 2016[60]; Jiravisitkul, 2017[61]; Ngan, 2017[62]; El-Chimi, 2017[63]; El-Fattah, 2017[64]; Kirpalani, 2019[65]; La Verde, 2019[66]	1502	Low	0.93 (0.79–1.10); 8%	19/1000 fewer patients developed bronchopulmonary dysplasia when PPV was initiated with sustained inflation(s) >1 s compared with initiating PPV with intermittent inflations lasting ≤1 s per breath (58 fewer to 27 more per 1000)
Intraventricular hemorrhage Grade 3 or 4	Linder, 2005[57]; Lista, 2015[58]; Schwaberger, 2015[59]; Mercadante, 2016[60]; Jiravisitkul, 2017[61]; Ngan, 2017[62]; El-Fattah, 2017[64]; Kirpalani, 2019[65]; La Verde, 2019[66]	1390	Low	0.88 (0.63–1.23); 0%	11/1000 fewer developed intraventricular hemorrhage Grade 3 or 4 when PPV was initiated with sustained inflation(s) >1 s compared with initiating PPV with intermittent inflations lasting ≤1 s per breath (35 fewer to 22 more per 1000)
Retinopathy of prematurity Stage 3 or higher	Linder, 2005[57]; Lista, 2015[58]; Schwaberger, 2015[59]; Mercadante, 2016[60]; Jiravisitkul, 2017[61]; Ngan, 2017[62]; El-Fattah, 2017[64]; Kirpalani, 2019[65]; La Verde, 2019[66]	1342	Low	0.83 (0.62–1.11); 19%	22/1000 fewer patients developed retinopathy of prematurity Stage 3 or higher when PPV was initiated with sustained inflation(s) >1 s compared with initiating PPV with intermittent inflations lasting ≤1 s per breath (49 fewer to 14 more per 1000)
Use of mechanical ventilation during hospitalization	Lista, 2015[58]; Mercadante, 2016[60]; Jiravisitkul, 2017[61]; El-Chimi, 2017[63]; El-Fattah, 2017[64]; La Verde, 2019[66]	813	Low	0.87 (0.74–1.02); 0%	51/1000 fewer patients received mechanical ventilation during their hospitalization when PPV was initiated with sustained inflation(s) >1 s compared with initiating PPV with intermittent inflations lasting ≤1 s per breath (103 fewer to 8 more per 1000)

(*Continued*)

Table 2. Continued

Outcome	Article With Outcome of Interest	Total, n	Certainty of Evidence	RR (95% CI); I^2	Absolute Difference (95% CI)
Airleak during hospitalization	Linder, 2005[57]; Lista, 2015[58]; Schwaberger, 2015[59]; Mercadante, 2016[60]; Jiravisitkul, 2017[61]; Ngan, 2017[62]; El-Chimni, 2017[63]; El-Fattah, 2017[64]; La Verde, 2019[66]	1076	Low	1.26 (0.72–2.21); 17%	9/1000 more patients developed airleak during their hospitalization when PPV was initiated with sustained inflation(s) >1 s compared with initiating PPV with intermittent inflations lasting ≤1 s per breath (9 fewer to 41 more per 1000)

DR indicates delivery room; PPV, positive-pressure ventilation; RCT, randomized controlled trial; and RR, relative risk.

Excluding Studies That Allowed Only a Single Sustained Inflation During Resuscitation. For the critical outcome of death before discharge, low-certainty evidence (downgraded for risk of bias and imprecision) from 9 RCTs[57–63,65,66] enrolling 1402 preterm newborns who received PPV for bradycardia or ineffective respirations at birth showed no significant benefit or harm from initiating PPV with sustained inflation greater than 1 second compared with initiating PPV with intermittent inflations lasting 1 second or less per breath (RR, 1.17; 95% CI, 0.88–1.55; I^2, 22%; 18 more patients/1000 died before hospital discharge with sustained inflation(s) [95% CI, 13 fewer to 58 more per 1000]).

Sustained Inflation With Mask Only. When considering only studies where a face mask was used to deliver initial sustained inflation, for the critical outcome of death before discharge, low-certainty evidence (downgraded for risk of bias and imprecision from 9 RCTs[58–66] enrolling 1441 preterm newborns who received PPV for bradycardia or ineffective respirations at birth showed no significant benefit or harm from initiating PPV with sustained inflation(s) greater than 1 second compared with initiating PPV with intermittent inflations lasting 1 second or less per breath (RR, 1.06; 95% CI, 0.61–1.39; I^2, 42%; 7 more patients/1000 died before hospital discharge with sustained inflations [95% CI, 44 fewer to 44 more per 1000]).

Treatment Recommendations

For preterm newborn infants who receive PPV for bradycardia or ineffective respirations at birth, we suggest against the routine use of initial sustained inflation(s) greater than 5 seconds (weak recommendation, low-certainty evidence). A sustained inflation may be considered in research settings.

For term or late preterm infants who receive PPV for bradycardia or ineffective respirations at birth, it is not possible to recommend any specific duration for initial inflations due to the very low confidence in effect estimates.

Justification and Evidence-to-Decision Framework Highlights

This topic was prioritized by the NLS Task Force after completion of a large RCT[65] published after the 2015 CoSTR.[1,9,10] In making these recommendations, the NLS Task Force considered the potential for increased death within 48 hours in preterm infants and increased death before discharge in preterm infants less than 28+0 weeks, a predefined subgroup of the systematic review.[53a] The task force recognizes that the outcome of death within 48 hours was influenced primarily by 1 study for which death within 48 hours was one of multiple secondary outcomes.[65] The NLS Task Force also considered the absence of evidence for either benefit or harm after sustained inflation at birth for all other critical and important outcomes.

The study comparisons were compromised by methodological heterogeneity across studies, including indication, duration, the use of different inspiratory pressures during sustained inflation and different inflation durations. No study was identified comparing short duration sustained inflation (less than 5 seconds) with intermittent inflations by using inspiratory time of 1 second or less. There is no new evidence to support or refute the practice of inflations less than 5 seconds immediately after birth. Hunt et al[67] was excluded from this systematic review because the control group received short duration sustained inflations (5 inflations of 2–3 seconds each) and the intervention group received sustained inflations of 15 seconds duration (and thus did not meet predefined inflation duration criteria for the comparator group).

A patent airway is necessary for effective lung inflation or ventilation. A recent study demonstrated that preterm rabbit pups are prone to closure of the larynx (ie, it opens only briefly during a spontaneous breath); this impedes noninvasive PPV after birth.[53] Studies in preterm infants have shown that very little gas enters the lungs in the absence of spontaneous breathing, suggesting that the same phenomenon occurs in preterm infants.[68,69] This SysRev[53a] (and most studies it identified) focused on use of sustained inflation in newborns who are not breathing effectively, so inadequate

laryngeal patency could explain the absence of benefit from sustained inflation immediately after birth in preterm infants. In addition, the NLS Task Force noted that the trials included in the systematic review were pragmatic in design and did not include respiratory function monitors to assess actual pressure and volume delivered or the actual duration of the sustained inflation. It remains unknown if mask leak or airway obstruction influenced the effectiveness of the sustained inflations. This further decreases the confidence in the effect estimates, especially for the subgroup analyses.

See Supplement Appendix A-2 for the evidence-to-decision table for this SysRev.

Knowledge Gaps

- How much of a role does glottis closure play in determining the effectiveness of sustained inflation in newborn infants of different gestational ages?
- What is the optimal duration, optimal inspiratory pressure, and number of sustained inflation maneuvers that allow establishment of functional residual capacity without barotrauma?
- The NLS Task Force recognizes that the total number of infants studied thus far is insufficient to have confidence in the estimate of effect. Larger multicenter trials are needed in both term and preterm newborns to determine whether there are benefits or harms from sustained inflations.
- Studies comparing short duration sustained inflation (less than 5 seconds) with intermittent inflations (inspiratory time 1 second or less) are needed. This is an important knowledge gap as the European Resuscitation Council currently recommends using inflations of a 2- to 3-second duration for the first 5 breaths in infants who are gasping or not breathing.
- Is there a role for sustained inflation for other situations in resuscitation, such as during cardiac compressions? (For more detail, see EvUp for NLS 895 CPR Ratios)

PEEP Versus No PEEP (NLS 897: EvUp)

During resuscitation after birth, PPV is provided to inflate and ventilate the lungs. The lungs of sick or preterm newborns tend to collapse as they are not supported by a stiff chest wall and the infant's breathing efforts may be weak; the lungs may also be immature and surfactant-deficient.[70] PEEP provides low positive pressure to the airway, which helps prevent lung collapse at the end of expiration. PEEP maintains lung volume during PPV in animal studies and improves lung function and oxygenation.[71,72] PEEP may be beneficial during neonatal resuscitation, but the evidence from human studies is limited. The previously reported evidence for use of PEEP was evaluated as part of the 2015 CoSTR for NLS.[1,9,10] In 2020, The NLS Task Force undertook an EvUp to determine whether additional evidence published after 2015 warranted consideration of a new SysRev.

The evidence update (see Supplement Appendix C-4) identified no evidence that would suggest the need for a new SysRev or a change in the 2015 treatment recommendation.[1,9,10] Most of the new studies identified confirm the 2015 recommendation for use of PEEP during PPV in the delivery room.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Preterm/term newborn infants who do not establish spontaneous respiration at birth
- Intervention: Use of PEEP as part of the initial ventilation strategy
- Comparator: No PEEP
- Outcome[21]:
  - Survival to discharge (critical)
  - 5-minute Apgar scores (important)
  - Time for heart rate to rise above 100/min (important)
  - Intubation rate in the delivery room (important)
  - Chest compressions in the delivery room (important)
  - Incidence of air leaks (important)
  - Oxygen saturation/oxygenation (important)
  - F_{IO_2} exposure in the delivery room (important)
  - Mechanical ventilation in the first 72 hours (important)
  - Bronchopulmonary dysplasia (any) (important)

Treatment Recommendation

This treatment recommendation has not changed from 2015.[1,9,10]

We suggest using PEEP for the initial ventilation of premature newborn infants during delivery room resuscitation (weak recommendation, low-quality evidence).

We cannot make any recommendation for term infants because of insufficient data.

CPAP Versus Intermittent Positive Pressure Ventilation (NLS 590: EvUp)

Newborn infants who breathe spontaneously need to establish a functional residual capacity after birth.[73] Some newborn infants experience respiratory distress, which manifests as labored breathing or persistent cyanosis. Continuous positive airway pressure (CPAP), a form of respiratory support, helps prevent atelectasis in newborns. CPAP is especially helpful for preterm newborn infants with breathing difficulty after birth or after resuscitation.[74] CPAP may also reduce the risk of death or bronchopulmonary dysplasia in very preterm infants when compared with endotracheal intubation and PPV.[75–79] For the newborn infant, CPAP is a less-invasive form of respiratory support than intubation and PPV.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Spontaneously breathing preterm newborn infants with respiratory distress requiring respiratory support in the delivery room
- Intervention: CPAP
- Comparator: Intubation and intermittent PPV
- Outcome[21]:
  - Death or bronchopulmonary dysplasia (critical)
  - Death (critical)
  - Bronchopulmonary dysplasia[54] (important)
  - Air leak (important)
  - Necrotizing enterocolitis (important)
  - Severe intraventricular hemorrhage[55] (critical)
  - Severe retinopathy of prematurity[56] (critical)

This topic was last reviewed in the 2015 CoSTR.[1,9,10] The NLS Task Force sought an EvUp to identify any studies published after the 2015 CoSTR. The EvUp did not identify any new studies that would potentially change the current recommendation. The 2015 CoSTR treatment recommendation remains in effect.[1,9,10]

The entire EvUp can be reviewed in Supplement Appendix C-5.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2010.[1,9,10]

For spontaneously breathing preterm newborn infants with respiratory distress requiring respiratory support in the delivery room, we suggest initial use of CPAP rather than intubation and intermittent PPV (weak recommendation, moderate certainty of evidence).

T-Piece Resuscitator Versus Self-Inflating Bag for Ventilation (NLS 870: ScopRev)

Rationale for Review

In 2015, the ILCOR Neonatal 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.[1,9,10] 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 NLS Task Force decided to reevaluate this topic through a ScopRev[79a] to determine whether sufficient new evidence had been published after the 2015 CoSTR[1,9,10] to justify a new SysRev.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Newborn infants receiving ventilation (PPV) during resuscitation
- Intervention: T-piece resuscitator
- Comparator: Self-inflating bag
- Outcome[21]:
  - Survival to hospital discharge (critical)
  - Air leak (important)
  - Development of stable spontaneous breathing (no need for intubation in delivery room) (important)
  - Bronchopulmonary dysplasia (any) (important)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion.
- Time frame: All years and languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. Literature search was updated to January 3, 2020.

Summary of Evidence

Using the 2015 search strategy, this ScopRev[79a] identified 2 additional studies: 1 RCT[80] and 1 observational study[81] published after the review for the 2015 CoSTR was completed. When these 2 studies were added to the 2 studies identified in the 2015 CoSTR for NLS,[1,9,10] a total of 4 clinical studies could be included in the data analysis, representing a total of 2889 newborns (927 in 3 RCTs and 1962 in 1 observational study).[80–83]

The 4 studies investigated different populations; 2 studies included term and preterm infants,[80,83] and 2 studies enrolled preterm infants only.[81,82] The studies also differed in reported outcomes and were from diverse geographical areas. The large observational study found that use of a T-piece resuscitator increased survival and decreased bronchopulmonary dysplasia and intubation in the delivery room.[81] The latest RCT also found decreased intubation in the delivery room when T-piece resuscitators were used.[80]

The ScopRev can be reviewed in its entirety in Supplement Appendix B-3.

Task Force Insights

Data from a substantial number of additional patients reported in 1 RCT and 1 large observational study suggest improved survival, less need for intubation, and a lower incidence of bronchopulmonary dysplasia when a T-piece resuscitator is used (compared with a self-inflating resuscitator bag) during PPV at birth, particularly in preterm infants. The NLS Task Force concludes that these findings justify a new SysRev of the use of a T-piece resuscitator versus self-inflating bag for administering PPV at birth. The task force anticipates that not only the strength, but the direction of evidence may be changing toward support for using T-piece devices. Until a new SysRev is completed and results are analyzed by the NLS Task Force, the 2015 treatment recommendation remains in effect.[1,9,10]

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[1,9,10]

There is insufficient evidence regarding the use of T-piece resuscitator or self-inflating bag for initial PPV at birth, so the recommendation of one device over another would be purely speculative because the confidence in effect estimates is so low.

Oxygen for Preterm Resuscitation (NLS 864: 2019 CoSTR)

Preterm newborn infants are vulnerable to oxidative stress as a result of reduced antioxidant defenses and frequent exposure to oxygen during stabilization in the delivery room.[84] Many common preterm morbidities, such as bronchopulmonary dysplasia, retinopathy of prematurity and intraventricular hemorrhage are directly associated with oxygen toxicity. In the delivery room, it is imperative that clinicians prevent hypoxia while limiting hyperoxia. In 2019, the NLS Task Force published a SysRev with meta-analysis of the relevant available evidence on this topic,[85] and published an ILCOR CoSTR statement.[86,87]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Preterm newborn infants (less than 35 weeks' estimated gestational age) who receive respiratory support at birth
- Intervention: Lower initial oxygen concentration (50% or less O_2)
- Comparator: Higher initial oxygen concentration (more than 50% O_2)
- Outcome[21]:
  - Primary: All-cause short-term mortality (in hospital or 30 days) (critical)
  - Secondary:
    - All-cause long-term mortality (1–3 years) (critical)
    - Long-term NDI (1–3 years) (critical)
    - Retinopathy of prematurity (Stages III–V)[56] (critical)
    - Necrotizing enterocolitis Stage II (pneumatosis) or III (surgical)[88] (important)
    - Bronchopulmonary dysplasia (moderate to severe)[54] (critical)
    - Major intraventricular hemorrhage (Grade III–IV)[55] (critical)
    - Time to heart rate more than 100/min (important)
- Study design: RCTs, quasi-RCTs and nonrandomized studies included; animal studies, unpublished studies, and published abstracts (eg, conference abstracts) excluded
- Time frame: Literature search was from 1980 to August 10, 2018.
- PROSPERO Registration: CRD42018084902

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2019.[86,87]

For preterm newborn infants (less than 35 weeks' gestation) who receive respiratory support at birth, we suggest starting with a lower oxygen concentration (21% to 30%) rather than higher initial oxygen concentration (60% to 100%) (weak recommendation, very low-certainty evidence).

We suggest the range of 21% to 30% oxygen because all trials used this for the low oxygen concentration group. Subsequent titration of oxygen concentration using pulse oximetry is advised (weak recommendation, very low-certainty evidence).

Oxygen for Term Resuscitation (NLS 1554: 2019 CoSTR)

Administration of high oxygen concentrations leads to free radical formation and may be toxic to many tissues and organs of the newborn. Questions persist about the risks of hypoxia versus risks of exposure to excess oxygen for late preterm and term newborn infants who receive respiratory support in the delivery room. In 2019, the NLS Task Force published a SysRev with meta-analysis of the relevant available evidence on this topic[89] and also published an NLS CoSTR.[86,87] For complete review of the consensus on science for the secondary outcomes and subgroup analyses, please see the NLS Task Force section of the recently published 2019 CoSTR summary.[86,87]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Newborn infants (35 weeks' or greater gestation) who receive respiratory support at birth
- Intervention: Lower initial oxygen concentration (50% O_2 or less)
- Comparator: Higher initial oxygen concentration (greater than 50% O_2)
- Outcome[21]:
  - Primary: All-cause short-term mortality (in hospital or 30 days) (critical)
  - Secondary: All-cause long-term mortality (1–3 years) (critical)
  - Long-term NDI (1–3 years) (critical)
  - HIE (Sarnat Stage 2–3)[90] (critical)
- Study design: RCTs, quasi-RCTs, and nonrandomized studies included; animal studies, unpublished studies, and published abstracts (eg, conference abstracts) excluded
- Time frame: Literature search was from 1980 to August 10, 2018.
- PROSPERO Registration: CRD42018084902

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2019.[86,87]

For newborn infants at 35 weeks' or greater gestation receiving respiratory support at birth, we suggest starting with 21% oxygen (air) (weak recommendation, low certainty of evidence). We recommend against starting with 100% oxygen (strong recommendation, low certainty of evidence).

CIRCULATORY SUPPORT

For each of the following topics, the EvUps were performed to identify any evidence relevant to the topic that was published after the most recent NLS CoSTR on the topic. The goal was to determine if there was sufficient evidence to suggest a need for a SysRev that might change recommendations about performance of cardiac compressions for the few neonates who require circulatory support at birth.

CPR Ratios for Neonatal Resuscitation (NLS 895: EvUp)

Chest compressions administered in a 3:1 compression-to-ventilation ratio are recommended for resuscitation of newborn infants.[1,9,10] At birth, the fluid filling the lungs of the newborn must be absorbed during the initial breaths. Lung aeration triggers an increase in pulmonary blood flow. If a newborn infant has sufficient compromise in gas exchange to cause severe bradycardia or cardiac arrest, successful resuscitation must first achieve adequate lung aeration and ventilation to avoid circulation of blood with progressively lower oxygen saturation.

Many newborn infants, even those who are asphyxiated, will respond to respiratory support alone. As a result, the focus of newborn resuscitation is aimed first at establishing effective ventilation, and support of circulation is provided only for those who have persistent bradycardia or asystole. When circulatory support is needed, it is important that it be as effective as possible. This EvUp was performed to identify the most effective compression-to-ventilation ratio for neonatal resuscitation.

Most studies identified by the EvUp (see Supplement Appendix C-6) either supported the 2015 treatment recommendations or did not refute it. As a result, the NLS Task Force agreed that no SysRev is needed and there is no change to the 2015 treatment recommendation.[1,9,10] The NLS Task Force is aware of an ongoing study of a new neonatal compression technique, with compressions delivered while maintaining a sustained inflation (NCT02858583 at Clinicaltrials.gov). The NLS Task Force agreed that a SysRev may be indicated after publication of the results of that study.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: In newborn infants receiving cardiac compressions
- Intervention: other ratios (5:1. 9:3, 15:2, synchronous, etc)
- Comparator: 3 compressions, 1 ventilation
- Outcome[21]:
  - Return of spontaneous circulation (ROSC) (critical)
  - Survival (critical)
  - Neurodevelopmental impairment (critical)
  - Time to ROSC (critical)
  - Perfusion (important)
  - Gas exchange (important)
  - Tissue injury (important)
  - Compressor fatigue (important)

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[1,9,10]

We suggest continued use of a 3:1 compression-to-ventilation ratio for neonatal CPR (weak recommendation, very low-quality evidence).

2-Thumb Versus 2-Finger Compressions for Neonatal Resuscitation (NLS 605: EvUp)

In the past, providers used a variety of techniques to perform chest compressions during resuscitation of newborn infants. The most common techniques used 2 thumbs with the remaining fingers surrounding the lateral and posterior chest, or 2 fingers placed vertically on the lower sternum. The most recent review of the topic of chest compressions was included in the 2015 CoSTR for NLS.[1,9,10] This EvUp was performed to identify any evidence published after the 2015 CoSTR that would suggest the need for a new SysRev and reevaluation of the treatment recommendation.

The only new evidence identified by the EvUp (see Supplement Appendix C-7) supports the 2015 treatment recommendations.[1,9,10] Thus, no new SysRev or change in the 2015 treatment recommendation is warranted.

The task force noted that initial reports of a few alternative compression techniques (vertical thumbs, thumb and index finger, 2 thumbs with fisted hands) have been studied in manikin models. Studies testing any of these in a comparative trial in human infants may prompt a future SysRev.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: In newborn infants receiving cardiac compressions
- Intervention: 2-thumb technique
- Comparator: 2-finger technique
- Outcome[21]:
  - ROSC (critical)
  - Survival (critical)
  - Neurodevelopmental impairment (critical)
  - Perfusion (important)

- Gas exchange (important)
- Compressor fatigue (important)

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[1,9,10]

We suggest that chest compressions in the newborn infant should be delivered by the 2-thumb, hands-encircling-the-chest method as the preferred option (weak recommendation, very low-certainty evidence).

DRUG AND FLUID ADMINISTRATION

Although seldom needed, the short list of medications and fluids used for delivery room resuscitation of the newborn includes epinephrine and volume expanders.

Epinephrine (Adrenaline) for Neonatal Resuscitation (NLS 593: SysRev)

When the heart is hypoxic and depleted of energy substrate to the point of cardiac arrest, providers must re-establish effective perfusion of the myocardium with oxygenated blood.[91] Epinephrine (adrenaline) causes vasoconstriction, which increases the amount of oxygenated blood entering the coronary arteries and improves myocardial blood flow. Perfusion of the myocardium with oxygenated blood facilitates the synthesis of ATP within myocardial mitochondria, thus enhancing cell viability, contractility, and ROSC.[91]

In 2010, the NLS CoSTR summarized the evidence comparing the endotracheal route with the intravenous (IV) route for delivery of epinephrine (adrenaline) and concluded that the IV route was preferable.[12–14] The NLS Task Force has never conducted a SysRev to evaluate the evidence for epinephrine dose, dose interval, or other routes of delivery. In 2019, the NLS Task Force initiated a new SysRev to identify the evidence addressing these gaps.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Among neonates (of any gestation) less than 28 days of age who have no detected cardiac output or who have asystole or heart rate less than 60/min despite ventilation and chest compressions
- Intervention: Any nonstandard dose, interval, or route of epinephrine (adrenaline)
- Comparator: Epinephrine (adrenaline) doses of 0.01 to 0.03 mg/kg via IV at intervals of every 3 to 5 minutes
- Outcome[21]:
  - Mortality before hospital discharge (critical)
  - Survival to neonatal unit admission (critical)
  - ROSC: incidence and time until (critical)
  - HIE stage moderate to severe (term infants only)[90] (critical)
  - Intraventricular hemorrhage Grades 3 to 4 (preterm infants only) (critical)[55]
  - Necrotizing enterocolitis[92] (important)
  - Retinopathy of prematurity[56] (important)
  - Bronchopulmonary dysplasia[54] (important)
  - Periventricular leukomalacia (critical)
  - Neurodevelopmental outcomes (critical)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Cohort studies may compare different interventions or include only 1 arm receiving 1 intervention. They were eligible for this review if they were considered representative of a defined population (eg, infants born at a hospital between specified dates). Otherwise, they were considered to be (ineligible) case series. All languages were eligible if there was an English abstract. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: Literature search was from inception of the searched databases to March 6, 2019.
- PROSPERO Registration: CRD42019132219

Consensus on Science

The SysRev identified 2 eligible studies including 97 newborn infants.[92a] A draft CoSTR document based on the SysRev was posted on the ilcor.org website for a 2-week public commenting period on February 18, 2020.

Only 2 observational studies were found that addressed any of the comparisons prespecified in the PICOST.[7,93] They included both preterm and term infants from the same neonatal unit, although the participants were from different epochs. The overall certainty of evidence was rated as very low for all outcomes, primarily for a very serious risk of bias and very serious imprecision. The individual studies were at a critical risk of bias due to confounding.

For the critical outcome of mortality before hospital discharge, we identified very low-certainty evidence (downgraded for very serious risk of bias and very serious imprecision) from 1 observational study[7] of 50 neonates treated with epinephrine (adrenaline). In this study, there was no benefit associated with initial endotracheal versus IV epinephrine (adrenaline) dose. This lack of benefit was observed despite the fact that larger initial doses of epinephrine (adrenaline) were given via the endotracheal route (0.03–0.05 mg endotracheal dose compared with 0.01 mg/kg per IV dose). See Table 3 for statistical data.

In a post hoc analysis, we identified very low-certainty evidence (downgraded for very serious risk of bias and very serious imprecision) from 2 observational studies[7,93] of 97 neonates treated with epinephrine (adrenaline). These studies showed no significant association between route of administration of first dose and receipt of a second dose (RR, 1.94; 95% CI, 0.18–20.96;

Table 3. Meta-Analysis of Outcomes After Initial Endotracheal Versus Intravenous Epinephrine

Outcome	Study With Outcome of Interest	Total, n	Certainty of Evidence	RR (95% CI); I^2	Absolute Difference (95% CI)
Neonatal Outcomes					
Mortality before hospital discharge	Halling, 2017[7]	50	Very low	1.03 (0.62–1.71); NA	17/1000 more neonates died when initial endotracheal (0.05–0.1 mg/kg) versus initial IV (0.01–0.03 mg/kg) epinephrine was used (209 fewer–391 more per 1000)
Failure to achieve ROSC	Halling, 2017[7] Barber, 2006[93]	97	Very low	0.97 (0.38–2.48); 0	7/1000 fewer failed to achieve ROSC when initial endotracheal (0.05–0.1 mg/kg) versus initial IV (0.01–0.03 mg/kg) epinephrine was used (135 fewer–322 more per 1000)
Time to ROSC (minutes)	Halling, 2017[7]	50	Very low		ROSC was 2 min later when initial endotracheal (0.05–0.1 mg/kg) versus initial IV (0.01–0.03 mg/kg) epinephrine was used (0.6 min earlier–4.6 min later)

IV indicates intravenous; NA, not applicable; ROSC, return of spontaneous circulation; and RR, relative risk.

P=0.59; absolute risk difference, 654 more newborn infants; 95% CI, 570 fewer to 1000 more per 1000 newborn infants would receive additional epinephrine (adrenaline) dose or doses after the first). This occurred despite infants receiving larger doses given via the endotracheal route in one of the studies.[7]

No studies specifically reported the critical outcome of survival to neonatal unit admission, but this was likely similar to the inverse of the reported outcome "failure to achieve ROSC." We found only 1 eligible study comparing different doses of IV epinephrine (adrenaline).[7] This study of 30 neonates who received initial endotracheal epinephrine (adrenaline) allowed a post hoc comparison of 30 newborn infants who received 2 different doses (0.03 versus 0.05 mg/kg per dose) of endotracheal epinephrine (adrenaline) in different epochs of the study. Although no statistically significant difference was found, there was such serious imprecision as to prevent any conclusion.

We did not find any eligible studies comparing different routes of administration other than the comparisons between IV versus endotracheal epinephrine (adrenaline).

We did not find any eligible studies comparing different intervals of epinephrine (adrenaline) administration.

We did not find any eligible studies that allowed comparison of any other prespecified important outcomes (HIE stage moderate-severe[90] [term infants only]; intraventricular hemorrhage Grades 3–4[55] [preterm infants only]; other morbidities in early infancy [eg, necrotizing enterocolitis,[92] retinopathy of prematurity,[56] bronchopulmonary dysplasia,[54] periventricular leukomalacia] or neurodevelopmental outcomes).

The NLS Task Force agreed that the key 2010 CoSTR recommendations about epinephrine (adrenaline) administration remain valid.[12–14] The 2020 treatment recommendations include some minor editorial revisions in the indications for epinephrine (adrenaline) administration and more specific dose information and guidance about repeat doses than were contained in the 2010 treatment recommendations.

Treatment Recommendations

If the heart rate has not increased to 60/min or greater after optimizing ventilation and chest compressions, we suggest the administration of intravascular epinephrine (adrenaline) (0.01–0.03 mg/kg) (weak recommendation, very low-certainty evidence).

If intravascular access is not yet available, we suggest administering endotracheal epinephrine (adrenaline) at a larger dose (0.05–0.1 mg/kg) than the dose used for IV administration (weak recommendation, very low-certainty evidence). The administration of endotracheal epinephrine (adrenaline) should not delay attempts to establish vascular access (weak recommendation, very low-certainty evidence).

We suggest the administration of further doses of epinephrine (adrenaline) every 3 to 5 minutes, preferably intravascularly, if the heart rate remains less than 60/min (weak recommendation, very low-certainty evidence).

If the response to endotracheal epinephrine (adrenaline) is inadequate, we suggest that an intravascular dose be given as soon as vascular access is obtained, regardless of the interval after any initial endotracheal dose (weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

This topic was prioritized by the NLS Task Force because epinephrine (adrenaline) administration is considered to have a key role for newborns who have not responded to all previous steps in resuscitation. The last of NLS CoSTR addressing epinephrine (adrenaline) administration was conducted a decade ago,[12–14] at a time when the ILCOR evidence evaluation did

not use the GRADE assessment tools. Finally, the NLS Task force was aware of new cohort studies published after 2010.

In making these recommendations, the NLS Task Force considered the fact that the very limited human infant evidence does not demonstrate greater effect of endotracheal versus IV epinephrine (adrenaline). Although the population identified for this SysRev was human neonates, the task force reviewed 1 animal study. In a RCT of term lambs undergoing perinatal transition with asphyxia-induced cardiopulmonary arrest,[94] peak plasma epinephrine (adrenaline) concentrations were higher and were achieved sooner after central venous epinephrine (adrenaline) (right atrium 470±250 ng/mL or low umbilical venous cord 450±190 ng/mL at 1 minute) than after endotracheal epinephrine (adrenaline) (130±60 ng/mL at 5 minutes; *P*=0.03), despite lower administered central venous than endotracheal doses (0.03 mg/kg central venous IV dose versus 0.1 mg/kg endotracheal dose). In the same study, central venous compared with endotracheal epinephrine (adrenaline) administration resulted in a shorter median time (interquartile range) to achieve ROSC (2 [95% CI, 1.9–3] versus 4.5 [95% CI, 2.9–7.4] minutes; *P*=0.02), using a lower dose for central venous than for endotracheal administration. In addition, central venous compared with endotracheal epinephrine (adrenaline) administration resulted in higher rates of ROSC (86% [19/22] versus 54% [12/22]; *P*=0.02, respectively), using the same lower central venous compared with endotracheal doses.[94]

Subgroup Considerations

There was no evidence to suggest any variation in recommendations for subgroups of infants (eg, term versus preterm).

Implementation Considerations

This recommendation is similar to the 2010 treatment recommendation (ie, route and dose of epinephrine [adrenaline] NLS-008A, NLS-008B, NRP-009A, NRP-009B),[12–14] so the task force agreed that there are no new implications for implementation.

Monitoring and Implementation

We recommend that health services monitor the use of epinephrine (adrenaline) for newborn resuscitation, together with the outcomes of epinephrine (adrenaline) treatment reported in this review. Wherever possible, this monitoring should include the characteristics of the infants, the resuscitation measures they have received before epinephrine (adrenaline), the dose(s), route(s) and treatment intervals, and any adverse effects of treatment. It is unlikely there will be clinical trials to provide high-certainty evidence on which to base future treatment recommendations about epinephrine (adrenaline) doses, administration time intervals, and delivery routes. However, collection and publication of clinical observational studies can increase the volume of good-quality data to validate or improve treatment recommendations. Finally, the task force agreed that frequency of epinephrine (adrenaline) administration during resuscitation may reflect the quality of earlier steps in intrapartum management and resuscitation.

See Supplement Appendix A-3 for the evidence-to-decision table associated with this SysRev.

Knowledge Gaps

The NLS Task Force identified the following specific gaps in knowledge:

- Optimal (heart rate) thresholds for administration of epinephrine (adrenaline)
- Optimal dose and interval of epinephrine (adrenaline)
- Optimal epinephrine dose and intervals specific to gestational age
- Optimal route and method of epinephrine (adrenaline) administration
- Potential harms of epinephrine (adrenaline) (single or multiple doses)
- Effect of vasoactive drugs other than epinephrine (adrenaline)
- Human factors approach to achieve the timely administration of epinephrine (adrenaline)
- Neurodevelopmental outcomes after epinephrine (adrenaline) use

Providers must make the decision to administer epinephrine (adrenaline) rapidly during newborn resuscitation. In addition, epinephrine (adrenaline) use is uncommon and unpredictable. As a result, it may be difficult to perform adequate and ethical randomized trials of human newborn infants with prior parental informed consent. Prospective, multicenter cluster-randomized trials could be a good option.

Newborn animal studies are also needed to address pharmacokinetics and pharmacodynamics to determine the optimal dose and route of epinephrine (adrenaline) to inform the optimal design of human infant studies.

Intraosseous Versus Umbilical Vein for Emergency Access (NLS 616: SysRev)

In the rare circumstance where epinephrine (adrenaline) or volume is needed during neonatal resuscitation, vascular access is urgently required. There are questions as to the best route of vascular access to use. The last SysRev about this topic for neonates was in 2010 (NLS-020A intraosseous [IO] versus IV).[12–14] In 2020, the NLS Task Force joined the Advanced Life Support Task Force and the Pediatric Life Support Task Force to complete a joint SysRev with meta-analysis.[95]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Newborn infants in any setting (in-hospital or out-of-hospital) with cardiac arrest (includes severe bradycardia and inadequate perfusion requiring chest compressions)
- Intervention: Placement of an IO cannula with drug administration through this IO site during cardiac arrest
- Comparator: Placement of an IV cannula (umbilical vein in newborn infants) and drug administration through this IV during cardiac arrest
- Outcome[21]:
  - Death during event, within 24 hours and before hospital discharge (critical)
  - Long-term neurodevelopmental outcomes (critical)
  - ROSC: any signs of cardiac output with heart rate 60/min or greater, and time to ROSC (critical)
  - Brain injury (HIE Stage 2–3 Sarnat,[90] [term only], intraventricular hemorrhage Grades 3–4,[55] periventricular leukomalacia, preterm only) (critical)
  - Time to secure access (important)
  - Morbidity related to IO (osteomyelitis, fracture, epiphyseal plate injury, compartment syndrome) or to IV (extravasation, embolic phenomenon, phlebitis) (important)
- Study design:
  - Inclusion criteria: Randomized trials, non-RCTs, and observational studies (cohort studies and case-control studies) comparing IO with IV administration of drugs; randomized trials assessing the effect of specific drugs (eg, epinephrine [adrenaline]) in subgroups related to IO versus IV administration; studies assessing cost-effectiveness for a descriptive summary
  - Exclusion criteria: Ecological studies, case series, case reports, reviews, abstracts, editorials, comments, letters to the editor, or unpublished studies
  - Search: All years and languages were included if there was an English abstract. MEDLINE (Ovid interface), Embase (Ovid interface), and Cochrane Central Register of Controlled Trials literature search was conducted from 1946 to September 12, 2019, as well as ongoing trials on International Clinical Trials Registry Platform.

A Priori Subgroups to Be Examined

Cardiac and noncardiac causes of circulatory collapse; gestational age (preterm less than 37 weeks and term 37 weeks or greater); delivery room or other site; in-hospital or out-of-hospital; central or peripheral IV access; pediatric trained personnel versus non pediatric

PROSPERO Registration: CRD42020150877

Consensus on Science

Although small clinical series and case reports suggest that medications and fluids can be successfully delivered by the IO route during neonatal resuscitation,[96,97] case series also report complications with IO catheter insertion or use.[96,98–102] To determine if IO or intravascular access is more effective for neonatal resuscitation, evidence from neonatal literature was sought and considered by the NLS Task Force as part of a joint effort with the Adult Life Support and Pediatric Life Support Task Forces. No studies meeting the a priori inclusion criteria were found for newborn infants, precluding meta-analysis in this population. A draft CoSTR was developed that reflected the lack of data and was posted on the ILCOR website; the draft was viewed more than 2600 times, and more than 50 comments were posted. The majority were supportive of the conclusions.

No evidence was identified for newborn infants comparing use of IO and IV cannulas for drug administration in any setting (in-hospital or out-of-hospital) for any prespecified outcome of the review.

In 2010, the NLS Task Force said that temporary IO access to provide fluids and medications to resuscitate critically ill neonates may be indicated after unsuccessful attempts to establish IV vascular access or when caregivers are skilled at securing IO access.[12–14] The 2020 SysRev identified reports of serious complications after use of IO access in neonates.[96,98–102] As a result, the 2020 treatment recommendations are stronger in support of the umbilical venous route as the primary route for vascular access during delivery room resuscitation but continue to allow that in some circumstances the IO route is acceptable.

Treatment Recommendations

We suggest umbilical venous catheterization as the primary method of vascular access during newborn infant resuscitation in the delivery room. If umbilical venous access is not feasible, the intraosseous route is a reasonable alternative for vascular access during newborn resuscitation (weak recommendation, very low-certainty evidence).

Outside the delivery room setting, we suggest that either umbilical venous access or the IO route may be used to administer fluids and medications during newborn resuscitation (weak recommendation, very low-certainty evidence). The actual route used may depend on local availability of equipment, training, and experience.

Justification and Evidence-to-Decision Framework Highlights

In making this recommendation, we recognize the absence of data from human neonatal studies supporting any advantage of IO over umbilical venous access. There are a number of case reports of serious adverse effects of IO access in neonates, including tibial fractures and extravasation of fluid and medications resulting in compartment syndrome and amputation.[96,98–102]

The rate of adverse effects attributable to emergency umbilical venous catheterization is unknown. However, public feedback emphasized umbilical access as

the technique most commonly taught to and used by neonatal providers, recognizing that IO access may be helpful in out-of-hospital settings or later in the neonatal intensive care stay when the umbilical vein is no longer patent.

For further information, see the evidence-to-decision table in Supplement Appendix A-4.

Knowledge Gaps

The absence of clinical trials, cohort studies, and case-control studies leaves many gaps related to IO versus umbilical vein access during newborn resuscitation. We failed to identify even case series or case reports of IO use in neonatal resuscitation at delivery.

Specific research is required in preterm and term neonates:

- Determination of time from start of CPR to achieving successful IO placement
- Determination time from start of CPR to achieving successful IV placement in umbilical vein
- Optimal IO device suitable for newborn infants
- Optimal site (head of humerus, proximal tibia, other) for successful IO access and drug and fluid administration
- Short- and long-term safety of IO placement during newborn resuscitation
- Complications related to emergency umbilical venous catheterization
- Pharmacokinetics and plasma availability of drugs administered through IO compared with IV routes
- Optimal training for IO placement and IV umbilical vein placement during neonatal resuscitation
- How to best secure and maintain any emergency vascular access devices
- Optimal method to determine correct placement of any emergency vascular access device
- Whether results of studies in animal and simulation models apply to clinical practice
- IO access during neonatal resuscitation outside the delivery room

Volume Infusion During Neonatal Resuscitation (NLS 598: EvUp)

In the absence of a history of blood loss, there is limited evidence of benefit from administration of volume during resuscitation of newborns who have not responded to chest compressions and epinephrine (adrenaline). This topic was most recently reviewed by the NLS Task Force in 2010.[12–14] In 2020, the NLS Task Force undertook an EvUp to see if additional literature warranted consideration of a request for a new SysRev.

The EvUp identified no human studies and a single animal RCT (see Supplement Appendix C-8); the results of this study supported the 2010 CoSTR for NLS treatment recommendations.[12–14] The NLS Task Force agreed that there is no reason at this time to suggest a new SysRev or a change in the 2010 treatment recommendations.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Term and preterm newborn infants who receive resuscitation immediately after birth and who have a heart rate less than 60/min after chest compressions and epinephrine (adrenaline) and/or suspected hypovolemia based on history and examination.
- Intervention: Blood volume expansion with blood (red cells or whole blood), colloid (eg, albumin, plasma), crystalloid (eg, 0.9% sodium chloride) or other solution
- Comparator: No blood volume expansion
- Outcome[21]:
  - Survival (to any stage) (critical)
  - Neurodevelopmental outcomes (with age-appropriate, validated tools) (critical)
  - Time to ROSC (or heart rate 60/min or greater) (important)
  - Subsequent use of vasopressor infusion(s) (important)
  - Blood pressure at specified time (important)
  - Pulmonary edema (important)
  - Serious neonatal morbidity (including intraventricular hemorrhage, necrotizing enterocolitis, persistent pulmonary hypertension of the newborn, HIE, pulmonary hemorrhage) (critical)

Treatment Recommendation

These treatment recommendations are unchanged from 2010.[12–14]

Early volume replacement with crystalloid or red cells is indicated for newborn infants with blood loss who are not responding to resuscitation.

There is insufficient evidence to support the routine use of volume administration in the newborn infant with no blood loss who is refractory to ventilation, chest compressions, and epinephrine. Because blood loss may be occult, a trial of volume administration may be considered in newborn infants who do not respond to resuscitation.

Sodium Bicarbonate During Neonatal Resuscitation (NLS 606: EvUp)

In 2019, a request was made by members of the European Resuscitation Council for the NLS Task Force to consider an EvUp concerning the use of sodium bicarbonate during neonatal resuscitation. Since 2005, inconsistency has developed internationally as to whether sodium bicarbonate is even mentioned in council guidelines. The 2010 CoSTR briefly mentioned that sodium bicarbonate may very rarely be useful after resuscitation.[12–14] In 2020, the NLS Task Force undertook

an EvUp to determine if additional evidence published after 2020 warranted consideration of a new SysRev.

The EvUp (see Supplement Appendix C-9) identified only evidence that supported the 2010 treatment recommendations.[12–14]

Thus, the task force agreed that no SysRev or change in the 2010 treatment recommendation is warranted.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Newborn infants who are receiving resuscitation in the hospital
- Intervention: Sodium bicarbonate administration
- Comparator: No sodium bicarbonate
- Outcome[21]:
  - Survival (to hospital discharge or as defined by authors) (critical)
  - ROSC (critical)
  - HIE stage moderate to severe[90] (term infants only) (critical)
  - Intraventricular hemorrhage Grades 3 to 4[55] (preterm only) (critical)
  - Other morbidities in early infancy (eg, necrotizing enterocolitis,[92] retinopathy of prematurity,[56] bronchopulmonary dysplasia,[54] periventricular leukomalacia) (important)
  - Neurodevelopmental outcomes (critical)

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[12–14]

Sodium bicarbonate is discouraged during brief CPR but may be useful during prolonged arrests after adequate ventilation is established and there is no response to other therapies.

PROGNOSTICATION DURING CPR

Impact of Duration of Intensive Resuscitation (NLS 896: SysRev)

It can be difficult for clinicians to decide how long resuscitative efforts should continue in a newborn infant with no heart rate and/or absent respirations with a very low heart rate after sustained resuscitative efforts.[12–14] This critical decision involves knowing when to redirect the care of the newborn infant from resuscitation to the provision of comfort and contact with the parents. If such a decision is made too early, some infants with potential to survive with good neurodevelopmental outcome may die. If the decision is made too late, there is likely to be a diminishing potential for survival, especially without severe neurological injury.

In recent years, long-term outcomes for survivors requiring prolonged resuscitation have improved somewhat. In 2015, the CoSTR focused on the following question: "In infants with a gestational age of 36 weeks or greater and an Apgar score of 0 for 10 minutes or longer, despite ongoing resuscitation, what is the rate of survival to NICU admission and death or neurocognitive impairment at 18 to 22 months?" In 2019, the NLS Task Force revised the question slightly to better reflect the questions clinicians and families ask in such a crisis situation.

The current PICOST attempts to reduce the emphasis on the Apgar score at 10 minutes and puts more focus on the incremental time of resuscitation exposure from birth as related to outcome.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Newborn infants presenting with at least 10 minutes of asystole, bradycardia (heart rate less than 60/min), or pulseless electric activity after birth for which CPR is indicated
- Intervention: Ongoing CPR for incremental time intervals beyond 10 minutes after birth
- Comparator: CPR discontinued at 10 minutes after birth
- Outcome[21]:
  - Survival (to any age) (critical)
  - Neurodevelopmental outcomes (critical)
  - Composite of survival to any age without moderate or severe neurodisability (critical)
- Study design: Cross-sectional or cohort studies were eligible for inclusion. Ancillary analyses of RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies, case series) were eligible for inclusion. All years and languages were included if there was an English abstract. Conference abstracts and trial protocols were excluded.
- Time frame: All years were included from inception of the searched databases to October 17, 2019.

A Priori Subgroups to Be Examined

Hypothermia postresuscitative care among newborn infants 36 weeks' or greater gestational age; 36 weeks' or greater gestational age versus less than 36 weeks'; birthweight 2500 g or greater; infants enrolled in population-level cohort studies

PROSPERO Registration: CRD42020157370

Consensus on Science

The SysRev[102a] identified 15 studies that included 470 infants (see Figure 2).

For the critical outcome of survival until last follow up, we identified very low-certainty evidence (downgraded for risk of bias and inconsistency) from 15 studies[103–117] reporting outcomes of 470 newborns to last known follow-up (range: 4 months–8 years of age). The number of enrolled newborns ranged from 3 to 177 per study. Across studies, reported survival rates to last follow up ranged from 1.7% to 100%. Among all 470 newborns reported in the literature, including studies that required survival

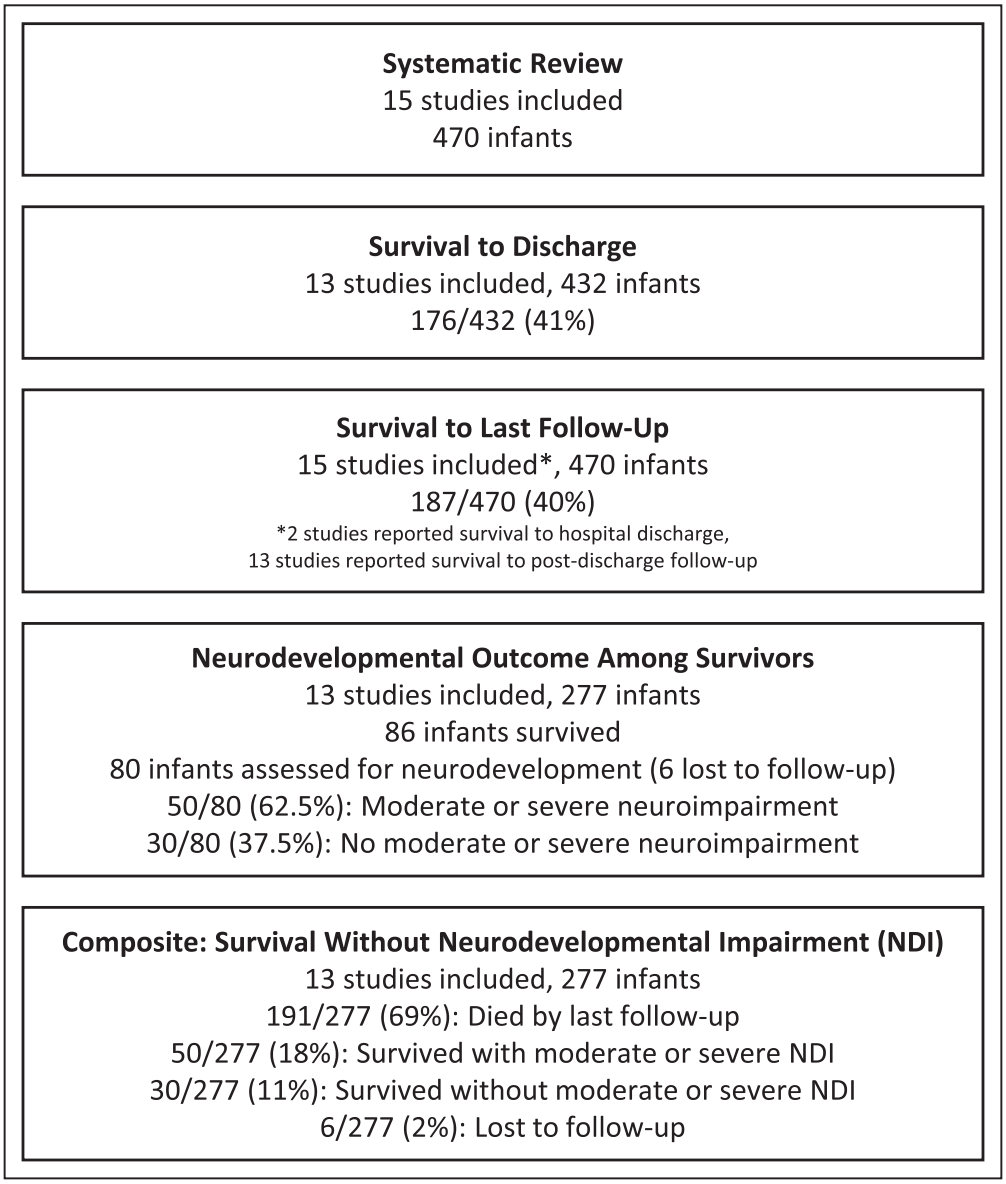

Figure 2. Modified flow diagram of number of studies and infants included for each specified outcome for infants experiencing resuscitation that exceeded 10 minutes.
Moderate to severe NDI was defined by each study.

to NICU admission or enrollment in a cooling protocol for inclusion, 187 (39.8%) survived to last follow-up. The decision was made not to calculate confidence intervals as a result of heterogeneity across included studies.

For the critical outcome of neurodevelopmental outcomes among survivors, we identified very low-certainty evidence (downgraded for risk of bias and inconsistency) from 13 studies including 277 infants.[103,104,106–112,114–117] Neurodevelopmental outcomes were assessed in 80 survivors. Thirty infants among 80 survivors (37.5%) did not have moderate or severe NDI (range: 0% to 100%). There was important heterogeneity across studies (and in some cases within studies) about the timing and tools used to assess neurodevelopmental outcomes that precluded calculation of confidence intervals.

For the composite critical outcome of survival without NDI, we identified very low-certainty evidence (downgraded for risk of bias and inconsistency) from 13 studies of 277 infants[103,104,106–112,114–117] reporting neurodevelopmental outcomes. Among all 277 infants reported in these studies, 69% died before last follow up, 18% survived with moderate to severe impairment, and 11% survived without moderate to severe impairment (2% lost to follow up). There was important heterogeneity across studies (and in some cases, within studies) about the timing and tools used to assess neurodevelopmental outcomes that precluded calculation of confidence intervals.

Note: Neurodevelopmental outcomes in postdischarge follow-up were reported in 13 studies using structured exams.[103,104,106–112,114–117] In 11 studies, these assessments used validated developmental assessment

tools.[106–112,114–117] These tools included developmental assessment tools such as the Bayley Scales of Infant and Toddler Development (any version) or a Japanese version of the Bayley Scales (Kyoto Scale of Psychological Development); motor assessment tools such as Gross Motor Function Classification System or Peabody Developmental Motor Scales; and cognitive evaluation tools such as Stanford-Binet Test, Griffiths Scales of Child Development (any version), or Wechsler Preschool and Primary Scale of Intelligence (any version). Two studies[103,104] reported only a formal neurological evaluation of the survivors. Auditory and visual assessment varied among studies. Of note, children assessed only by screening tools (such as Denver Developmental Screening Test) in any study were analyzed as lost to follow-up. Time of follow-up for the 80 survivors assessed for NDI was 12 months or greater in 83% (66/80) of the infants (range: 12 months–8 years) and less than 12 months in 6% (5/80) of the infants. Time of assessment was not reported in 1 study[114] with 11% (9/80) survivors. Moderate and severe NDI were defined by each study.

Subgroup Considerations

Prespecified subgroup analyses for the specified critical outcomes of survival to last follow-up, survival without NDI, and the composite of survival without moderate to severe NDI are depicted in Table 4. Insufficient details about birthweight precluded the planned subgroup analysis based on birthweight.

Given the small sample sizes and heterogeneity of study characteristics, there is no strong evidence on which to base recommendations for specific subgroups of infants.

Treatment Recommendations

Failure to achieve return of spontaneous circulation in newborn infants despite 10 to 20 minutes of intensive resuscitation is associated with a high risk of mortality and a high risk of moderate-to-severe neurodevelopmental impairment among survivors. However, there is no evidence that any specific duration of resuscitation consistently predicts mortality or moderate-to-severe neurodevelopmental impairment. If, despite provision of all the recommended steps of resuscitation and excluding reversible causes, a newborn infant requires ongoing cardiopulmonary resuscitation (CPR) after birth, we suggest discussion of discontinuing resuscitative efforts with the clinical team and family. A reasonable time frame to consider this change in goals of care is around 20 minutes after birth. (Weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

In making this recommendation, we recognize the need to balance the risk of ceasing resuscitation too early, when ROSC and long-term survival may still be achievable, and continuing resuscitation for too long, when ROSC may occur but survival is associated with a high risk of severe neurological injury. The appreciable number of survivors without moderate or severe NDI after 10 minutes or greater of resuscitation suggests that early cessation of resuscitation may preclude survival of some infants who may have a good outcome.

While an Apgar score of 0 or 1 at 10 minutes is a strong predictor of mortality and morbidity, recent case reports and series have reported favorable outcomes among newborn infants with Apgar scores of 0 or 1 at 10 minutes after birth who achieved ROSC and received therapeutic hypothermia. In this subgroup of newborns with severe depression at birth, both survival and survival without moderate-to-severe impairment have been reported. Among 105 such infants reported in the literature with Apgar scores 0 or 1 who were successfully resuscitated, were treated with therapeutic hypothermia, and were assessed after discharge, 20% of all infants survived without moderate-to-severe NDI, and 37% of the survivors did not have moderate or severe NDI.[107,109–112,116,117]

The evidence supporting this recommendation is of very low certainty. However, we value the possibility of survival and intact survival after ongoing resuscitation. In a large multisite cohort of 659 newborn infants who survived to discharge after more than 1 minute of chest compressions in the delivery room, 25% of survivors received 10 minutes or more of resuscitation.[118] This study did not specifically report on infants with 10-minute Apgar scores of 0 or 1. While these data indicate that survival to discharge is possible after a lengthy duration of CPR, neurodevelopmental outcomes among survivors in this study were not reported.

Extremely limited data are available about outcomes of newborn infants who received 20 or more minutes of CPR after birth. Five studies included in this systematic review[110–112,116,117] reported results for 39 newborn infants in whom first detectable heart rate or heart rate 100/min or greater occurred at or beyond 20 minutes after birth. Of these, 38% (15/39) survived until last follow up and 40% (6/15) of survivors did not have moderate or severe neuroimpairment.

The task force agreed that in addition to considering duration of resuscitation, it was important to consider whether all recommended resuscitation interventions were provided. Studies suggest that the time taken to accomplish steps of a resuscitation up to the point of administration of 1 or more doses of epinephrine varies widely across studies but may take as long as 20 minutes.[7,93,111,119] The variation in the interval from birth to completion of these steps may depend on the characteristics and time to attendance of the resuscitation team. Thus, using a single time interval after birth to discontinue intensive resuscitation for all newborns might mean in some cases that the full repertoire of

Table 4. Subgroup Analyses for Specified Outcomes for Infants Who Had Resuscitation That Exceeded 10 Minutes

Subgroup	Studies Contributing	Infants, n	Survival to Last Follow-up	Assessed for NDI	Survivors Assessed Without Moderate or Severe NDI	Composite: Survival Without Moderate or Severe NDI
Population level studies	Casalaz, 1998[104] Harrington, 2007[103] Jain, 1991[106] Sproat, 2017[111] Zhang, 2019[117]	131	13% (17/131)	88% (15/17)	60% (9/15)	7% (9/131)
Therapeutic hypothermia	Ayerapetyan, 2019[116] Kasdorf, 2015[107] Natarajan, 2013[108] Sarkar, 2010[109] Shah, 2015[110] Shibasaki, 2020[112] Sproat, 2017[111] Zhang, 2019[117] Zhong, 2019[113]	206	60% (122/206)	47% (57/122)	37% (21/57)	20% (21/105)*
Gestational age ≥36 wk	Ayerapetyan, 2019[116] Casalaz, 1998[104] Harrington, 2007[103] Kasdorf, 2015[107] Natarajan, 2013[108] Patel, 2004[114] Sarkar, 2010[109] Shah, 2015[110] Shibasaki, 2020[112] Sproat, 2017[111] Zhang, 2019[117] Zhong, 2019[113]	286	51% (146/286)	50% (73/146)	32% (23/73)	14% (23/166)†
Gestational age <36 wk	Casalaz, 1998[104] Harrington, 2007[103] Shah, 2015[110] Sproat, 2017[111] Zhang, 2019[117] Zhong, 2019[113]	99	34% (34/99)	24% (8/34)	63% (5/8)	12% (5/42)‡

*Eight studies with 105 infants reported postdischarge outcomes.
†Eleven studies with 166 infants reported postdischarge outcomes.
‡Five studies with 42 infants reported postdischarge outcomes.
NDI indicates neurodevelopmental impairment.

recommended resuscitation interventions were not provided before cessation of resuscitation.

Another issue considered by the task force was the potential impact on infants and their families. Among the included studies, most deaths occurred either in the delivery room/birth suite or during the initial hospitalization. In this systematic review, rates of survival to discharge were similar to rates of survival to last follow up (see Figure 2). For those infants who ultimately die in early infancy, achieving even this short-term survival may provide the family the time and opportunity to participate in decision-making and care of their infant. Moreover, intact survival is possible among surviving infants. In this systematic review, 38% of surviving infants did not have moderate or severe impairment.

Given these considerations, we do not recommend a specific duration of resuscitation after which point resuscitative efforts should cease. Instead, we suggest that providers consider changing the goals of care if a newborn infant has not responded to all recommended steps of resuscitation that are appropriate to the given setting. We acknowledge that cultural and religious differences, including different perceptions of the value of extending life, the quality of life, and the acceptance of comfort care as an option, may influence the decision.[120–122]

Ultimately, the decision to initiate and continue resuscitative efforts should be individualized and informed by factors such as gestational age, the presence of congenital anomalies, the timing of perinatal insult (if known), the perceived adequacy of resuscitative interventions, the family's stated preferences and values, and the availability of postresuscitative resources, such as neonatal intensive care, and neuroprotective strategies, such as therapeutic hypothermia. Finally, in low-resource settings, where emphasis is given to face-mask ventilation with 21% oxygen for nonbreathing neonates,[123] advanced resuscitation procedures and prolonging resuscitation may not be an option. Therefore, caution must be taken in the global adoption of this treatment recommendation as local/regional discussion and customization are necessary.

Implementation Considerations

Acceptability of the intervention should be thoroughly discussed in the different settings according to cultural, ethical, and moral standards that prevail in each country or region. High-quality resuscitation should be available for infants in need, and training of skills and team performance are critical to achieve it. Communication with families should be optimized, and whenever possible, parents' wishes and values must be considered, even in urgent and stressful situations. Availability of neonatal intensive care and neuroprotective strategies for postresuscitation care is another aspect that may be considered in the decision-making process.

Monitoring and Implementation

It is important to monitor both short- and long-term outcomes for infants who had a prolonged interval between birth and ROSC. In addition, although health equity was not objectively reported for prolonged neonatal resuscitation, it is possible that prolonged resuscitation may be offered to a higher proportion of infants in higher-resource settings; outcomes may also be better in settings with full availability of intensive care and neuroprotective strategies.

Prolonged CPR after birth is relatively rare, so an international registry of events, with detailed description of procedures and their timing in the delivery room, postresuscitation care, and neurological outcomes assessed in follow-up, would provide essential evidence to inform the discussion of how long is too long. Such a registry would also provide valuable information about variability in practice regarding duration of resuscitation in different settings.

For more information, refer to the evidence-to-decision table in Supplement Appendix A-5.

Knowledge Gaps

Many studies reported only outcomes of infants who survived resuscitation and met a specific study eligibility criterion, such as NICU admission or initiation of therapeutic hypothermia. Therefore, estimates of mortality after prolonged resuscitation are likely to underestimate the true rate of death after prolonged resuscitation because this would need to also include infants for whom resuscitation had failed. Studies that account for the full population of newborn infants who receive CPR after birth by using consistent definitions of stillbirths and resuscitation failures are needed to identify the incidence of death and NDI after prolonged resuscitation of term and preterm infants.

In addition, the extent and timing of resuscitation interventions were not reported in most studies; therefore, prognosis of newborn infants after prolonged resuscitation at birth is inferred from the available data. Further, most available studies characterized the infant's response to resuscitation using the Apgar score at 10 minutes, which is prone to subjective assessment and does not provide information about ongoing assessments or responses to resuscitation beyond 10 minutes. More granular information about the interval from birth to detectable heart rate that uses objective measures such as ECG and time to ROSC is needed to inform more precise recommendations about the duration of intensive resuscitation after birth. Additionally, as the ECG is used more frequently in the delivery room environment, additional information about the presenting rhythm (bradycardia, asystole, pulseless electric activity) preceding chest compressions will be helpful to identify outcomes after these varied presentations.

Therefore, studies that report outcomes on the full population of infants who present without signs of life and receive intensive resuscitation are needed with the following:

- A priori definitions of stillbirths and completeness of resuscitation attempts
- Complete description of cointerventions (resuscitation procedures), timing of procedures at birth, and interventions in postresuscitative care
- Description of methods to assess the heart rate during resuscitation by using objective measures, such as ECG, and report of timing for detection of heart rate and heart rate 60/min or greater and 100/min or greater
- Complete follow-up of survivors with accurate and consistent methods of assessment of neurodevelopment, comparable across studies and population

POSTRESUSCITATION CARE

Rewarming of Hypothermic Newborns (NLS 858: EvUp)

The most recent review of this topic was published in the 2015 CoSTR for NLS.[1,9,10] In 2020, the NLS Task Force undertook an EvUp to determine if any additional evidence was published after 2015 that would necessitate consideration of a new SysRev.

An EvUp (see Supplement Appendix C-10) identified 133 studies; of these, 2 were considered eligible for inclusion. Although the EvUp identified no new prospective trials of rates of rewarming, the 2 new retrospective studies[124,125] increased the number of infants in observational trials nearly 4-fold to 379 infants. Both studies found that the rate of rewarming (after adjustment for confounders) was not associated with the critical outcomes identified in each study. However, 1 study[125] suggested that rapid rewarming reduces the risk for respiratory distress syndrome.

The NLS Task Force agreed that a SysRev that includes the new studies analyzed by using GRADE criteria will likely allow the development of a weak recommendation in relation to the rate of rewarming of hypothermic infants, as opposed to the "no recommendation" that was made in 2015. As a result, the task force will consider prioritization of a SysRev in the near future. Until

the completion of a new SysRev, the 2015 recommendation remains in effect.[1,9,10]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Newborn infants who are hypothermic (less than 36.0°C) on admission
- Intervention: Rapid rewarming
- Comparator: Slow rewarming
- Outcome[21]:
  - Survival (to hospital discharge or as defined by authors) (critical)
  - Convulsions/seizures (critical)
  - Hemorrhage/pulmonary hemorrhage (critical)
  - Need for respiratory support (important)
  - Hypoglycemia (important)
  - Episodes of apnea (important)

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[1,9,10]

The confidence in effect estimates is so low that a recommendation for either rapid rewarming (0.5°C/h or greater) or slow rewarming (0.5°C/h or less) of unintentionally hypothermic newborn infants (temperature less than 36°C) at hospital admission would be speculative.

Induced Hypothermia in Settings With Limited Resources (NLS 734: EvUp)

This topic was most recently reviewed in 2015.[1,9,10] In 2020, the NLS Task Force undertook an EvUp to identify any studies published after 2015.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Newborn infants with HIE managed in limited-resource settings
- Intervention: Therapeutic hypothermia delivered by passive hypothermia and/or ice packs
- Comparator: Standard care
- Outcome[21]:
  - Survival (critical)
  - Neurodevelopmental impairment (any) (important)

The EvUp (see Supplement Appendix C-11) identified 142 studies; 13 of these were thought worthy of inclusion.[126–138] The NLS Task Force agreed that these 13 studies did not identify sufficient new evidence to consider a new SysRev and, even if added to previous studies, would not likely add to the level of certainty of the evidence summarized in 2015.[1,9,10]

It is becoming increasingly difficult (as a result of clinician and parent preferences) to perform large, multicenter randomized trials with a "no-therapeutic hypothermia" control group. However, a protocol was published for 1 such study in hospitals in India, Bangladesh, or Sri Lanka; a multicenter RCT of therapeutic hypothermia using a servo-controlled cooling device compared with standard care without therapeutic hypothermia has a planned enrollment of 418 infants.[139] When completed, such a study (NCT02387385) could provide valuable additional information. Accumulation of data from such a study or from a group of smaller studies might warrant an updated SysRev.

Future studies of this subject should ideally try to examine the contributions of population characteristics, cooling method, and availability of concomitant intensive care to outcomes. Interestingly, a survey of hospitals in California identified a range of practices and opinions about the additional services (specialized nurses, video electroencephalogram monitoring, pediatric neurology and neuroradiology services, developmental follow-up services, etc) that should be required of centers providing neonatal therapeutic hypothermia.[140] In addition to wide variation in opinions about necessary resources such as electroencephalogram monitoring, only 92% of centers reported using an evidence-based protocol, and there was a lack of universal agreement that therapeutic hypothermia centers should treat a minimum volume of patients annually. Considering this variation across high-resource locations, it is not surprising that there is lack of certainty supporting recommendations for when and how to provide therapeutic hypothermia for low- and middle-income countries.

Treatment Recommendation

This recommendation (below) is unchanged from 2015.[1,9,10]

We suggest that newborn infants at term or near-term with evolving moderate-to-severe hypoxic-ischemic encephalopathy in low-income countries and/or other settings with limited resources may be treated with therapeutic hypothermia (weak recommendation, low-quality evidence).

Cooling should only be considered, initiated, and conducted under clearly defined protocols with treatment in neonatal care facilities with the capabilities for multidisciplinary care and availability of adequate resources to offer intravenous therapy, respiratory support, pulse oximetry, antibiotics, anticonvulsants, and pathology testing. Treatment should be consistent with the protocols used in the randomized clinical trials in developed countries, ie, cooling to commence within 6 hours, strict temperature control at 33°C to 34°C for 72 hours and rewarming over at least 4 hours.

Postresuscitation Glucose Management (NLS 607: EvUp)

The most recent review of this topic was published in the 2010 CoSTR.[12–14] In 2020, the NLS Task Force undertook an EvUp to determine if any additional studies were published after 2015 that would necessitate an update to the prior SysRev.

The EvUp (see Supplement Appendix C-12) identified 648 studies; 52 were reviewed and, of those, 13

were worthy of inclusion. Overall, this EvUp suggests the need to maintain vigilance for neonatal hypoglycemia and hyperglycemia in the aftermath of resuscitation, that the use of protocols for blood glucose management may avoid both hypoglycemia and hyperglycemia, and that these protocols may also avoid large swings in blood glucose concentration that have also been associated with harm. The NLS Task Force agreed that the EvUp highlights the fact that research is needed to determine the optimal protocols for glycemic management for preterm and term infants in the aftermath of resuscitation, and identifying the optimal target glucose range should be a high priority. Because the most recent review of the topic was published in 2010, the NLS Task Force agreed that there has been sufficient new evidence published about glucose management after newborn resuscitation to consider prioritizing a SysRev on the topic of blood glucose management.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Newborn infants who have received drugs for resuscitation
- Intervention: Glucose infusion
- Comparator: No glucose infusion
- Outcome[21]:
  - Survival (to hospital discharge or as defined by authors) (critical)
  - Convulsions/seizures (critical)
  - Hemorrhage/pulmonary hemorrhage (critical)
  - Need for respiratory support (important)
  - Hypoglycemia (important)
  - Episodes of apnea (important)

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[12–14]

Intravenous glucose infusion should be considered as soon as practical after resuscitation, with the goal of avoiding hypoglycemia.

TOPICS NOT REVIEWED IN 2020

- Term umbilical cord management (NLS 1551-SysRev in process)
- Preterm umbilical cord management (NLS 787-Sys Rev in process)
- Babies born to mothers who are hypothermic or hyperthermic (NLS 804)
- Stimulation for apneic newborns (NLS 1558)
- Respiratory function monitoring in the delivery room (NLS 806)
- Laryngeal mask for neonatal resuscitation (NLS 618)
- Less-invasive surfactant administration (New)
- CPAP versus increased oxygen for term infants in the delivery room (NLS 1579)
- Optimal peak inspiratory pressure (NLS New)
- Oxygen saturation target percentiles (NLS 1580)
- Use of feedback CPR devices for neonatal cardiac arrest (NLS 862)
- Oxygen use post-ROSC for newborns (NLS 1569)
- Oxygen delivery during CPR (Neonatal) (NLS 738)
- Hypovolemia (risk factors for newborns) (NLS 1555)
- Effect of monitoring technology on team function (NLS 1559)

ARTICLE INFORMATION

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Disclosures

Appendix 1. Writing Group Disclosures

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(*Continued*)

Appendix 1. Continued

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
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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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Taylor Sawyer	Seattle Children's Hospital/University of Washington	None	None	None	None	None	None	None
Birju A. Shah	University of Oklahoma	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.

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Circulation

Education, Implementation, and Teams

2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

ABSTRACT: For this *2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations*, the Education, Implementation, and Teams Task Force applied the population, intervention, comparator, outcome, study design, time frame format and performed 15 systematic reviews, applying the Grading of Recommendations, Assessment, Development, and Evaluation guidance. Furthermore, 4 scoping reviews and 7 evidence updates assessed any new evidence to determine if a change in any existing treatment recommendation was required. The topics covered included training for the treatment of opioid overdose; basic life support, including automated external defibrillator training; measuring implementation and performance in communities, and cardiac arrest centers; advanced life support training, including team and leadership training and rapid response teams; measuring cardiopulmonary resuscitation performance, feedback devices, and debriefing; and the use of social media to improve cardiopulmonary resuscitation application.

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Key Words: AHA Scientific Statements ■ basic life support ■ education ■ opioid overdose

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CONTENTS

The *2020 International Consensus on Cardiopulmonary Resuscitation* (CPR) *and Emergency Cardiovascular Care Science With Treatment Recommendations* (CoSTR) is the fourth in a series of annual summary publications from the International Liaison Committee on Resuscitation (ILCOR). This 2020 CoSTR for education, implementation, and teams (EIT) includes new topics addressed by systematic reviews (SysRevs) performed within the past 12 months. It also includes updates of the EIT treatment recommendations published from 2010 through 2019,[1–6] as needed, that are based on additional evidence evaluations. As a result, this 2020 CoSTR for EIT represents the most comprehensive update since 2010. The 3 major types of evidence evaluation supporting this 2020 publication are the SysRev, the scoping review (ScopRev), and the evidence update (EvUp).

The SysRev is a rigorous process following strict methodology to answer a specific question, and each of these ultimately resulted in generation of the task force CoSTR included in this publication. The SysRevs were performed by an expert systematic reviewer or by the EIT Task Force, and many have resulted in separate published SysRevs.

To begin the SysRev, the question to be answered was phrased in terms of the PICOST (population, intervention, comparator, outcome, study design, time frame) format. The methodology used to *identify* the evidence was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[7] The approach used to *evaluate* the evidence was based on that proposed by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group.[8] Using this approach for each of the predefined outcomes, the task force rated as high, moderate, low, or very low the certainty/confidence in the estimates of effect of an intervention or assessment across a body of evidence. Randomized controlled trials (RCTs) began the analysis as high-certainty evidence, and observational studies began the analysis as low-certainty evidence; examination of the

evidence using the GRADE approach could result in downgrading or upgrading the certainty of evidence. For additional information, refer to Evidence Evaluation Process and Management of Potential Conflicts of Interest in this supplement.[9,9a] Disclosure information for writing group members is listed in Appendix 1. Disclosure information for peer reviewers is listed in Appendix 2.

Where a pre-2015 CoSTR treatment recommendation was not updated, the language used differs from that used in the GRADE approach, because GRADE was not used before 2015.[10–12]

It important to note that GRADE, which was designed for clinical studies, was applied across different types of literature to maintain consistency throughout the ILCOR review process. There were challenges in applying GRADE to the evaluation of educational studies, and ILCOR will continue to consider alternative approaches for future evidence reviews.

Draft 2020 CoSTRs for EIT were posted on the ILCOR website[13] for public comment between December 31, 2019, and February 18, 2020, with comments accepted through March 3, 2020. The 14 EIT Task Force draft CoSTR statements received 15 277 views and 18 comments. All comments were reviewed by the EIT Task Force, but none of the comments led to any change in the treatment recommendations.

This summary statement contains the final wording of the CoSTR statements as approved by the ILCOR task forces and by the ILCOR member councils after review and consideration of comments posted online in response to the draft CoSTRs. Within this publication, each topic includes the PICOST as well as the CoSTR, an expanded section on justification and evidence-to-decision framework highlights, and a list of knowledge gaps requiring future research studies. An evidence-to-decision table is included for each CoSTR in Appendix A in the Supplemental Materials.

The second major type of evidence evaluation performed to support this 2020 CoSTR for EIT is a ScopRev. ScopRevs are designed to identify the extent, range, and nature of evidence on a topic or a question, and they were performed by topic experts in consultation with the EIT Task Force. The task force assessed the identified evidence and determined its value and implications for resuscitation practice or research. The rationale for the ScopRev, the summary of evidence, and task force insights are all highlighted in the body of this publication. The most recent treatment recommendation is included. The task force notes whether the ScopRev identified substantive evidence that may result in a change in ILCOR treatment recommendations. If sufficient evidence was identified, the task force suggested consideration of a future SysRev to supply sufficient detail to support the development of an updated CoSTR. All ScopRevs are included in their entirety in Appendix B in the Supplemental Materials.

The third type of evidence evaluation supporting this CoSTR for EIT is an EvUp. EvUps are generally performed for topics previously reviewed by ILCOR, to identify new studies published after the most recent ILCOR evidence evaluation, typically through use of search terms and methodologies from previous reviews. Several EvUps for new topics deemed to be important but missing from the existing reviews were also undertaken (by using a PubMed/Medline search only) by one or more of the member resuscitation councils. The EvUps were performed by task force members, collaborating experts, or members of Council writing groups. The EvUps are cited in the body of this publication with a note as to whether the evidence suggested the need to consider a SysRev. The existing ILCOR treatment recommendation was reiterated. In this publication, no change in ILCOR treatment recommendations resulted from an EvUp; if substantial new evidence was identified, the task force recommended consideration of a SysRev. All EvUps are included in their entirety in Appendix C in the Supplemental Materials.

The following topics have been reviewed:

Training for Treatment of Opioid Overdose

- Opioid overdose first aid education (EIT 4001: ScopRev)

Basic Life Support (BLS) Including Automated External Defibrillator (AED) Training

- Willingness to perform bystander CPR (EIT 626: ScopRev)
- Prehospital termination of resuscitation (TOR) (EIT 642: SysRev)
- In-hospital termination of resuscitation (TOR) (EIT 4002: SysRev)
- Deliberate practice and mastery learning (EIT 4004: EvUp)
- Layperson training (EIT 4009: EvUp)
- Timing for retraining (EIT 628: EvUp)

Measuring Implementation/Performance in Communities, Cardiac Arrest Centers

- System performance improvements (EIT 640: SysRev)
- Community initiatives to promote BLS implementation (EIT 641: ScopRev)
- Cardiac arrest centers (EIT 624: SysRev, 2019 CoSTR)
- Out-of-hospital CPR training in low-resource settings (EIT 634: ScopRev)
- Disparities in education (EIT 4003: EvUp)

Advanced Life Support (ALS) Training, Including Team and Leadership Training, and Medical Emergency Teams (METs) and Rapid Response Teams (RRTs)

- Spaced learning (EIT 1601: SysRev)
- Emergency medical services (EMS) experience and exposure (EIT 437: SysRev)

- Cognitive aids during resuscitation education (EIT 629: SysRev)
- Team and leadership training (EIT 631: SysRev)
- Precourse preparation for advanced courses (EIT 637: SysRev)
- Rapid response systems (RRSs) in adults (EIT 638: SysRev)
- End-of-course testing versus continuous assessment (EIT 643: SysRev)
- Virtual reality, augmented reality, and gamified learning (EIT 4005: EvUp)
- In situ training (EIT 4007: EvUp)
- High-fidelity manikins for ALS training (EIT 623: EvUp)

Measuring CPR Performance, Feedback Devices, and Debriefing

- Debriefing of resuscitation performance (EIT 645: SysRev)
- CPR feedback devices during training (EIT 648: SysRev)
- Patient outcomes as a result of a member of the resuscitation team attending an ALS course (EIT 4000: SysRev)

Use of Social Media

- First responder engaged by technology (EIT 878: SysRev)

TRAINING FOR TREATMENT OF OPIOID OVERDOSE

Opioid Overdose First Aid Education (EIT 4001: ScopRev)

Rationale for Review

In 2015, the ALS Task Force recommended the use of naloxone for individuals in cardiac arrest caused by opioid toxicity (strong recommendation, very low quality of evidence).[14,15] Because of lack of evidence, in 2015 the BLS Task Force did not make a treatment recommendation for using naloxone for suspected opioid overdose. However, the BLS Task Force did 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 certainty evidence).[16,17] The EIT Task Force chose to identify the scope of current opioid overdose response education programs reporting outcomes to recommend further SysRevs or identify gaps in the existing literature on education of the use of naloxone in possible opioid overdose.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: First aid providers responding to opioid overdose
- Intervention: Education on response or care of an individual in an opioid overdose emergency
- Comparator: Any other or no specialized education
- Outcome: Any clinical or educational outcome; survival, first aid provided, skills, attitude, knowledge
- Study design: RCTs and nonrandomized studies (interrupted time series, controlled before-and-after studies, cohort studies) were included. Studies that did not specifically answer the question, unpublished studies (eg, conference abstracts, trial protocols), and studies only published in abstract form, unless accepted for publication, were excluded.
- Time frame: All years and all languages were included if there was an English abstract; literature search was updated to November 13, 2019.

Summary of Evidence

The full ScopRev is included in Supplement Appendix B-1.

We found insufficient data to warrant consideration of a SysRev comparing one educational intervention with another or with no education.

Eight[18–25] out of 59 studies finally identified, from a systematic search of 2057, used a comparator group. The 1 RCT reported first aid/naloxone use at 8 of 13 witnessed overdoses within 3 months after interventions; 2 of the 5 overdoses witnessed by an individual in the facilitator-trained group administered naloxone compared with 0 of 3 individuals in the comparison group who received only a pamphlet.[18]

Task Force Insights

The EIT Task Force identified several limitations in the evidence relating to opioid overdose education: inconsistent reporting of educational interventions makes comparison between studies challenging. The use of the Guideline for Reporting Evidence-Based Practice Educational Interventions and Teaching checklist for educational interventions would help standardize future analysis.[26]

With only 1 RCT[18] and 7 other studies with control groups,[19–25] a lack of experimental rigor limits comparison and the strength of any future recommendations.

First aid and survival outcomes were self-reported by people generally coming in for a refill of their prescription for naloxone. The verifiability of this data were not reported. A prospective means to validate self-reported use of first aid/naloxone in these emergencies should be developed. For example, if EMS was called, corroborating the status of the poisoned victim, naloxone administration, and outcome could help establish validity. This is challenging because there is debate about the need for hospitalization after reversal of the overdose.

Brief training (less than 15 minutes) for people who use opioids nonmedically without knowing

first aid skills appears beneficial for survival, perhaps because of personal and social experience with drugs. Stand-alone education (16–60 minutes) with skill training on administering first aid/naloxone for people who use opioids medically and nonmedically and for first responders is associated with improved outcomes for poisoned victims. The EIT Task Force found no evidence to change the current treatment recommendation.

Treatment Recommendation

This treatment recommendation from the BLS Task Force (below) is unchanged from 2015.[16,17]

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.

BLS INCLUDING AED TRAINING

Willingness to Perform Bystander CPR (EIT 626: ScopRev)

Rationale for Review

The 2010 CoSTR included a narrative review on this topic and described both positive and negative factors impacting the willingness of bystanders (both lay rescuers and healthcare providers) to provide CPR.[1,2] The 2015 CoSTR recommended the use of BLS training interventions that focus on high-risk populations, on the basis of their willingness to be trained and the fact that there is little harm and high potential benefit (strong recommendation, low-certainty evidence).[3,4]

This topic of willingness of bystanders to perform CPR was chosen for a 2020 ScopRev by the EIT Task Force because of the low incidence of provision of CPR and AED use by bystanders in most areas of the world.[27–30] Understanding the barriers and facilitators of bystander CPR and AED might lead to increased use of AEDs. These facilitators or barriers to performing CPR can be categorized into personal factors, CPR knowledge, and procedural issues.[31]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Out-of-hospital cardiac arrest (OHCA) bystanders (laypersons)
- Intervention: Factors increasing the willingness of bystanders to perform CPR
- Comparator: Factors that decrease the willingness of bystanders to perform CPR
- Outcome: Resulting in bystander CPR performance in an actual situation and willingness to provide CPR in an actual situation
- Study design: RCTs and nonrandomized studies (eg, interrupted time series, controlled before-and-after studies, cohort studies) investigating factors associated with an increase or decrease in bystander CPR in actual settings. Exclusion criteria were simulation studies, unpublished studies (eg, conference abstracts, trial protocols), letters, editorials, comments, case reports, SysRevs, any gray literature, or studies overlapping other ILCOR SysRevs/ScopRevs (eg, dispatcher-instructed CPR, community initiatives to improve CPR, etc).
- Time frame: All years and all languages were included if there was an English abstract; literature search was updated to January 4, 2020.

Summary of Evidence

The full ScopRev is included in Supplement Appendix B-2.

We found insufficient data to warrant consideration of a SysRev. Studies had significant heterogeneity among study populations, study methodologies, definitions of factors associated with willingness to provide CPR, outcome measures used, and outcomes reported. There were no RCTs and 18 observational studies[31–48] reporting factors associated with the willingness of actual bystanders to perform CPR.

Task Force Insights

The EIT Task Force decided to perform a ScopRev with a narrative summary to gain insight into factors associated with bystanders' actions in actual emergencies.

On the basis of this ScopRev and the discussion of the task force, it was suggested that although the 2010 treatment recommendation remains valid, the following proposals should be given further consideration:

- All BLS training, as well as regional and national education programs for lay rescuers, should include information to overcome potential barriers to CPR faced by lay rescuer (eg, panic, disagreeable physical characteristics of the victim, CPR on a female patient)
- When providing CPR instructions, EMS dispatchers should recognize lay rescuers' personal factors (emotional barriers and physical factors that may make them reluctant to perform CPR) and support them in starting and continuing CPR.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2010.[1,2]

To increase willingness to perform CPR, laypeople should receive training in CPR. This training should

include the recognition of gasping or abnormal breathing as a sign of cardiac arrest when other signs of life are absent. Laypeople should be trained to start resuscitation with chest compressions in adult and pediatric victims. If unwilling or unable to perform ventilation, rescuers should be instructed to continue compression-only CPR. EMS dispatchers should provide CPR instructions to callers who report cardiac arrest. When providing CPR instructions, EMS dispatchers should include recognition of gasping and abnormal breathing.

Prehospital Termination of Resuscitation (EIT 642: SysRev)

Rationale for Review

There has been no recent ILCOR recommendation addressing prehospital TOR rules after OHCA. Individual TOR rules have been developed and implemented in a variety of EMS systems, but there has been little study of the impact of these rules in prehospital practice. A SysRev addressing the question "Do prehospital TOR rules reliably predict in-hospital outcome following OHCA?" has been completed.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children in cardiac arrest who do not achieve return of spontaneous circulation (ROSC) in the out-of-hospital environment
- Intervention: TOR rules
- Comparator: In-hospital outcomes (died/survived), and favorable/unfavorable neurological outcome
- Outcome: Ability of TOR to predict death in hospital (critically important) and unfavorable neurological outcome (critically important)
- Study design:Cross-sectional or cohort studies are eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: All years and all languages were included if there was an English abstract. The search was completed on July 10, 2019.
- International Prospective Register of Systematic Reviews (PROSPERO) registration CRD42019 131010

Consensus on Science

The SysRev identified 34 studies[49–82] addressing the use of TOR rules. To facilitate improved insight into context and usefulness of the various TOR rules, studies were grouped as follows across the 2 outcomes: 1) prediction of death in-hospital and 2) prediction of poor neurological outcome.

For the Critically Important Outcome of Prediction of Death in Hospital

a) Studies reporting the derivation and internal validation of a TOR rule to predict death after arrival at hospital

Table 1. Sensitivity and Specificity of Derivation and Internal Validation Studies (Death)

Author (TOR Rule)	Sensitivity [95% CI]	Specificity [95% CI]
Bonnin et al, 1993 (no-ROSC TOR)[49]	0.77 [0.74, 0.79]	0.93 [0.86, 0.98]
Chiang et al, 2016 (tCPA TOR)[52]	0.17 [0.15, 0.20]	1.00 [0.91, 1.00]
Glober et al, 2019 (Glob1 TOR)[57]	0.14 [0.13, 0.16]	1.00 [0.98, 1.00]
Goto et al, 2019 (Goto1 TOR)[58]	0.11 [0.11, 0.11]	1.00 [0.99, 1.00]
Haukoos et al, 2004 (Haukoos1 TOR)[61]	0.68 [0.64, 0.71]	0.92 [0.78, 0.98]
Lee et al, 2019 (KOCARC1 TOR)[66]	0.31 [0.29, 0.32]	0.97 [0.96, 0.99]
Lee et al, 2019 (KOCARC2 TOR)[66]	0.32 [0.31, 0.34]	0.98 [0.96, 0.99]
Marsden et al, 1995 (Marsden TOR)[81]	0.58 [0.53, 0.63]	1.00 [0.03, 1.00]
Morrison et al, 2007 (ALS TOR)[67]	0.51 [0.50, 0.53]	1.00 [0.98, 1.00]
Petrie et al, 2001 (Petrie TOR)[82]	0.39 [0.38, 0.40]	0.98 [0.97, 0.99]
SOS-Kanto, 2017 (SOS_Kanto1 TOR)[76]	0.50 [0.49, 0.50]	0.95 [0.93, 0.96]
Verbeek et al, 2002 (BLS TOR)[77]	0.65 [0.62, 0.69]	1.00 [0.75, 1.00]
Yoon et al, 2019 (KoCARC1 TOR)[80]	0.53 [0.51, 0.54]	0.92 [0.89, 0.94]
Yoon et al, 2019 (KoCARC2 TOR)[80]	0.53 [0.51, 0.54]	0.89 [0.86, 0.91]
Yoon et al, 2019 (KoCARC3 TOR)[80]	0.39 [0.38, 0.41]	0.95 [0.93, 0.97]

ALS indicates advanced life support; BLS, basic life support; ROSC, return of spontaneous circulation; and TOR, termination of resuscitation.

b) Studies reporting external validation of a TOR rule to predict death after arrival at hospital

c) Studies reporting clinical validation of a TOR rule to predict death after arrival at hospital

Studies Reporting the Derivation and Internal Validation of a TOR Rule to Predict Death in Hospital. We identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 12 nonrandomized studies.[49,52,57,58,61,66,67,76,77,80–82] These studies derived and internally validated 15 distinct TOR rules to predict death after arrival at hospital. Studies by Lee et al[66] and Yoon et al[80] derived multiple TOR rules. There was considerable heterogeneity in patient population, clinician population, and EMS system design; thus, meta-analysis was not appropriate. Reported sensitivities and specificities of included papers are listed in Table 1.

Studies Reporting External Validation of a TOR Rule to Predict Death in Hospital. We identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from

Table 2. Sensitivity and Specificity of External Validation Studies (Death)

Author (TOR Rule)	Sensitivity [95% CI]	Specificity [95% CI]
Cheong et al, 2016 (BLS TOR)[50]	0.66 [0.64, 0.68]	0.93 [0.85, 0.98]
Cheong et al, 2016 (ALS TOR)[50]	0.28 [0.26, 0.30]	0.99 [0.93, 1.00]
Chiang et al, 2016 (BLS TOR)[51]	0.64 [0.62, 0.66]	0.74 [0.67, 0.80]
Chiang et al, 2016 (ALS TOR)[51]	0.58 [0.56, 0.59]	0.76 [0.69, 0.81]
Cone et al, 2005 (NAEMSP TOR)[53]	0.58 [0.54, 0.63]	1.00 [0.74, 1.00]
Diskin et al, 2014 (ALS TOR)[54]	0.27 [0.21, 0.32]	1.00 [0.91, 1.00]
Drennan et al, 2014 (uTOR)[55]	0.43 [0.42, 0.45]	0.89 [0.83, 0.94]
Fukada et al, 2014 (BLS TOR)[56]	0.70 [0.62, 0.78]	0.83 [0.36, 1.00]
Fukada et al, 2014 (ALS TOR)[56]	0.19 [0.08, 0.35]	1.00 [0.40, 1.00]
Goto et al, 2019 (BLS TOR)[58]	0.91 [0.91, 0.91]	0.62 [0.60, 0.63]
Grunau et al, 2017 (Shib 1 TOR)[59]	0.72 [0.71, 0.73]	0.91 [0.89, 0.93]
Grunau et al 2019 (Shib 1 TOR)[48,60]	0.90 [0.89, 0.91]	1.00 [1.00, 1.00]
Jordan et al, 2017 (uTOR)[62]	0.24 [0.16, 0.34]	1.00 [0.83, 1.00]
Kajinno et al, 2013 (BLS TOR)[63]	0.79 [0.79, 0.79]	0.88 [0.87, 0.88]
Kajinno et al, 2013 (ALS TOR)[63]	0.31 [0.30, 0.31]	0.92 [0.92, 0.93]
Kashiura et al, 2016 (BLS TOR)[64]	0.82 [0.81, 0.83]	0.92 [0.88, 0.94]
Kashiura et al, 2016 (ALS TOR)[64]	0.29 [0.28, 0.30]	0.91 [0.87, 0.95]
Kim et al, 2015 (BLS TOR)[65]	0.74 [0.72, 0.75]	0.70 [0.65, 0.74]
Lee et al, 2019 (BLS TOR)[66]	0.72 [0.70, 0.73]	0.78 [0.74, 0.81]
Lee et al, 2019 (ALS TOR)[66]	0.21 [0.20, 0.23]	0.97 [0.95, 0.98]
Lee et al, 2019 (Goto 1 TOR)[66]	0.39 [0.37, 0.40]	0.95 [0.93, 0.97]
Lee et al, 2019 (SOS-Kanto 1 TOR)[66]	0.27 [0.26, 0.28]	0.98 [0.97, 0.99]
Morrison et al, 2007 (BLS TOR)[67]	0.51 [0.50, 0.53]	1.00 [0.98, 1.00]
Morrison et al, 2009 (ALS TOR)[68]	0.33 [0.31, 0.35]	1.00 [0.97, 1.00]
Morrison et al, 2009 (uTOR)[68]	0.57 [0.55, 0.60]	1.00 [0.97, 1.00]
Ong et al, 2006 (BLS TOR)[70]	0.53 [0.52, 0.54]	1.00 [0.99, 1.00]
Ong et al, 2006 (Marsden TOR)[70]	0.19 [0.19, 0.20]	1.00 [0.99, 1.00]
Ong et al, 2006 (Petrie TOR)[70]	0.10 [0.09, 0.10]	1.00 [0.99, 1.00]
Ong et al, 2007 (BLS TOR)[71]	0.69 [0.67, 0.71]	0.81 [0.64, 0.93]
Ong et al, 2007 (Marsden TOR)[71]	0.65 [0.63, 0.67]	0.91 [0.75, 0.98]
Ong et al, 2007 (Petrie TOR)[71]	0.32 [0.30, 0.34]	0.94 [0.79, 0.99]
Sasson et al, 2008 (BLS TOR)[72]	0.51 [0.49, 0.52]	0.99 [0.97, 1.00]
Sasson et al, 2008 (ALS TOR)[72]	0.23 [0.22, 0.24]	1.00 [0.99, 1.00]
Skrifvars et al, 2010 (ALS TOR)[75]	0.27 [0.26, 0.27]	0.99 [0.97, 1.00]
Skrifvars et al, 2010 (ERC TOR)[75]	0.94 [0.94, 0.95]	0.95 [0.91, 0.97]
Skrifvars et al, 2010 (Helsinki TOR)[75]	0.55 [0.54, 0.56]	0.74 [0.68, 0.80]
SOS-Kanto 2017 (BLS TOR)[76]	0.78 [0.77, 0.79]	0.89 [0.86, 0.91]
SOS-Kanto 2017 (Goto 2 TOR)[76]	0.50 [0.49, 0.51]	0.95 [0.93, 0.96]
SOS-Kanto 2017 (SOS-Kanto 2)[76]	0.44 [0.43, 0.45]	0.97 [0.96, 0.98]
SOS-Kanto 2017 (SOS-Kanto 3)[76]	0.41 [0.40, 0.42]	0.99 [0.97, 0.99]
Verhaert et al, 2016 (ALS TOR)[78]	0.07 [0.05, 0.10]	1.00 [0.96, 1.00]
Yates et al, 2018 (uTOR)[79]	0.34 [0.27, 0.41]	0.17 [0.04, 0.41]
Yoon et al, 2019 (uTOR)[80]	0.70 [0.69, 0.72]	0.81 [0.77, 0.84]

ALS indicates advanced life support; BLS, basic life support; ERC, European Resuscitation Council; TOR, termination of resuscitation; and uTOR, universal termination of resuscitation.

24 nonrandomized studies.[50,51,53–56,58–60,62–68,70–72,75,76,78–80] These studies externally validated 14 distinct TOR rules to predict death after arrival at hospital. There was considerable heterogeneity across TOR variables, patient populations, clinician populations, and EMS systems; thus, meta-analysis was not appropriate. However, performance of 3 TOR rules (BLS TOR rule, ALS TOR rule, universal TOR rule) was reported in multiple papers (see below). Reported sensitivities and specificities of included papers are listed in Table 2.

We identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 13 nonrandomized studies[50,51,56,58,63–66,68,70–72,76] reporting the accuracy of the BLS TOR rule to predict in-hospital death. There was considerable heterogeneity across patient populations, clinician populations, and EMS systems; thus, meta-analysis was not appropriate. We calculated estimates of effect per 1000 patients based on the range of sensitivities, specificities, and prevalence in the studies (Table 2).

On the basis of the lowest prevalence of 88.3%,[66] the estimate of false positives (TOR rule predicts death, but patient will survive) per 1000 patients tested ranged from 0 to 36. On the basis of the highest prevalence of 98.6%,[71] the estimate of false positives per 1000 patients tested ranged from 0 to 4.

We identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 11 nonrandomized studies[50,51,54,56,63,64,66,68,72,75,78] reporting the accuracy of the ALS TOR rule to predict in-hospital death. There was considerable heterogeneity across patient populations, clinician populations, and EMS systems; thus, meta-analysis was not appropriate. We calculated estimates of effect per 1000 patients based on the range of sensitivities, specificities, and prevalence in the studies (Table 2).

On the basis of the lowest prevalence of 84.9%,[78] the estimate of false positives (TOR rule predicts death, but patient will survive) per 1000 patients tested ranged from 0 to 36. On the basis of the highest prevalence of 99.0%,[75] the estimate of false positives (TOR rule predicts death, but patient will survive) per 1000 patients tested ranged from 0 to 3.

We identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 6 nonrandomized studies[55,59,62,68,79,80] reporting the accuracy of the universal TOR rule to predict in-hospital death. There was considerable heterogeneity across patient populations, clinician populations, and EMS systems; thus, meta-analysis was not appropriate. We calculated estimates of effect per 1000 patients based on the range of sensitivities, specificities, and prevalence in the studies (Table 2). On the basis of the lowest prevalence of 82.0%,[62] the estimate of false positives (TOR rule predicts death, but patient will survive) per 1000 patients tested ranged from 0 to 149. On the basis of the highest prevalence of 97.6%,[55] the estimate of false positives (TOR rule predicts death, but patient will survive) per 1000 patients tested ranged from 0 to 9.

Studies Reporting Clinical Validation of a TOR Rule to Predict Death in Hospital. We identified very low-certainty evidence (downgraded for indirectness) from 1 nonrandomized study[69] reporting a clinical validation of the universal TOR rule to predict in-hospital death. Sensitivity was 0.64 (95% CI, 0.61–0.68), and specificity was 1.00 (95% CI, 0.92–1.00). Of 954 patients enrolled, the BLS TOR rule recommended transport in 367 cases. Of these, 44 survived to discharge and 323 died in hospital. Of the remaining 586, 388 had resuscitation terminated in the field. Of 198 cases transported to hospital despite termination being recommended, no patient survived.

For the Critically Important Outcome of Prediction of Poor Neurological Outcome

a) Studies reporting the derivation and internal validation of a TOR rule to predict poor neurological outcome
b) Studies reporting external validation of a TOR rule to predict poor neurological outcome
c) Studies reporting clinical validation of a TOR rule to predict poor neurological outcome

Table 3. Sensitivity and Specificity of Derivation and Internal Validation Studies (Poor Neurological Outcome)

Author (TOR Rule)	Sensitivity [95% CI]	Specificity [95% CI]
Glober et al, 2019 (Glob 2 TOR)[57]	0.19 [0.17, 0.21]	1.00 [0.98, 1.00]
Goto et al, 2019 (Goto 1 TOR)[58]	0.11 [0.10, 0.11]	1.00 [1.00, 1.00]
Haukoos et al, 2004 (Haukoos 2 TOR)[61]	0.57 [0.54, 0.61]	1.00 [0.79, 1.00]
Haukoos et al, 2004 (Haukoos 3 TOR)[61]	0.69 [0.66, 0.72]	1.00 [0.78, 1.00]
Haukoos et al, 2004 (Haukoos 4 TOR)[61]	0.69 [0.65, 0.72]	1.00 [0.48, 1.00]
Lee et al, 2019 (KOCARC 4 TOR)[66]	0.30 [0.28, 0.31]	1.00 [0.99, 1.00]
Lee et al, 2019 (KOCARC 5 TOR)[66]	0.31 [0.30, 0.33]	1.00 [0.99, 1.00]
Shibahashi et al, 2018 (Shib1 TOR)[74]	0.39 [0.38, 0.39]	0.95 [0.95, 0.96]
Shibahashi et al, 2018 (Shib2 TOR)[74]	0.59 [0.59, 0.59]	0.89 [0.88, 0.90]
Yoon et al, 2019 (KOCARC1 TOR)[80]	0.52 [0.50, 0.53]	0.99 [0.97, 1.00]
Yoon et al, 2019 (KOCARC2 TOR)[80]	0.52 [0.50, 0.53]	0.98 [0.96, 0.99]
Yoon et al, 2019 (KOCARC3 TOR)[80]	0.38 [0.37, 0.40]	1.00 [0.98, 1.00]

TOR indicates termination of resuscitation.

Studies Reporting the Derivation and Internal Validation of a TOR Rule to Predict Poor Neurological Outcome. We identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 6 nonrandomized studies[57,58,61,66,74,80] These studies derived and internally validated 12 distinct TOR rules to predict poor neurological outcome. Studies by Haukoos et al,[61] Lee et al,[66] Shibahashi et al,[74] and Yoon et al[80] derived multiple TOR rules. There was considerable heterogeneity in patient population, clinician population, and EMS system design; thus, meta-analysis was not appropriate. Reported sensitivities and specificities of included papers are listed in Table 3.

Studies Reporting External Validation of a TOR Rule to Predict Poor Neurological Outcome. We identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 9 nonrandomized studies[50,63–66,73,75,76,80]; externally validating 10 distinct TOR rules to predict poor neurological outcome. There was considerable heterogeneity across TOR rule variables, patient populations, clinician populations, and EMS systems; thus, meta-analysis was not appropriate. However, performance of 2 TOR rules (BLS TOR, ALS TOR) was reported in multiple papers (see below). Reported sensitivities and specificities of included papers are listed in Table 4.

We identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 6 nonrandomized studies[50,63–66,76] reporting the accuracy of the BLS TOR rule to predict poor neurological outcome. There was considerable heterogeneity across patient populations, clinician populations, and EMS systems; thus, meta-analysis was not appropriate. We calculated estimates of effect per 1000 patients based on the range of sensitivities, specificities, and prevalence in the studies (Table 4).

On the basis of the lowest prevalence of 92.1%,[66] the estimate of false positives (TOR predicts poor neurological outcome, but patient has favorable neurological outcome) per 1000 patients tested ranged from 0 to 6. On the basis of the highest prevalence of 98.0%,[50] the estimate of false positives per 1000 patients tested ranged from 0 to 1.

We identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and

Table 4. Sensitivity and Specificity of External Validation Studies (Poor Neurological Outcome)

Author (TOR Rule)	Sensitivity [95% CI]	Specificity [95% CI]
Cheong et al, 2016 (BLS TOR)[50]	0.66 [0.64, 0.68]	1.00 [0.92, 1.00]
Cheong et al, 2016 (ALS TOR)[50]	0.27 [0.25, 0.29]	1.00 [0.92, 1.00]
Kajino et al, 2013 (BLS TOR)[63]	0.78 [0.78, 0.78]	0.97 [0.96, 0.97]
Kajino et al, 2013 (ALS TOR)[63]	0.30 [0.30, 0.30]	0.98 [0.97, 0.99]
Kashiura et al, 2016 (BLS TOR)[64]	0.81 [0.80, 0.82]	0.97 [0.94, 0.99]
Kashiura et al, 2016 (ALS TOR)[64]	0.28 [0.27, 0.29]	0.94 [0.87, 0.98]
Kim et al, 2015 (BLS TOR)[65]	0.72 [0.71, 0.73]	0.90 [0.85, 0.94]
Lee et al, 2019 (BLS TOR)[66]	0.71 [0.70, 0.72]	0.93 [0.89, 0.95]
Lee et al, 2019 (ALS TOR)[66]	0.21 [0.20, 0.22]	0.99 [0.97, 1.00]
Lee et al, 2019 (Goto 1 TOR)[66]	0.27 [0.26, 0.28]	0.98 [0.97, 0.99]
Lee et al, 2019 (SOS-Kanto 1 TOR)[66]	0.39 [0.37, 0.40]	0.95 [0.93, 0.97]
SOS-Kanto 2017 (BLS TOR)[76]	0.77 [0.76, 0.78]	0.96 [0.94, 0.98]
SOS-Kanto 2017 (ALS TOR)[76]	0.49 [0.48, 0.50]	0.98 [0.96, 0.99]
SOS-Kanto 2017 (SOS-Kanto 1)[76]	0.49 [0.48, 0.50]	0.97 [0.95, 0.99]
SOS-Kanto 2017 (SOS-Kanto 2)[76]	0.44 [0.43, 0.44]	0.99 [0.97, 1.00]
SOS-Kanto 2017 (SOS-Kanto 3)[76]	0.40 [0.39, 0.41]	0.99 [0.98, 1.00]
Ruygrok et al, 2008 (ALS TOR)[73]	0.24 [0.21, 0.27]	1.00 [0.92, 1.00]
Ruygrok et al, 2008 (uTOR)[73]	0.34 [0.31, 0.38]	1.00 [0.92, 1.00]
Ruygrok et al, 2008 (Haukoos 3 TOR)[73]	0.06 [0.04, 0.08]	1.00 [0.92, 1.00]
Skrifvars et al, 2010 (ALS TOR)[75]	0.27 [0.26, 0.27]	1.00 [0.97, 1.00]
Skrifvars et al, 2010 (ERC TOR)[75]	0.94 [0.94, 0.95]	0.96 [0.93, 0.98]
Skrifvars et al, 2010 (Helsinki TOR)[75]	0.55 [0.54, 0.56]	0.79 [0.73, 0.85]
Yoon et al, 2019 (uTOR)[80]	0.69 [0.68, 0.71]	0.94 [0.91, 0.96]

ALS indicates advanced life support; BLS, basic life support; ERC, European Resuscitation Council; TOR, termination of resuscitation; and uTOR, universal termination of resuscitation rule.

imprecision) from 6 nonrandomized studies[50,63,64,66,73,75] reporting the accuracy of the ALS TOR rule to predict poor neurological outcome. There was considerable heterogeneity across patient populations, clinician populations, and EMS systems; thus, meta-analysis was not appropriate. We calculated estimates of effect per 1000 patients based on the range of sensitivities, specificities, and prevalence in the studies.

On the basis of the lowest prevalence of 92.1%,[66] the estimate of false positives (TOR rule predicts poor neurological outcome, but patient has favorable neurological outcome) per 1000 patients tested ranged from 0 to 6. On the basis of the highest prevalence of 98.0%,[50] the estimate of false positives per 1000 patients tested ranged from 0 to 1.

Studies Reporting Clinical Validation of a TOR Rule to Predict Poor Neurological Outcome. We identified very low-certainty evidence (downgraded for indirectness) from 1 nonrandomized study[69] reporting a clinical validation of the universal TOR rule to predict poor neurological outcome. Sensitivity was 0.63 (95% CI, 0.61–0.68), and specificity was 1.00 (95% CI, 0.92–1.00). Of 953 patients included, the BLS TOR rule recommended transport in 367 cases. Of these, 17 survived with poor neurological outcome (Cerebral Performance Category 3 or 4) and 323 died in hospital.

Treatment Recommendations

We conditionally recommend the use of TOR rules to assist clinicians in deciding whether to discontinue resuscitation efforts out of hospital or to transport to hospital with ongoing CPR (conditional recommendation/very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-1. The majority of studies describe either the derivation and internal validation of individual TOR rules or the external validation of previously published TOR rules. We identified only 1 study addressing clinical validation (the use of a TOR rule in clinical practice) of a TOR rule by emergency medical technicians with defibrillators. Robust evidence to support the widespread implementation of TOR rules in clinical practice is therefore weak. Despite several studies reporting a specificity of 1.0, the task force acknowledges that implementation of a TOR rule, in isolation, may result in missed survivors.

The task force recognizes that TOR is common practice in many EMS systems. We support the principle of discontinuing resuscitation when treatment is futile because it preserves the dignity of the recently deceased, reduces risk for EMS providers, and protects scarce healthcare resources. However, the task force also acknowledges that identification of futile cases is challenging and is often informed by both clinical guidelines and clinician insight.

The task force advocates the adoption of TOR guidelines that take into account the patients' prior wishes and/or expectations, consideration of patient preexisting comorbidities, and quality of life both before and after the cardiac arrest event. Such TOR guidelines may be informed by the inclusion of an evidence-based TOR rule; however, the task force believes a TOR rule should not be the sole determinant of when to discontinue resuscitation.

In those EMS systems that do implement prehospital TOR rules, the EMS system must ensure that there is no conflict with legislation prohibiting nonphysicians from discontinuing resuscitation and must have appropriate governance arrangements to monitor practice. Where an evidence-based TOR rule is included to inform practice, the EMS system should consider the training needs of EMS crews in communicating bad news and supporting the relatives of the recently deceased, in addition to consideration of the generalizability of the chosen TOR rule to its healthcare system. In some healthcare systems, it may be appropriate for EMS systems to communicate with organ donation teams before implementing change.

The task force acknowledges that prehospital TOR may not be feasible in some instances. In some locations, the legal infrastructure may require EMS clinicians to provide resuscitation in all but a very few circumstances (eg, in the presence of rigor mortis). In other areas, it may not be culturally acceptable for nonphysicians to make a clinical decision to stop resuscitation in the prehospital environment. Where this is the case, or where clinical governance arrangements are insufficient to monitor practice, we suggest transport to hospital with ongoing CPR may be preferable.

The 2010 CoSTR recommended validated TOR rules in adults,[1,2] but the topic was not addressed in 2015. This 2020 CoSTR for EIT softens the recommendation, taking into consideration the social acceptability of excluding potential survivors from in-hospital treatment and the very limited clinical validation of such rules.

Knowledge Gaps

There is little evidence addressing use of TOR rules in clinical practice. Studies are required to address the following:

- Use of TOR rules in actual clinical practice
- Compliance with out-of-hospital TOR rules
- Implementation strategies of TOR for EMS that are based on evidence
- Health economic implications of TOR implementation
- Societal perceptions and acceptance of TOR rules

- TOR rules specific for children
- Impact of TOR rules on non–heart-beating organ donation

In-Hospital TOR (EIT 4002: SysRev)

Rationale for Review

There are no current ILCOR recommendations on clinical decision rules to terminate resuscitation during in-hospital cardiac arrest (IHCA). Almost half of all in-hospital resuscitation attempts are terminated without ROSC.[83] Knowing when to terminate resuscitation is, therefore, an important clinical question. The EIT Task Force defined *clinical decision rules* as cardiac arrest characteristics to be applied during resuscitation to predict survival (ROSC, survival to hospital discharge) and thereby terminate resuscitation if deemed futile. Measures of prediction were negative predictive value, sensitivity, specificity, and positive predictive value.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with IHCA
- Intervention: Use of any clinical decision rule
- Comparator: No clinical decision rule
- Outcome: No ROSC, death before hospital discharge, survival with unfavorable neurological outcome, and death within 30 days
- 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), animal studies, simulation studies, and studies not in English were excluded.
- Time frame: All years until November 11, 2019

Consensus on Science

We found 3 studies investigating the usability of the UN10 rule to predict survival to hospital discharge on the basis of the unwitnessed arrest, a nonshockable rhythm, and 10 minutes of CPR without ROSC.[84–86] All studies were cohort studies, and no studies used randomization or prospective implementation of a clinical decision rule.

For the critical outcomes of positive predictive value and sensitivity in predicting death before hospital discharge for adults with IHCA, we identified very low-certainty evidence from 3 historical cohort studies.[84–86] investigating the UN10 rule (downgraded for risk of bias, indirectness, imprecision, and inconsistency). Because of clinical heterogeneity in study cohorts, no meta-analysis was conducted. Positive predictive values and sensitivities are reported in Table 5.

For the important outcomes of specificity and negative predictive value in predicting death before hospital discharge for adults with IHCA, we identified very low-certainty evidence from 3 historical cohort studies.[84–86] investigating the UN10 rule (downgraded for risk of bias, indirectness, imprecision, and inconsistency). Specificities and negative predictive values are reported in Table 5.

For the important outcomes of positive predictive value, specificity, sensitivity, and negative predictive values in predicting survival to hospital discharge with unfavorable neurological outcome for adults with IHCA, we identified very low-certainty evidence from 1 observational study[86] investigating the UN10 rule (downgraded for risk of bias, indirectness, and imprecision). The study reported a positive predictive value of 95.2% (95% CI, 94.9%–95.6%), a specificity of 95.3% (95% CI, 95.0%–95.6%), a sensitivity of 18.8% (95% CI, 18.5%–19.0%), and a negative predictive value of 19.1% (95% CI, 18.8%–19.3%).[86]

We identified no studies predicting no ROSC or death within 30 days. We identified no studies on children with IHCA.

Table 5. Positive Predictive Values, Specificity, Sensitivity, and Negative Predictive Values for Prediction of Death Before Hospital Discharge

	Positive Predictive Value	Specificity	Sensitivity	Negative Predictive Value
Van Walraven, 1999[84]	100% (95% CI, 97.1% to 100%)	100% (95% CI, 97.1% to 100%)	12.2% (95% CI, 10.3%–14.4%)	10.8% (95% CI, 8.9–12.8%)
Van Walraven, 2001[85]	98.9% (95% CI, 96.5%–99.7%)	99.1% (95% CI, 97.1%–99.8%)	14.4% (95% CI, 12.4%–16.0%)	17.0% (95% CI, 15.3–18.7)
Petek, 2019[86]	93.7% (95% CI, 93.3%–94.0%)	94.6% (95% CI, 94.3%–94.9%)	19.1% (95% CI, 18.8%–19.3%)	22.0% (95% CI, 21.9%–22.0%)

Treatment Recommendations

We did not identify any clinical decision rule that was able to reliably predict death after IHCA. We recommend against using the UN10 rule as a sole strategy to terminate in-hospital resuscitation (strong recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-2. In making this recommendation, the EIT Task Force considered the following: several other scores have been developed that aim at predicting the chance of survival on the basis of prearrest factors only, including the GO-FAR score[87] and comorbidity scores.[88] While these scores may be suitable to trigger do-not-resuscitate discussions, they are not aimed at deciding when to terminate resuscitation during a resuscitation attempt and were therefore not included in this review.

The Resuscitation Predictor Scoring Scale[89] aimed to identify patients with low likelihood of surviving a cardiac arrest after 15 minutes of resuscitation. This score was not included in the review because the score aimed

at identifying patients with low likelihood but not patients with no likelihood of surviving the cardiac arrest.

Several studies (primarily prehospital) have looked at other factors such as end-tidal carbon dioxide (CO_2) and echocardiographic findings to terminate resuscitation. These have been included in reviews by the ILCOR ALS Task Force. End-tidal carbon dioxide and echocardiographic findings may be considered together with other factors to decide when to terminate in-hospital resuscitation.

All identified studies were based on historical cohorts and carry a risk of a self-fulfilling prophecy bias as clinicians may have terminated resuscitation on patients who potentially had a chance of surviving in the observed studies. Prospective studies are needed to reliably assess the effect of such clinical decision rules.

Two of the studies[84,85] included patients resuscitated in the 1980s and 1990s, when resuscitation practices differed from present time and when reported survival rates were lower than now.[90] The third study[86] included patients resuscitated between 2000 and 2016, but a large proportion of the arrests occurred before 2010. As previously stated, survival rates are now higher than in previous decades.

The task force prioritized a perfect positive predictive value (no survivors among those predicted to be dead) for any clinical prediction rule because of the risk of terminating resuscitation of a patient who could have survived. The task force discussed that it is reasonable not to terminate resuscitation as long as the patient has a shockable rhythm. No single clinical factor or no single decision rule has been identified as sufficient to terminate resuscitation. Therefore, the EIT Task Force members suggested that a decision to terminate an IHCA resuscitation should continue to be based on a combination of factors that are known to be associated with a low chance of survival, eg, end-tidal carbon dioxide, cardiac standstill on echocardiography, duration of resuscitation, patient age, and patient comorbidities.

ILCOR has not previously made a treatment recommendation on an in-hospital TOR rule. Unfortunately, the existing evidence is insufficient to recommend an in-hospital TOR rule. Clinicians have to rely on clinical examination, their experience, and the patient's conditions and wishes to inform their decision to terminate resuscitation efforts.

Knowledge Gaps

- There are no clinical decision tools to predict the absence of ROSC during in-hospital resuscitation.
- There are clinical decision tools that combine existing decision tool elements such as resuscitation duration and cardiac arrest rhythm with end-tidal carbon dioxide and/or findings on cardiac ultrasound.
- No studies were found on the use of a clinical decision tool to terminate resuscitation for pediatric IHCA.
- There is a lack of prospective clinical validation studies and randomized trials investigating the use of a clinical decision tool to terminate resuscitation during IHCA.
- It is unknown how the use of a clinical decision tool affects resuscitation practices, cost benefit, or how it affects survival outcomes.

Deliberate Practice and Mastery Learning (EIT 4004: EvUp)

One EvUp (Supplement Appendix C-1) identified several studies that suggest the need for consideration of a SysRev, especially because no former assessment of this educational strategy has been done by ILCOR and no treatment recommendation has been made as of January 31, 2020.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Students/healthcare providers taking BLS or ALS training
- Intervention: Use of deliberate practice and/or mastery learning
- Comparator: No such teaching strategies
- Outcome: Improve knowledge/skill performance at course conclusion, knowledge/skill retention beyond course conclusion, clinical performance in actual resuscitations, or patient outcomes (critically important); intact neurological outcome (critically important)
- Study design: Cross-sectional or cohort studies were eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: All articles published before 2013 were excluded, and all languages were included if there was an English abstract. The search was completed on October 22, 2019.

An EvUp was conducted for 2020 to identify recent published evidence. A search conducted in PubMed yielded 30 studies, and 12 were identified as relevant. See the complete EvUp in Supplement Appendix C-1.

Treatment Recommendation

The EvUp did not enable a treatment recommendation to be made.

Layperson Training (EIT 4009: EvUp)

An EvUp was performed (Supplement Appendix C-2) and identified several studies suggesting the need to consider a SysRev. To date, no SysRev on the training of laypeople has been done by ILCOR, and no treatment

recommendation has been made as of January 31, 2020.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Laypeople (nonprofessional responders)
- Intervention: Participating in CPR training
- Comparator: Compared with no training
- Outcome: Change willingness to perform CPR in actual resuscitations, skill performance quality, and/or patient outcomes
- Study design: Cross-sectional or cohort studies are eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: All articles published between January 1, 2018, and October 10, 2019, and all languages were included if there was an English abstract.

A search conducted in PubMed yielded 372 studies, and 25 were identified as relevant. See Supplement Appendix C-2 for the full EvUp.

Treatment Recommendation

The EvUp did not enable a treatment recommendation to be made.

Timing for Retraining (EIT 628: EvUp)

The topic of timing for retraining was last reviewed in 2015.[3,4] An EvUp was performed (Supplement Appendix C-3) with several studies identified that suggest the need for consideration of a SysRev. The 2015 treatment recommendation[3,4] will then be reevaluated.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Students who are taking BLS courses
- Intervention: Any specific interval for update or retraining
- Comparator: Compared with standard practice (ie, 12 or 24 monthly)
- Outcome: Improve patient outcomes, skill performance in actual resuscitations, skill performance at 1 year, skill performance at course conclusion, and cognitive knowledge
- Study design: Cross-sectional or cohort studies are eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: All articles published between January 1, 2014, and January 7, 2020, and all languages were included if there was an English abstract

An EvUp was conducted for 2020 by the RCA. A search conducted in PubMed and Embase yielded 1002 studies, and 5 were identified as relevant. See Supplement Appendix C-3 for the complete EvUp.

Treatment Recommendation

The treatment recommendation from 2015 (below) is unchanged.[3,4]

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 months 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).

MEASURING IMPLEMENTATION/ PERFORMANCE IN COMMUNITIES, CARDIAC ARREST CENTERS

System Performance Improvements (EIT 640: SysRev)

Rationale for Review

The task force considered improvements at the system level of health care that would have the greatest potential to increase the survival rate after cardiac arrest. Studies associated with system performance improvement for personnel in organizations or systems caring for patients with cardiac arrest were included. *System performance improvement* was defined as hospital-level, community-level, or country-level improvement related to structure, care pathways, process, and quality of care.

Population, Intervention, Comparator, and Outcome

- Population: Resuscitation systems who are caring for patients in cardiac arrest in any setting
- Intervention: System performance improvements
- Comparator: Compared with no system performance improvements
- Outcome: Survival with favorable neurological outcome at discharge, survival to hospital discharge, skill performance in actual resuscitations, survival to admission, and system-level improvement
- Study Designs: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies, case-control studies). All years and all languages were included as long as there was an English abstract associated with system performance improvement for personnel in organizations or systems caring for patients with cardiac arrest. *System performance improvement* is defined as hospital-level, community-level, or country-level improvement related to structure, care pathways, process, and quality of care.
- Exclusion: Unpublished studies (eg, conference abstracts, trial protocols), letters, editorials, comments, and case reports.
- Time Frame: The new search included studies from November 1, 2013, to November 14, 2019.

Table 6. Interventions Among Included Studies

Study	Interventions
Hostler, 2011[91] (RCT) (OHCA)	Real-time audiovisual feedback on CPR provided by the monitor-defibrillator among EMS from 3 sites within the Resuscitation Outcomes Consortium in the United States (King County, Washington; Pittsburgh; and Westmoreland County, Pennsylvania) and Canada (Thunder Bay, Ontario)
Adabag, 2017[117] (OHCA)	Minnesota Resuscitation Consortium, a statewide integrated resuscitation program, established in 2011, to provide standardized, evidence-based resuscitation and postresuscitation care
Anderson, 2016[103] (IHCA)	Assess the hospital process composite performance score for IHCA using 5 guideline-recommended process measures
Bradley, 2012[109] (IHCA)	Get With The Guidelines-Resuscitation (formerly known as the *National Registry of CPR*), a data registry and quality improvement program for IHCA supported by the AHA
Couper, 2015[101] (IHCA)	Phase 1: Quality of CPR and patient outcomes were measured with no intervention implemented Phase 2: 1. Hospital 1: staff received real-time audiovisual feedback 2. Hospital 2: staff received real-time audiovisual feedback supplemented by postevent debriefing 3. Hospital 3: no intervention was implemented
Davis, 2015[92] (IHCA)	Advanced resuscitation training program implementation since Spring 2007
Del Rios, 2019[105] (OHCA)	System-wide initiatives in Chicago since 2013, including telephone-assisted and community CPR training programs; high-performance CPR and team-based simulation training; new postresuscitation care and destination protocols; and case review for EMS providers
Edelson, 2008[112] (IHCA)	Resuscitation with actual performance-integrated debriefing: weekly debriefing sessions of the prior week's resuscitations, between March 2006 and February 2007, reviewing CPR performance transcripts obtained from a CPR-sensing and feedback-enabled defibrillator
Ewy, 2013[108] (OHCA)	Continuous quality improvement, instituted cardiocerebral resuscitation in community and EMS. Community: prompt recognition and activation, CO-CPR, teaching and advocating CO-CPR, CO-CPR for healthcare providers, DA-CPR. EMS: endotracheal intubation delayed, passive ventilations, epinephrine administration
Grunau, 2018[106] (OHCA)	British Columbia OHCA quality improvement strategy, since 2005
Hopkins, 2016[98] (OHCA)	System-wide restructuring high-quality CPR program (CPR Quality Improvement Initiatives, Simplified Medication Algorithm Adopted, EMS Crew Team Training) from the Salt Lake City Fire Department in September 2011
Hubner, 2017[99] (OHCA)	Postresuscitation feedback protocol (implemented on August 1, 2013)
Hunt, 2018[114] (IHCA)	Study of the quality of chest compressions delivered to children during a 3-year period simultaneous with development and implementation of a resuscitation-quality bundle (evolved into the CODE ACES2)
Hwang, 2017[93] (OHCA)	System-wide CPR program in 2011, including DA-CPR protocol, medical control for regional EMS, provision of high-quality ACLS with capnography and extracorporeal CPR, and the standard post–cardiac arrest care protocol
Kim, 2017[96] (OHCA)	Phase 1 (2009–2011): after implementing 3 programs (national OHCA registry, obligatory CPR education, and public report of OHCA outcomes) Phase 2 (2012–2015): after implementing 2 programs (telephone-assisted CPR and EMS quality assurance program)
Knight, 2014[104] (IHCA)	Code team members were introduced to Composite Resuscitation Team Training and continued training throughout the intervention period (January 1, 2010–June 30, 2011)
Lyon, 2012[116] (OHCA)	Resuscitation symposium, collecting transthoracic impedance data via telemetry from ambulance service defibrillators, postresuscitation feedback, and monthly resuscitation training
Nehme, 2015[111] (OHCA)	Surveillance in the Australian Southeastern state of Victoria for patients with OHCA of presumed cardiac pathogenesis, with CPR awareness program, telephone-assisted CPR instruction, and prehospital hypothermia
Olasveengen, 2007[115] (OHCA)	Providing CPR performance evaluation
Park, 2018[97] (OHCA)	Implementation of 3 new CPR programs in Seoul Metropolitan City in January 2015: 1. A high-quality DA-CPR program 2. A multitier response program using fire engines or BLS vehicles 3. A feedback CPR program with professional recording and feedback of CPR process
Pearson, 2016[94] (OHCA)	Implementation of team-focused CPR; widespread incorporation began in 2011 with an optional statewide protocol introduced in July 2012
Spitzer, 2019[110] (IHCA)	"Pit crew" model for IHCA resuscitation, including ACLS training and mock code events
Sporer, 2017[95] (OHCA)	Specific implementation of specific therapies focused on perfusion during CPR and cerebral recovery after ROSC (mechanical adjuncts and protective postresuscitation care with in-hospital therapeutic hypothermia)
Stub, 2015[102] (OHCA)	Assess composite performance score with 5 selected individual ILCOR/AHA guideline recommended, hospital based postresuscitative therapies performance measures
van Diepen, 2017[107] (OHCA)	HeartRescue project, a multistate public health initiative, established in 5 states (Arizona, Minnesota, North Carolina, Pennsylvania, and Washington) in 2010

(*Continued*)

Table 6. Continued

Study	Interventions
Weston, 2017[113] (OHCA)	Initiation of the individualized CPR feedback program
Wolfe, 2014[100] (IHCA)	Structured, quantitative, audiovisual, interdisciplinary debriefing of chest compression events with frontline providers; real-time feedback in actual resuscitation in both periods

ACLS indicates advanced cardiovascular life support; AHA American Heart Association; BLS, basic life support; CO-CPR, chest compression–only CPR; CPR, cardiopulmonary resuscitation; DA-CPR, dispatcher-assisted CPR; EMS, emergency medical services; IHCA, in-hospital cardiac arrest; ILCOR, International Liaison Committee on Resuscitation; OHCA, out-of-hospital cardiac arrest; RCT, randomized controlled trial; and ROSC, return of spontaneous circulation.

The studies included in the 2015 SysRev[3,4] were reviewed against the new inclusion/exclusion criteria and included where appropriate.

Consensus on Science

The interventions among the studies are summarized in Table 6. For the critical outcome of survival with favorable neurological outcome at discharge, we identified moderate-certainty evidence from 1 cluster-randomized trial[91] (downgraded for imprecision) and very low-certainty evidence from 18 non-RCTs[92–109] (downgraded for risk of bias). Among these studies, different interventions for system performance improvement were implemented in different contexts (IHCA versus OHCA); the heterogeneity of the studies precludes any meta-analysis. Thirteen of these studies[92–97,99,100,102,103,105,106,108] showed an association of significantly higher chance of survival with favorable neurological outcome at discharge with implementation of interventions for system performance improvement. The other 6 studies,[91,98,101,104,107,109] including 1 cluster-randomized trial,[91] showed no significant improvement after interventions were implemented.

For the critical outcome of survival to hospital discharge, we identified moderate-certainty evidence from 1 cluster-randomized trial[91] (downgraded for imprecision) and very low-certainty evidence from 21 non-RCTs[92–112] (downgraded for risk of bias). The heterogeneity of the studies precludes any meta-analysis. Fourteen of these studies[92–94,96,97,99,100,102–106,108,111] showed an association of significantly higher chance of survival to hospital discharge with implementation of interventions for system performance improvement. The other 8 studies,[91,95,98,101,107,109,110,112] including 1 cluster-randomized trial,[91] showed no significant improvement after interventions were implemented.

For the important outcome of skill performance in actual resuscitations, we identified moderate-certainty evidence from 1 cluster-randomized trial[91] (downgraded for risk of bias) and very low-certainty evidence from 13 non-RCTs[93,99–101,104,106,109,110,112–116] (downgraded for risk of bias). The heterogeneity of the studies precludes any meta-analysis. The interventions of these studies all consisted of strategies to improve the quality of resuscitation, including skills of BLS and ALS. Twelve of these studies,[91,93,99,100,104,106,109,110,112–114,116] including 1 cluster-randomized trial,[91] reported that rescuers had significantly improved skill performance in actual resuscitations after interventions were implemented. The other 2 studies[101,115] showed no significant improvement after interventions were implemented.

For the important outcome of survival to admission, we identified moderate-certainty evidence, from 1 cluster-randomized trial[91] (downgraded for imprecision) and very low-certainty evidence from 5 non-RCTs[94,95,98,105,111] (downgraded for risk of bias). The heterogeneity of the studies precludes any meta-analysis. Three of these studies[94,105,111] reported that patients had significantly higher chance of survival to admission after interventions for system performance improvement were implemented. The other 3 studies,[91,95,98] including 1 cluster-randomized trial,[91] showed no significant improvement after interventions were implemented.

For the important outcome of system-level improvement, we identified very low-certainty evidence (downgraded for risk of bias) from 11 non-RCTs.[92,93,95–98,105–107,111,117] The heterogeneity of the studies precludes any meta-analysis. All studies included individual interventions to improve specific system-level variables, and all studies achieved all or partial goals. These system-level variables included rate of bystander CPR or use of AEDs, rate of prehospital or in-hospital therapeutic hypothermia, and the use of automatic CPR devices and CPR feedback devices.

Treatment Recommendations

We recommend that organizations or communities that treat cardiac arrest evaluate their performance and target key areas with the goal to improve performance (strong recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-3. The EIT Task Force recognizes that the evidence in support of this recommendation comes mostly from studies of moderate to very low certainty of evidence. However, the majority of studies reported that interventions to improve system performance not only improved system-level variables and skill performance in actual resuscitations among rescuers but also clinical outcomes of patients with OHCA or IHCA, such as

survival to hospital discharge and survival with favorable neurological outcome at discharge.

Such interventions need money, personnel, and stakeholder buy-in to improve system performance. Some systems may not have adequate resources to implement system performance improvement. In making this recommendation, the EIT Task Force places increased value on the benefits of system performance improvement, which have no known risks, given our knowledge that system performance improvement could show substantial benefit.

In 2010, the EIT treatment recommendation stated the insufficiency of the evidence to make recommendations supporting or refuting the effectiveness of specific performance measurement interventions to improve processes of care and/or clinical outcomes in resuscitation systems.[1,2] In 2015, a suggestion was made to use performance measurement and quality improvement initiatives in organizations that treat cardiac arrest on the basis of a weak recommendation and very low-certainty evidence.[3,4] The evidence evaluation in 2020 led to a recommendation to evaluate performance, with the goal of improving performance (strong recommendation, very low-certainty evidence).

Knowledge Gaps

- Identify the most appropriate strategy to improve system performance.
- Better understand the influence of local community and organizational characteristics.
- Evaluate the cost-effectiveness of the individual interventions for improving system performance.

Community Initiatives to Promote BLS Implementation (EIT 641: ScopRev)

Rationale for Review

This evidence evaluation is an update from the 2010 CoSTR.[1,2] In 2015, a SysRev addressed the crucial role of communities in providing and promoting bystander CPR.[3,4] Because several specific interventions have been investigated, the EIT Task Force decided to look into how community initiatives promote BLS implementation. For the purpose of this review, the term *community* was defined as the general population of the studied area (ie, a group of neighborhoods, 1 or more cities/towns or regions, a part of or a whole nation) in which individuals can act as potential witnesses or bystanders of a cardiac arrest (eg, a group of populations with no duty to respond in case of a cardiac arrest). The role of healthcare providers or first responders with any duty to respond was excluded. The term *initiative* includes all interventions aimed at increasing the engagement of the community in providing BLS, including early defibrillation.

Interventions improving the community response to cardiac arrest are evaluated in other specific PICOs of the 2020 evidence evaluation process—like dispatcher-assisted CPR or telephone-CPR; public access defibrillator programs and AED dissemination; simplification of CPR protocols (ie, chest compression–only CPR); and mobile apps to localize and engage first responders and/or the nearest AED—and are not addressed in this review.

The aim of this SysRev was to assess the impact of any other intervention involving the community, which can affect BLS implementation in terms of bystander CPR and other consistent clinical outcomes. Because of the high heterogeneity among found studies, the task force considered a ScopRev with a narrative description of the results as an appropriate way to summarize the results of this evidence evaluation.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Within the general population of children and adults suffering an OHCA
- Intervention: Community initiatives to promote BLS implementation
- Comparator: Current practice
- Outcome: Survival to hospital discharge with good neurological outcome, survival to hospital discharge, ROSC, time to first compressions, bystander CPR rate, and proportion of population trained
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion.
- Time Frame: No limit; search ended November 10, 2019

Summary of Evidence

The complete ScopRev is included in Supplement Appendix B-3.

Of the 17 studies identified, 7 had a cross-sectional design,[48,118–123] 5 were before-and-after studies,[93,124–127] 4 were cohort studies,[128–131] and 1 was an RCT.[132] All OHCA cases included adult populations only. The main settings where the interventions took place were workplaces, schools, governmental offices, major civic events, and community-shared spaces.

Task Force Insights

Bystander CPR rate was reported in nearly all the studies, and almost all reported a benefit with implementation of community initiatives. This was more pronounced with bundled interventions than with training or mass media, but only 40% of studies reported an increase in survival at hospital discharge. Studies assessing bundled interventions also reported other outcomes that could

not be included in the report, because the outcomes could not be associated with a specific intervention.

On the basis of the results of our review, we propose a SysRev be conducted, because it appears that the implementation of community initiatives such as CPR training involving a large portion of the population or bundle of interventions may improve the layperson bystander CPR rate.

Treatment Recommendation

The treatment recommendation (below) remains unchanged from 2015.[3,4]

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).

Cardiac Arrest Centers (EIT 624: SysRev, 2019 CoSTR)

Cardiac arrest centers were considered hospitals providing evidence-based postresuscitation treatments, namely targeted temperature management and cardiac intervention (eg, coronary angiography).[14,15] A SysRev on this topic has been published[133] and was included in the 2019 CoSTR summary.[5,6]

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults with attempted resuscitation after nontraumatic IHCA or OHCA
- Intervention: Treatment at a specialized cardiac arrest center
- Comparator: Treatment in a healthcare facility not designated as a specialized cardiac arrest center
- Outcome: 30-day survival with favorable neurological outcome (defined as Cerebral Performance Category 1 or 2, modified Rankin Scale score 0–3), survival at hospital discharge with favorable neurological outcome, survival at 30 days, and survival at hospital discharge and ROSC after hospital admission
- Study designs: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) were excluded, as well as studies reporting pediatric cardiac arrests (18 years old or younger) and cardiac arrest secondary to trauma.
- Time frame: All years and all languages are included, provided there was an English abstract. Unpublished studies (eg, conference abstracts, trial protocols) were excluded. Literature search updated to the August 1, 2018.

Treatment Recommendations

We suggest adult patients with nontraumatic OHCA be cared for in cardiac arrest centers rather than in non–cardiac arrest centers in settings where this can be implemented (weak recommendation, very low-certainty evidence).

For patients with IHCA, we found no evidence to support an EIT and ALS Task Force recommendation for or against the intervention.

For patient subgroups with either shockable or nonshockable initial cardiac rhythm, the current evidence is inconclusive, and confidence in the effect estimates is currently too low to support a separate EIT and ALS Task Force recommendation. For regional triage of OHCA patients to a cardiac arrest center by primary EMS transport or secondary interfacility transfer subgroups, the current evidence is inconclusive and confidence in the effect estimates is currently too low to support a separate EIT and ALS Task Force recommendation.[5,6]

Out-of-Hospital CPR Training in Low-Resource Settings (EIT 634: ScopRev)

Rationale for Review

Scientific statements and treatment recommendations have in the past been formulated from a perspective of an ideally resourced environment. Little attention has been paid to the applicability of statements from such high-resource or high-income areas in the daily practice of lower-income countries and/or lower-resource emergency care systems. In many parts of the world, the standard of care available in high-resource settings is unavailable because of lack of money. For example, the absence of an EMS system or the low-quality performance of an EMS system[134–137] or an EMS system under development[138] are barriers to the implementation of resuscitation guidelines. ILCOR's aim of creating internationally valid statements should consider that recommendations should also support systems with more limited resources.[139] This ScopRev aims to raise awareness of gaps in emergency care services around the world, to identify gaps in the literature, and to suggest future research priorities to address these gaps.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children living in low-resource settings
- Intervention: Prehospital resuscitation
- Comparator: No comparator
- Outcome: Improved clinical outcomes
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) are

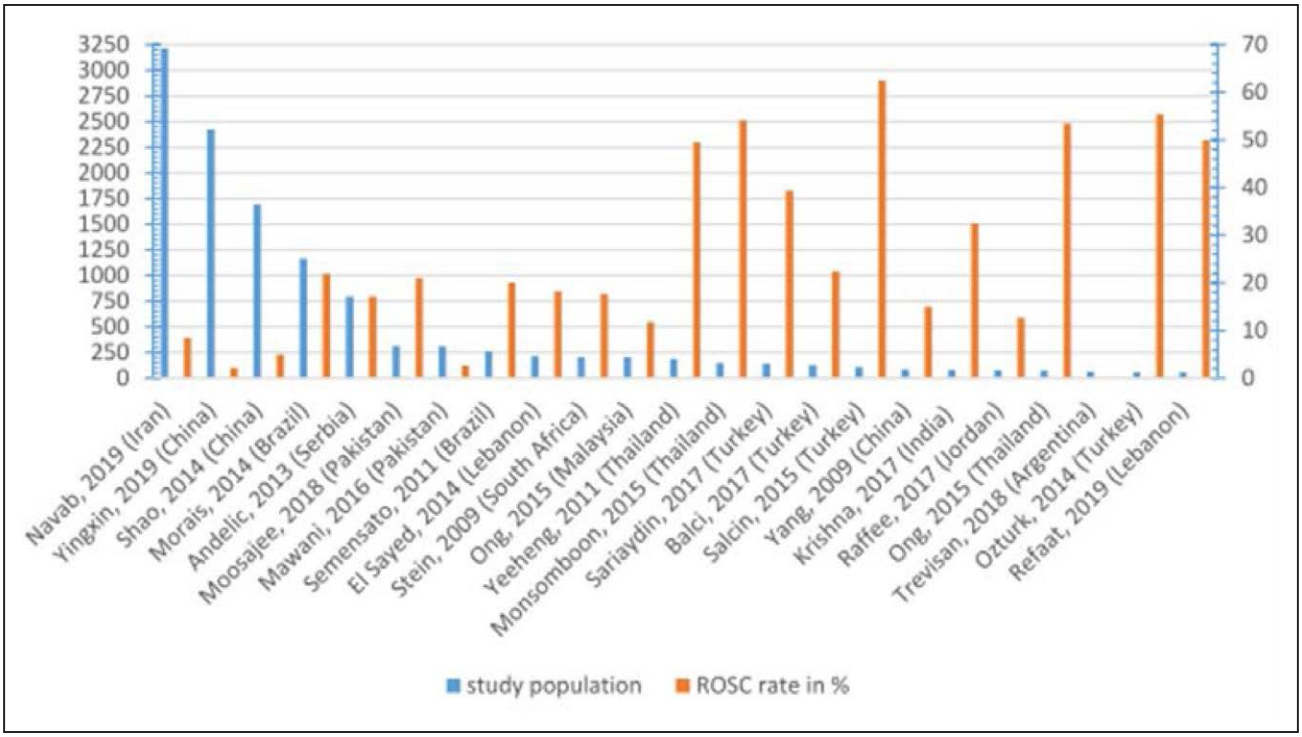

Figure. Number of patients studied (blue) and ROSC rates in % (orange) for included studies.
X axis: first author, year of publication (country); Y axis left: number of patients studied; Y axis right: % return of spontaneous circulation (ROSC). Guo 2017 was excluded from the figure because only a range of ROSC rates were reported.

eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: All years and all languages were included if there was an English abstract.

Summary of Evidence

The full ScopRev is included in Supplement Appendix B-4.

Low-resource settings were defined according to the World Bank definition by gross national income per capita, and all data except those coming from high-income economies were rated as low-resource for this ScopRev. The 24 identified studies[140–163] originated from diverse geographical areas, and there were large differences in the number of studies per region. No studies from low-income countries were eligible; 4 studies were from lower–middle income countries[144,145,158,159] all others were from upper–middle income economies.

Only 4 studies reported data on over 1000 patients.[140,143,150,154] With the exception of 7 studies,[141,142,148,154,159,160,163] most data were derived from prospective or retrospective observational studies.

The ROSC rates varied considerably across studies, from 0% to 62%. Fifteen studies (63%)[142–146,148,151,154–161] reported on longer-term outcomes such as survival to hospital discharge or neurological status. Longer-term outcomes were usually worse than those reported in patients from high-resource countries.[164] The Figure shows ROSC rates and the number of patients studied. The 3 largest studies[140,143,154] reported low ROSC rates compared with many of the smaller studies that reported high ROSC rates.

Task Force Insights

This ScopRev of prehospital resuscitation in low-resources settings searched for evidence from adult and pediatric studies. Members of the ILCOR EIT Task Force are from mainly high-income settings. Experts with a background in or who are from low-resource settings were consulted and gave their opinions and insights, but they did not participate in the selection of the studies and in the data extraction. For this same reason, we could not consider non-English full-text articles, thereby creating a selection bias.

After the data extraction phase, the EIT Task Force decided to exclude studies on trauma, children, and neonates to reduce the complexity of this review. The EIT Task Force also decided to exclude articles published before January 1, 2009, thereby limiting the results to the last decade (this included 71% of all screened abstracts). We did this because low- and middle-income countries develop over time, and conclusions based on older studies may therefore be no longer relevant. The EIT Task Force acknowledges the heterogeneity of the reported data. This may have derived from the lack of resources that EMS systems, emergency departments, and researchers in low-resource areas can devote to standardize the reporting of outcome after

resuscitation. Organizations responsible for emergency care in low-resource environments should be encouraged and supported to introduce measures of data collection, such as registries with outcome documentation, preferably also considering Utstein-style reporting. We acknowledge that there are costs associated with such data collection, and this should be prioritized locally depending on competing health expenditures. Data collection, in turn, may lead to improved comparability of data, support research specific to such settings, and generate scientific statements and recommendations specific for these areas. For future work, regional experts and clinicians should be involved in global initiatives such as ILCOR to maximize both local acceptability and applicability of such recommendations.

The question arises if prehospital resuscitation is feasible, cost-effective, or even ethically justifiable in the regions considered. CPR in OHCA has limited success, even in high-income economies. Considering the scarcity of resources in low-income countries, the feasibility of full ALS and postresuscitation care is controversial. Local determination of where to prioritize health system development should outweigh outside influence to focus on resuscitation to the detriment of other areas of health. So far, the information from the studies identified seems too heterogenous and was considered insufficient to make recommendations on OHCA in low-resource settings.

Treatment Recommendations

This treatment recommendation (below) is unchanged from 2015.[3,4]

We suggest that alternative instructional strategies would be reasonable for BLS or ALS teaching in low-income countries (weak recommendation, very low quality of evidence). The optimal strategy had yet to be determined.

Disparities in Education (EIT 4003: EvUp)

The topic of disparities in CPR education has not previously been reviewed by ILCOR, and there was no treatment recommendation as of January 31, 2020. An EvUp was performed (Supplement Appendix C-4), and several studies were identified that suggest the need for a SysRev.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Laypeople (nonprofessional responders)
- Intervention: Racial, ethnic, socioeconomic, or gender disparities
- Comparator: None
- Outcome: Impact resuscitation education and/or contribute to barriers in bystander CPR
- Study design: Cross-sectional or cohort studies are eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols), letters, editorials, and pediatric studies were excluded.
- Time frame: All articles published before October 8, 2019, and all languages were included if there was an English abstract

An EvUp was conducted for 2020. A search conducted in PubMed yielded 398 studies, and 24 were identified as relevant. The complete EvUp is included in Supplement Appendix C-4.

Treatment Recommendation

The EvUp did not enable a treatment recommendation to be made.

ALS TRAINING, INCLUDING TEAM AND LEADERSHIP TRAINING, AND METS AND RRTS

Spaced Learning (EIT 1601: SysRev)

Rationale for Review

The spaced learning principle is supported by evidence from both the cognitive science and neuroscience literature.[165] There are few data to support which method of resuscitation training is most effective.[3,4] Formats using spaced learning are increasingly being developed, aiming to enhance educational impact and flexibility of teaching. Educational theory strongly supports advantages of spaced learning.[166–170] Potential advantages may include the additional time to reflect and elaborate on the learning content between the learning sessions (eg, constructivist theories) and memory consolidation effects by recall/retraining.

Spaced learning is defined as the following (from the AHA scientific statement "Resuscitation Education Science: Educational Strategies to Improve Outcomes From Cardiac Arrest"[171]): "Spaced or distributed practice involves the separation of training into several discrete sessions over a prolonged period with measurable intervals between training sessions (typically weeks to months), whereas massed practice involves a single period of training without rest over hours or days."[171]

While this evidence evaluation did not specifically address the timing of retraining, we included studies comparing spaced with massed learning in contexts of retraining (refresher training).

The comparisons in the literature revealed 2 types: (1) The use of spaced learning, which involved the separation of training into several discrete sessions over a prolonged period with measurable intervals between training sessions (typically weeks to months). The learning content can be distributed across different sessions or repeated at each session. The number of repetitions and time intervals between repetitions can vary. (2) The use of booster training, which describes distributed practice after initial completion of training and

is generally related to low-frequency tasks such as the provision of CPR. The terms *just-in-time training*, *just-in-place training*, and *refreshers* describe training that is included in this category.

Because of the high heterogeneity among studies including clinical heterogeneity (such as types, format of intervention, and methods of outcome assessments) and methodologic heterogeneity (outcome assessments, duration of follow-up, and timing of assessment), the EIT Task Force was unable to perform a meta-analysis but reports a narrative synthesis of the findings structured around each outcome; spaced learning and booster training are discussed separately.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: All learners taking resuscitation courses (all course types and all age groups) and/or first aid courses
- Intervention: Trained or retrained distributed over time (spaced learning)
- Comparator: Compared with training provided at 1 single time point (massed learning)
- Outcome: Educational outcomes (skill performance 1 year after course conclusion, skill performance between course conclusion and 1 year, and knowledge at course conclusion) and clinical outcomes (quality of performance in actual resuscitations and patient survival with favorable neurological outcome)
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: All years and all languages were included if there was an English abstract; literature search was updated to December 2, 2019.
- PROSPERO registration CRD42019150358

Consensus on Science

Seventeen studies in courses with manikins and simulation were included in the narrative synthesis: 13 randomized studies[172–184] and 4 nonrandomized studies.[185–188] As shown in Table 7 for spaced learning and Table 8 for booster learning, the included studies covered a range of resuscitation courses: 8 studies in BLS,[173,174,177,178,180–182,186] with the latter 3 studies reporting results from the same cohort of participants; 3 studies in pediatric ALS[172,175,185]; 5 studies in neonatal life support[176,179,183,184,188]; and 1 study in emergency medicine skills course.[187]

In all identified studies, practical skills were assessed using manikins.

The overall certainty of evidence was rated as very low for all outcomes primarily because of a very serious risk of bias. The individual studies were all at moderate to serious risk of bias because of confounding. Because of this and a high degree of clinical heterogeneity (such as types, format of intervention, methods of outcome assessments) and methodologic heterogeneity (outcome assessments, duration of follow-up, timing of assessment), no meta-analyses could be performed.

For the critical outcome of skill performance 1 year after course conclusion, we identified very low-certainty evidence (downgraded for risk of bias, inconsistency, and imprecision) from 4 RCTs,[173,174,178] which all reported the use of spaced learning in BLS to evaluate the number of participants able to provide chest compressions of adequate depth (defined as greater than 50 mm) at 1 year. One RCT[174] (n=87) reported that more participants were able to perform chest compressions of adequate depth with spaced learning than with massed learning. At 12 months' testing, the spaced learning group was superior to the control group for proportion of excellent CPR (control, 6/41 [14.6%], intervention 25/46 [54.3%]; $P<0.001$; odds ratio [OR], 6.94; 95% CI, 2.45–19.69). This study also reported improvement in other measures of quality of chest compressions: percentage of chest compressions at the correct rate (100–120/min) improved from 78.0% (95% CI, 70.8%–85.1%) to 92.7% (95% CI, 86.0%–99.4%), and percentage of chest compressions with complete recoil improved from 86.5% (95% CI, 81.6%–91.4%) to 97.4% (95% CI, 92.8%–100.0%). Similar improvements were also reported in pediatric CPR parameters.

In booster learning, 3 RCTs[173,178,182] (n=790) reported more participants were able to provide chest compressions of adequate depth compared with those who received no booster learning. One RCT[173] compared booster learning of different frequency (monthly, every 3 months, every 6 months, annually). This study reported improved chest compression performance across all booster groups, with monthly booster learning providing the best skill performance but the highest attrition rate.[173] Participants who trained monthly had a significantly higher rate of excellent CPR performance (15/26, 58%) than those in all other groups (12/46, 26% in the 3-month group, $P=0.008$; 10/47, 21% in the 6-month group, $P=0.002$; and 7/48, 15% in the 12-month group, $P<0.001$). *Excellent CPR* was defined as a 2-minute CPR session in which 3 metrics were achieved: (1) 90% of compressions with correct depth (50–60 mm); (2) 90% of compressions with correct rate (100–120/min); and (3) 90% of compressions with complete chest recoil. The Oermann study[178] also reported improved CPR performance in participants who received brief monthly practice compared with no monthly practice. In the booster learning group, students' mean compression depth was within acceptable range (mean, 40.3 mm; standard deviation [SD], 6.6) with 59.2% (SD, 36.6) of compressions with adequate depth and no skill decay over the 12 months ($P=0.31$). In contrast, the control group had a significant loss of ability to compress with adequate

Table 7. Characteristics of Included Studies Spaced Learning

Author, Year, Country	Study Design	Student	# Students	Course/Skills Taught	Intervention	Control	Primary Outcome(s)	Secondary Outcomes(s) If Any	Conclusion
Patocka, 2019,[172] Canada	Single-blinded RCT	Trained EMS providers (EMT or paramedics)	48	AHA/Heart and Stroke Foundation of Canada 2010 PALS	Spaced course (four 3.5-h weekly sessions over 1 mo)	Massed course (two sequential 7-h days)	GRS score for the 4 individual procedural skills (adult and infant CC, infant bag-mask ventilation, and IO) immediately after course and 3 mo later	Quantitative metrics of CPR, a MCQ test, and VAS scores for self-efficacy immediately after course and 3 mo later	3-mo retention of CC skills is similar regardless of training format, retention of other resuscitation skills may be better in spaced group
Lin, 2018,[174] Canada	RCT	Trained healthcare providers working in the ED	87	Just-in-time CPR training; AHA BLS	Distributed training at least 1/mo with real-time feedback without limited practicing time (AHA RQI program)	Annual standardized AHA BLS course 1/y	"Excellent CPR" (defined as achieving at least 90% of all AHA standards for CC depth, rate and recoil for each individual criterion.) after 1 y	Percentage of compression depth >50 mm for adult/child and compression depth >40 mm for infant; percentage of CC with rate of 100–120/min; percentage of CC with complete recoil. Every 3 mo up to 1 y	Spaced training improves quality of CPR
Patocka, 2015,[185] Canada	Prospective cohort	Third-year medical students	45	5-h pediatric resuscitation course based on PALS	4 weekly 1.25-h sessions (each with 1 wk spacing interval)	Single 5-h session	Performance on the multiple-choice examination knowledge assessment and procedural skill global rating scores. 4 wk following the completion of the last session	Procedural checklist scores and performance on a priori determined critical procedural elements	Spaced format may have better retention of skills and more rapid completion of critical tasks
Kurosawa, 2014,[175] Japan	Prospective randomized single-blind trial	Trained PICU nurses, respiratory therapists, and nurse practitioners	40	PALS recertification, based on AHA PALS renewal	Simulation-based modular PALS recertification training (reconstructed into six 30-min sessions conducted monthly) and two 15-min AED/CPR demonstration sessions, and up to 60 min for the written evaluation, for a total of 4.5 h	Standard 1-d simulation-based PALS recertification course 7.5 h	Skill performance measured by a validated clinical performance tool immediately after training	Teamwork (behavioral assessment tool), self-confidence and satisfaction immediately after training	Spaced training more effective for skill performance

(*Continued*)

Table 7. Continued

Author, Year, Country	Study Design	Student	# Students	Course/Skills Taught	Intervention	Control	Primary Outcome(s)	Secondary Outcomes(s) If Any	Conclusion
Tabangin, 2018,[176] Honduras	RCT	Clinic and hospital providers (doctors and nurses)	37	HBB	Monthly practice for 6 mo after initial training	3 consecutive practices at 3, 5, and 6 mo	The objective structured clinical examination score immediately after training, at 3 and 6 mo	Passing on the first attempt (performing 14 of 18 steps, including the required 4 essential steps) and the number of attempts until passing immediately after training, at 3 and 6 mo	Spaced training has better retention of skills
Sullivan, 2015,[177] USA	RCT	Trained nurses	66	CPR and defibrillation for IHCA	15 min in-situ IHCA training sessions every 2, 3, or 6 mo	Standard AHA training (2 y)	Time elapsed from call for help to (1) initiation of CC and (2) successful defibrillation in IHCA 6 mo after initial training	CCF and whether CPR adjuncts (stepstool and backboard) were used 6 mo after initial training	Spaced training improves initiation of CPR and defibrillation timings
Breckwoldt, 2016,[187] Switzerland	Quasi-experimental study	Fifth-year medical student	156	Students' procedural knowledge within intensive course in emergency medicine	26 teaching hours in 4.5 days	26 teaching hours in 3.0 days	The difference in overall key-feature test score within 8 d after training		Moderate improvement on learning seen with spaced learning

AED indicates automated external defibrillator; AHA, American Heart Association; BLS, basic life support; CC, chest compressions; CCF, chest compression fraction; CPR, cardiopulmonary resuscitation; ED, emergency department; EMS, emergency medical services; EMT, emergency medical technician; GRS, global rating scale; HBB, Helping Babies Breathe; IHCA, in-hospital cardiac arrest; IO, intraosseous; MCQ, multiple choice question; PALS, Pediatric Advanced Life Support; PICU, pediatric intensive care unit; RCT, randomized controlled trial; and VAS, visual analogue scale.

depth at 12 months (mean, 36.5 mm; SD, 7.7) and only 36.5% (SD, 33.6) of compressions with adequate depth (P=0.004). With booster learning, students in the spaced learning group had significantly higher percentage of ventilations with adequate volume (booster, 52.2%; SD, 30.9 versus no booster, 38.5%; SD 36.1; P<0.001). At 12 months, the mean ventilation volume was 565 mL (SD, 148) for the booster group compared with mean ventilation volume of 431 mL (SD, 232) for no booster group (P<0.0001). In a randomized study, Nishiyama et al compared BLS skill retention by laypeople trained with a 45-minute DVD-based program with and without a 15-minute refresher/booster learning at 6 months.[182] During a 2-minute evaluation performed at 12 months, the number of total chest compressions was significantly greater in the booster group than in the no-booster group (booster mean, 182.0 [SD, 41.7] versus no booster mean, 142.0 [SD, 59.1]; P<0.001). The number of appropriate chest compressions (with depth over 50 mm, correct hand position, complete recoil) performed was significantly greater in the booster group than in the no-booster group (booster mean, 68.9; SD, 72.3 versus no booster mean, 36.3; SD, 50.8; P=0.009). Time without chest compressions was also significantly shorter in the booster group (booster mean, 16.1 [SD, 2.1] seconds versus no booster, 26.9 [SD, 3.7] seconds; P<0.001). There were no significant differences in time to first chest compression between the 2 groups (booster mean, 29.6 [SD, 16.7] seconds versus no booster mean, 34.4±17.8 seconds; P=0.172) and AED operations.

For the critical outcome of skill performance between course conclusion and 1 year, we identified very low-certainty evidence (downgraded for risk of bias and imprecision) from 2 RCTs[174,178] (n=201) for number of participants able to perform chest compressions with adequate depth (greater than 50 mm) at 6 months.

In a randomized trial, Lin et al[174] reported the percentage of spaced learning participants who were able to perform chest compressions of adequate depth as mean 83.2 (95% CI, 74.4–92.1) compared with the control group mean 58.0 (95% CI, 48.5–67.4), group difference mean 25.3 (95% CI, 12.0–38.2); the percentage

Table 8. Characteristics of Included Studies With Booster Learning

Author, Year, Country	Study Design	Student	# Students	Course/ Skills Taught	Intervention	Control	Primary Outcome(s)	Secondary Outcome(s) If Any	Main Findings
Ernst, 2014,[179] USA	RCT	Third-year medical students	110	Neonatal intubation	Weekly (practice 1/wk for 4 consecutive wk), or consecutive day (practice 1/d for 4 consecutive days)	Standard (control; no practice sessions)	Equipment selection (preparation score), procedural skill steps (procedure score), length of intubation attempts (in seconds), and the number of attempts at 6 wk		Neither practice superior at 6 wk
Montgomery,* 2012,[180] USA	RCT	Nursing students	606	BLS	6 min of monthly practice on a voice advisory manikin after initial training	No practice after initial training	Survey related to CPR confidence, initial course length, and satisfaction at 1 y		Monthly practice improves confidence
Kardong-Edgren,* 2012,[181] USA	RCT	Nursing students	606	BLS	6 min of monthly practice on a voice advisory manikin after initial training	No practice after initial training	Correctly performed compressions; correctly performed ventilations at 12 mo		Even with monthly practice and accurate voice-activated manikin feedback, some students could not perform CPR correctly
O'Donnell, 1993,[186] UK	RCT	Trained nurses	100	CPR	Group 1: monthly refresher sessions, group 2: a single refresher at 3 mo	Group 3: no refresher training	Knowledge test and pass rate for the skill test 6 mo after initial training		Knowledge better in booster training; skills equally poor in both groups
Anderson, 2019,[173] Canada	RCT	Trained healthcare professionals in ICU, theater, ED, ward nurses	244	AHA's RQI program	Workplace-based CPR training at different intervals: group 1, monthly; group 2, every 3 mo; group 3, every 6 mo	Workplace-based CPR training at different intervals, every 12 mo	Proportion of participants performed "excellent CPR" at 12 mo	Individual CPR performance metrics at 12 mo	Booster training is effective in improving CPR performance, with monthly training more effective than training every 3, 6, or 12 mo
Cepeda Brito, 2017,[183] USA	Single-blinded, randomized longitudinal study	Trained staff from neonatal ICU	25	NRP	Rolling refresher training at 1-mo and 3-mo intervals	Rolling refresher training at 6-mo interval	Effective CC rate (>90 compressions/ min, >1/3 anteroposterior chest wall diameter, full recoil, interruptions <1.5 s; tested at 6 mo	CCF; CC rate; adjusted CC rate (results not given)	No statistically significant difference between groups

(*Continued*)

Table 8. Continued

Author, Year, Country	Study Design	Student	# Students	Course/ Skills Taught	Intervention	Control	Primary Outcome(s)	Secondary Outcome(s) If Any	Main Findings
Oermann,* 2011,[178] USA	RCT	Nursing students	606	BLS	6 min of monthly practice on a voice advisory manikin after initial training	No practice after initial training	Compression rate and depth, percent of compressions performed with adequate depth; percent of compressions with correct hand placement, ventilation rate and volume; and percent of ventilations with adequate volume; randomly selected to be tested every 3 mo to 1 y		Booster training may improve skill performance
Mduma, 2015,[188] Africa	Before and after study	Midwives, nurse students, operating nurses, and doctors	Number of students not reported; 4894 deliveries before, 4814 after intervention	NRP	Frequent brief (3–5 min weekly) on-site HBB simulation training on newborn resuscitation practices in the delivery room	No booster	Delivery room management of newborns and 24-h neonatal outcomes (normal, admitted to a neonatal area, death, or stillbirths); observed by research assistants		The number of stimulated neonates increased from 712 (14.5%) to 785 (16.3%) (P=0.016), those suctioned increased from 634 (13.0%) to 762 (15.8%) (P≤0.0005); neonates receiving bag mask ventilation decreased from 357 (7.3%) to 283 (5.9%) (P=0.005); mortality at 24 h decreased from 11.1/1000 to 7.2/1000 (P=0.040)
Bender, 2014,[184] USA	RCT	Residents (NICU and non-NICU)	50	NRP	Booster simulation 7 to 10 mo after NRP	No booster	Video recordings independently assessed procedural skill and teamwork behavior at 15 mo		The intervention group demonstrated better procedural skills (71.6 versus 64.4) and teamwork behaviors (18.8 versus 16.2).

(*Continued*)

Table 8. Continued

Author, Year, Country	Study Design	Student	# Students	Course/ Skills Taught	Intervention	Control	Primary Outcome(s)	Secondary Outcome(s) If Any	Main Findings
Nishiyama, 2015,[182] Japan	RCT	University employees and students (nonhealthcare)	112	BLS	15 min refresher course 6 mo after initial 45 min training	Initial 45 min BLS training; no refresher	The number of appropriate CC during a 2-min test period at 12 mo	The number of total CC, the proportion of appropriate CC, and time without CC; time from starting the presentation to first CC and time from arriving at AED beside the participant to the first defibrillation	The number of appropriate CC performed was significantly greater in the refresher training group (68.9±72.3) than in the control group (36.3±50.8; *P*=0.009); time without CC was significantly shorter in the refresher training group (16.1±2.1 s versus 26.9±3.7 s; *P*<0.001); there were no significant differences in time to CC and AED use between the groups

*Same study with different outcomes reported.

AHA indicates American Heart Association; BLS, basic life support; CC, chest compressions; CCF, chest compression fraction; CPR, cardiopulmonary resuscitation; ED, emergency department; HBB, Helping Babies Breathe; ICU, intensive care unit; NICU, neonatal intensive care unit; NRP, Neonatal Resuscitation Program; RCT, randomized controlled trial; and RQI, Resuscitation Quality Improvement.

of spaced learning participants able to perform chest compressions of correct rate mean 95.5 (95% CI, 90.0–100.0) compared with the control mean 79.3 (95% CI, 73.3–85.3), group difference mean 16.2 (95% CI, 8.1–24.4); and the percentage of spaced learning participants able to perform chest compressions with complete chest recoil mean 97.4 (95% CI, 94.1–100.0) compared with mean 88.9 (95% CI, 85.3–92.4), group difference mean 8.6 (95% CI, 3.7–13.4). Similar superior performance was reported in the spaced learning group across all testing time points (3, 6, 9, and 12 months).

A second study also reported improved CPR performance in participants who received brief monthly practice compared with no monthly practice.[178] In the booster learning group, the mean compression depths were maintained during 12 months of the study and ranged from 38.6 mm (SD, 6.7) at 3 months to 40.3 mm (SD, 6.6) at 12 months. In the no-booster group, there was significant skill decay with ability to compress with adequate depth, the mean depth at 9 months was 39.6 mm (SD 6.8) and at 12 months was 36.5 mm (SD 7.7, *P*=0.004). With booster learning, students in the spaced learning group improved their ability to ventilate with an adequate volume (6 months mean ventilation volume, 514.0 mL [SD, 208.4]; 12 months mean ventilation volume, 620.7 mL [SD, 211.0]). In the control group, the mean ventilation volumes remained less than the recommended minimum (500 mL) throughout the 12 months.

Other Studies Reporting Skill Performance Between Course Conclusion and 1 Year

Spaced Learning (3 Studies). Three studies examined spaced learning in pediatric ALS. The first study[175] recruited healthcare providers and found improved clinical performance score: maximum score of 42 made up of 21 items (each item was scored as 0=not performed, 1=performed inappropriately or not in a timely manner, and 2=performed correctly and in a timely manner). Scores in the spaced learning group increased (pre 16.3±4.1 to post 22.4±3.9) compared with scores in the standard massed learning group (pre 14.3±4.7 to post 14.9±4.4; *P*=0.006). Improvement was also found in the Behavioral Assessment Tool after learning but did not reach statistical significance (*P*=0.49).

The second study[172] randomized EMS providers to either a spaced (4 weekly sessions) or massed (2 sequential days) format. At 3 months' testing, infant and adult chest compressions were similar in both groups, but bag-mask ventilation and intraosseous insertion performance was superior in the spaced learning group (spaced learning group bag-mask ventilation score mean, 2.2 [SD, 7], *P*=0.005; intraosseous score mean, 3.1 [SD, 0.5], *P*=0.04; massed learning group bag-mask

ventilation score mean, 1.8 [SD, 0.5], *P*=0.98; intraosseous score mean, 2.7 (SD, 0.2), *P*=0.98).

In the third study, the same research group randomized medical students to a pediatric resuscitation course in either a spaced or massed format.[185] Four weeks after course completion, participants were tested with a knowledge examination and their ability to perform bag-mask ventilation, intraosseous insertion, and chest compressions. The study found no significant difference in knowledge and overall performance, but there was a trend toward more critical procedural steps performed by the spaced learning group.

Booster Learning (7 Studies). Sullivan et al randomized nurses into 4 groups: 1 group for standard AHA learning and 3 groups that participated in 15-minute in situ IHCA learning sessions every 2, 3, or 6 months.[177] The study found more frequent learning was associated with decreased median time (in seconds) to starting compressions (standard, 33 [interquartile range—IQR, 25–40] versus 6 months, 21 [IQR, 15–26] versus 3 months, 14 [IQR, 10–20] versus 2 months, 13 [IQR, 9–20]; *P*<0.001) and to defibrillation (standard, 157 [IQR, 140–254] versus 6 months, 138 [IQR, 107–158] versus 3 months, 115 [IQR, 101–119] versus 2 months, 109 [IQR, 98–129]; *P*<0.001])

Randomizing nursing students to monthly booster learning or no booster learning, Kardong-Edgren et al reported a higher percentage of compressions and ventilations without errors in the booster group: percentage of correct mean chest compressions (booster group mean, 49.2 [SD 33.2] versus no-booster group mean, 39.7 [SD 34.8]; *P*=0.003), percentage of correct ventilation (booster group mean, 48.0 [SD, 32.3] versus no-booster group, mean 36.7 [SD 33.7]; *P*<0.0001).[181] In the same cohort, participants also reported high satisfaction with the course.[180]

O'Donnell et al also compared monthly booster learning, booster learning every 3 months, and no booster learning among 100 nursing students undertaking BLS courses.[186] They found improved knowledge in the participant booster learning group but did not find improved skill performance at 6 months (theory score monthly practice mean, 11.5/14; practice every 3 months, 10.68/14; no practice, 9.50/14; *P*=0.05).

Repeated booster practice was tested in neonatal resuscitation by Tabangin, who randomized neonatal hospital providers to monthly practice for 6 months versus 3 consecutive practices at 3, 5 and 6 months.[176] The study concluded that repeated monthly testing resulted in improvements and maintenance of performance. Participants in the monthly practice group scored 1.3 points (SE, 0.42) higher on the objective structured clinical evaluation than those who practiced less frequently. Over 6 months, the monthly practice group had 2.9 times greater odds of passing on the first attempt compared with the group that practiced less frequently.

Ernst et al randomized students training in neonatal intubation to standard training, weekly booster learning, or 4-weekly booster learning.[179] Booster learning improved all aspects of neonatal intubation performance, including choosing the correct equipment, properly performing the skill steps, length of time to successful intubation, and success rate, for novice healthcare providers in a simulation setting. After training, the median preparation score (maximum, 11) for the weekly (median, 9; IQR, 8.0–9.5) and consecutive-day (median, 8.0; IQR, 7.5–9.0) groups was significantly higher than in the control group (median, 7.0; IQR, 6.0–8.0; *P*<0.001). The posttraining performance score (maximum, 8) was also significantly higher in the weekly (median, 7.0; IQR, 6.5–7.5) and consecutive-day (median, 7.0; IQR, 6.0–7.5) groups compared with the control group (median, 5.5; IQR, 4.0–6.0; *P*<0.001). First-attempt intubation success improvements from baseline to the final assessment were as follows: from 3 participants to 11 (20% increase) in the standard group, from 6 participants to 26 (62% increase) in the weekly practice group, and from 4 participants to 29 (67% increase) in the consecutive-day practice group (*P*<0.001 for all groups). First-attempt intubation times also improved (decreased) between the baseline and final assessments for participants in the 2 practice groups (weekly mean, 27 seconds decrease from 42.5 to 15.5 seconds; consecutive-day mean, 11.3 seconds decrease from 31.3 to 20.0 seconds; control mean, 6.5 seconds increase from 23.5–30.0 seconds; *P*<0.001). The researchers were unable to demonstrate whether one type of booster learning was superior to the others.

Bender et al conducted an RCT comparing booster learning 9 months after a neonatal resuscitation training program with no booster learning. In simulation testing at 15 months, the booster group scored significantly higher in procedural scores out of a maximum score of 107 (71.6 versus 64.4; *P*=0.02) and teamwork behaviors out of maximum score of 25 (18.8 versus 16.2; *P*=0.02). No difference in knowledge scores was found.[184]

Cepeda Brito et al randomized students in a neonatal resuscitation program to rolling refresher booster learning or no booster learning.[183] Participants in booster learning reported higher confidence in their performance at 6 months, but this was not statistically significant.

For the important outcome of knowledge at course conclusion, we found very low-certainty evidence (downgraded for risk of bias and imprecision) from 3 cohort studies. Breckwoldt et al designed an emergency medicine intensive course of 26 teaching hours and compared the knowledge of 156 students when the course was delivered over 4.5 days with a course delivered over 3.0 days.[187] At course conclusion, knowledge was tested with video case-based simulation. After the course, participants' procedural knowledge was assessed by a specifically developed video case-based key-feature test.

Participants from the spaced version reached a mean of 14.8 (SD, 2.0) out of 22 points, compared with 13.7 (SD, 2.0) in the massed version (*P*=0.002). In an RCT of spaced versus massed learning in EMS providers, a 33-question standardized Heart and Stroke Foundation of Canada pediatric ALS multiple choice questionnaire (MCQ) test was used immediately after training and 3 months after the course.[172] In the spaced group, there was no decay in the mean MCQ score 3 months after the course compared with the immediate postcourse score (immediately after, 30.3 [SD, 0.5] versus after 3 months, 29.7 [SD 0.5]; *P*=0.39); however, there was a statistically significant decay in the MCQ scores in the massed learning condition (immediately after, 31.1 [SD, 0.5] versus after 3 months, 29.6 [SD 0.5]; *P*=0.04).

O'Donnell compared monthly booster learning, booster learning every months, and no booster learning among 100 nursing students undertaking BLS courses.[186] They found improved knowledge among participants in the booster learning group but did not find improved skill performance at 6 months (theory score monthly practice mean 11.5/14, 3 monthly practice 10.68/14, no practice 9.50/14, *P*=0.05)

For the important outcome of quality of performance in actual resuscitations, we did not identify any studies.

For the important outcome of patient survival with favorable neurological outcome, we did not identify any studies.

While we did not find any study reporting performance at clinical resuscitation and patient survival with favorable neurological outcome, there was evidence from 1 observational study on the impact of booster learning on delivery room management of the newborn.[188] This study assessed the impact of frequent brief (3–5 minutes weekly) on-site simulation training on newborn management in the delivery room and the potential impact on 24-hour neonatal mortality. The number of stimulated neonates increased from 712 (14.5%) to 785 (16.3%) (*P*=0.016), and those suctioned increased from 634 (13.0%) to 762 (15.8%) (*P*≤0.0005). Mortality at 24 hours decreased from 11.1/1000 to 7.2/1000 (*P*=0.040).

Treatment Recommendations

For learners undertaking resuscitation courses, we suggest that spaced learning (training or retraining distributed over time) may be used instead of massed learning (training provided at 1 single time point) (weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-4. There is growing evidence suggesting that spaced learning can improve skill retention (performance 1 year after course conclusion), skill performance (performance between course completion and 1 year), and knowledge at course completion. We did not find any evidence to support either spaced or massed learning in skill performance during actual resuscitations or patient survival with favorable neurological outcomes.

In making this recommendation, the EIT Task Force (in collaboration with Neonatal Life Support Task Force) considered the following:

Our review has only found very low-certainty evidence to support spaced learning in resuscitation education derived mainly from BLS, pediatric, and neonatal life support courses. Nevertheless, the EIT Task Force is of the opinion that the benefits of spaced learning demonstrated in other areas of education would also apply in resuscitation training.

Our review did not evaluate the optimal format of spaced learning or effect of different retraining intervals. Any training intervention should be designed to deliver the learning objectives specific to a course, and it is unlikely that 1 specific format, design, or duration would fit all resuscitation training courses.

There were limited data from 2 studies that reported improved human factors with spaced learning.[175,184]

There may be concerns about increased costs and resources because of the organization required for faculty, equipment, and learners to implement spaced learning.[173] However, there is evidence from the gray literature that spaced learning can lead to cost savings.[189]

Participation in spaced learning requires ongoing motivation. It may be challenging to engage providers in repeated, effortful practice.[171]

The 2010 CoSTR described insufficient evidence to recommend any specific training intervention, compared with traditional lecture/practice sessions, to improve learning, retention, and use of ALS skills.[1,2] The issue of new teaching strategies was not assessed in 2015, but this 2020 evaluation suggests that spaced learning (distributed over time) may be useful for resuscitation training.

This CoSTR EIT 1601 is a new PICO and refers to the difference in education by a large initial teaching session compared with small inputs separated over time. The CoSTR EIT 628 refers to retraining after initial education. Both are different educational questions, and therefore, EIT decided to investigate these different questions.

Knowledge Gaps

- There were no studies examining spaced learning in adult ALS.
- There was a lack of data on the impact of spaced learning on quality of performance in actual resuscitations.
- There was a lack of data on impact of spaced learning on patient survival with favorable neurological outcome. In neonates, there were limited data on infant mortality at 24 hours after delivery.

There are currently no data on survival to hospital discharge or long-term survival in neonates.
- There were insufficient data to examine the effectiveness of spaced learning on skill acquisition compared with maintaining skill performance and/or preventing skill decay.
- There were insufficient data to examine the effectiveness of spaced learning on laypeople compared with healthcare providers.
- There were limited data on impact of spaced learning on human factors (team behaviors and nontechnical skills).
- There was no evidence on cost-effectiveness and resource implications of spaced learning.
- There is a need to understand how to address high attrition rates in spaced learning. For spaced learning to be effective, we will need to understand how to engage learners by using the learners' motivation and reduce their burden.

EMS Experience and Exposure (EIT 437: SysRev)

Rationale for Review

There are no current ILCOR recommendations on EMS experience and exposure to resuscitation. Resuscitation knowledge and skills are likely to degrade with time if not refreshed with regular use or training. A SysRev published in 2014[190] found very little evidence; however, several large studies have been published subsequently. EMS experience and exposure was chosen as a topic because there was emerging evidence that EMS exposure to resuscitation varied greatly both within and across organizations and that there was an association between this and patient outcomes.

The literature defines 2 main types of comparisons: first, exposure and years of career experience of the team performing resuscitation, and second, exposure and years of career experience of individuals within the team (eg, team leader or treating paramedic). Because of the considerable heterogeneity among studies, the EIT Task Force was unable to perform a meta-analysis but describes the findings in a narrative synthesis.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children who are in cardiac arrest in the out-of-hospital setting
- Intervention: Resuscitation by experienced EMS practitioners or practitioners with higher exposure to resuscitation
- Comparator: Resuscitation by less-experienced practitioners or practitioners with fewer exposures
- Outcome: Survival to hospital discharge/30 days with good neurological outcome, survival to hospital discharge/30 days, and survival to hospital (event survival) and prehospital ROSC
- Study design: RCTs, nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies), original research articles (both prospective and retrospective) were included with no language restrictions. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: All years and all languages were included if there was an English abstract up to October 14, 2019.
- PROSPERO registration CRD42019153599

Consensus on Science

Very-low-certainty evidence (downgraded for very serious risk of bias) was derived from 7 studies included in this narrative synthesis.[191–197] The critical risk of bias and a high degree of heterogeneity precluded meta-analyses.

Studies Examining Exposure to Resuscitation

For the critical outcome of survival with favorable neurological outcome at discharge/30 days, we identified very low-certainty evidence (downgraded for risk of bias and imprecision) from 1 non-RCT.[196] This study examined exposure for EMS-physicians and reported unadjusted data with insufficient numbers of events to be confident in the direction of the outcome estimates.

For the critical outcome of survival to discharge/30 days, we identified very low-certainty evidence (downgraded for risk of bias and imprecision) from 3 non-RCTs.[191,192,196] The largest and highest-quality non-RCT[192] reported adjusted outcomes and examined the whole resuscitating teams' exposure in the preceding 3 years. This study found that higher team exposure in the preceding 3 years was associated with increased survival to discharge: comparing the reference group with 6 exposures or fewer, with a group having more than 6 to 11 exposures (adjusted OR, 1.26; 95% CI, 1.04–1.54), group with 11 to 17 exposures (adjusted OR, 1.29; 95% CI, 1.04–1.59), and a third group having more than 17 exposures (adjusted OR, 1.50; 95% CI, 1.22–1.86).

The remaining 2 non-RCTs[191,196] reported unadjusted outcomes and used the average exposure of team leaders to resuscitation over 1-[196]and 3-year study periods.[191] These studies found no association between exposure to resuscitation, at thresholds of 5 exposures over 3 years for EMS-physicians[191] or 10 exposures over 1 year for the lead paramedic,[196] and unadjusted survival to hospital discharge.

Dyson et al[192] also found lower survival to discharge in patients treated by teams without an exposure in the preceding 6 months (adjusted OR, 0.70; 95% CI, 0.54–0.91) compared with those with recent exposure (less than 1 month).

For the critical outcome of event survival, we identified very low-certainty evidence (downgraded for risk

of bias and imprecision) from 2 non-RCTs.[191,196] These 2 studies reported unadjusted outcomes and used the average exposure of team leaders to resuscitation over 1-[196] and 3-year study periods.[191] These studies found no association between exposure to resuscitation, at cut-offs of 5 exposures over 3 years for EMS-physicians[191] or 10 exposures over 1 year for the lead paramedic,[196] and unadjusted event survival.

For the critical outcome of ROSC, we identified very low-certainty evidence (downgraded for risk of bias) from 2 non-RCTs.[195,196] The largest non-RCT[195] reported adjusted outcomes and examined the primary treating paramedic's exposure in the preceding 5 years. This study found higher exposure of the treating paramedic was associated with increased ROSC, compared with the reference group with fewer than 15 exposures and the group with 15 exposures or more (adjusted OR, 1.22; 95% CI, 1.11–1.36). The other non-RCT[196] also found an unadjusted association between 10 exposures or more for the lead paramedic over a 1-year period and achievement of ROSC (OR, 1.30; 95% CI, 1.01–1.69).

Studies Examining Years of Career Experience

For the critical outcome of survival with favorable neurological outcome at discharge/30 days, we identified no studies.

For the critical outcome of survival to discharge/30 days, we identified very low-certainty evidence (downgraded for risk of bias and imprecision) from 4 non-RCTs.[192–194,197] The largest and highest-quality non-RCT[192] reported adjusted outcomes and examined the treating teams' years of clinical experience and found no association with survival to hospital discharge: reference group with median 5 or fewer career years, group with 5 to 8 years (adjusted OR, 1.17; 0.99–1.39), group with 8 to 11 years (adjusted OR, 1.11; 0.93–1.34), and group with more than 11 years (adjusted OR, 1.09; 0.91–1.29). Two smaller non-RCTs examined subgroups of OHCAs and also found no association between survival to discharge and the experience of the individual treating paramedics or treating EMS team.[193,197] The remaining non-RCT reported an association between increased survival to hospital discharge and technicians with more than 4 years of experience (adjusted OR 2.58; 95% CI, 1.11–6.03; *P*=0.03) and paramedics with more than 1 year of experience (adjusted OR 2.68; 95% CI, 1.05–6.82; *P*=0.04).[194] However, this study did not fully account for the experience of the paramedics because it did not include the previous career experience of paramedics as EMTs.

For the critical outcomes of event survival and ROSC, we identified no studies.

Treatment Recommendations

We suggest that EMS systems (1) monitor their clinical personnel's exposure to resuscitation and (2) implement strategies, where possible, to address low exposure or ensure that treating teams have members with recent exposure (weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-5. In making this recommendation, the EIT Task Force prioritized the potential for improved patient outcomes through increased exposure and with the understanding that knowledge and skills degrade over time and without use. We recognize that the evidence in support of this recommendation comes from observational studies of very low certainty.

Potential strategies to improve exposure include rotating EMS personnel through higher OHCA volume areas and ensuring treating teams include EMS personnel with recent exposure. However, the strategies used are likely to vary among EMS systems.

The EIT Task Force discussed the maintenance of resuscitation skills through team simulation. Team simulation has been found to be effective for maintaining ALS skills in hospital settings and is associated with improved patient outcomes.[104,198] Such training may be a useful proxy for exposure in low-exposure settings and for rare OHCA cases (eg, pediatrics and neonates).

The EIT Task Force also discussed the possibility of providing a target level for ideal exposure. However, it was decided that more evidence is needed before exposure can be more accurately defined because the existing studies are conflicting. Dyson et al report a linear relationship between survival to hospital discharge and exposure,[192] whereas Tuttle et al report a leveling of ROSC at more than 15 exposures in the preceding 5 years.[195]

Knowledge Gaps

- Only short-term outcomes were evaluated. Future studies should document neurologically intact survival to hospital discharge/30 days and adjust for potential confounders.
- There is limited evidence to define low/ideal exposure to OHCA resuscitation.
- There is limited evidence of exposure to rare OHCA cases.
- There is a need to study this in other groups of healthcare professionals.
- There is a need for interventional studies implementing strategies to improve EMS exposure to resuscitation.

Cognitive Aids During Resuscitation Education (EIT 629: SysRev)

Rationale for Review

The 2010 CoSTR stated, "It is reasonable to use cognitive aids (eg, checklists) during resuscitation,

provided that they do not delay the start of resuscitative efforts."[1,2] Since then, many studies have been published.

For this review, *cognitive aids* were defined as the presentation of prompts aimed to encourage recall of information to increase the likelihood of desired behaviors, decisions, and outcomes.[199] Examples of cognitive aids include checklists, device apps, video clips, and pictures.

Our goal was to describe the impact of cognitive aids used during actual CPR attempts; however, no studies were found. Therefore, the task force decided to address the topic in 2 indirect ways: (1) actual trauma resuscitation, where the clinical environment may be sufficiently similar to cardiac arrest, and (2) simulated cardiac arrest environments. The outcomes listed below refer to these 2 types of studies.

There was high heterogeneity among studies (such as types, format of intervention, methods of outcome assessments, duration of follow-up, timing of assessment). We were unable to perform a meta-analysis and have conducted a narrative synthesis of the findings.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Patients requiring resuscitation or providers learning to deliver resuscitation
- Intervention: Use of a cognitive aid
- Comparator: No use of a cognitive aid
- Outcomes:
  - Patient survival
  - Quality of performance in actual resuscitations
  - Skill performance 1 year after course conclusion
  - Time to starting CPR between course conclusion and 1 year in simulated resuscitations
  - Chest compression rate between course conclusion and 1 year in simulated resuscitations
  - Chest compression depth between course conclusion and 1 year in simulated resuscitations
  - Chest compression fraction (CCF) between course conclusion and 1 year in simulated resuscitations
  - Ventilation between course conclusion and 1 year in simulated resuscitations
  - Time to starting CPR at course conclusion in simulated resuscitations
  - Chest compression rate at course conclusion in simulated resuscitations
  - Chest compression depth at course conclusion in simulated resuscitations
  - Chest compression fraction at course conclusion in simulated resuscitations
  - Ventilation at course conclusion in simulated resuscitations
  - Knowledge at course conclusion
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: All years and all languages were included if there is an English abstract. Initial search was run July 17, 2019. The search was updated December 30, 2019.
- PROSPERO registration submitted November 23, 2019

Consensus on Science

1. For the critical outcome of survival to hospital discharge, we identified no studies during cardiac arrest but found very low-certainty evidence for trauma resuscitation in 3 studies (1 randomized trial[200] and 2 observational studies[201,202]), downgraded for risk of bias, indirectness, and imprecision. These studies enrolled 4659 patients, but not all studies reported numbers of patients who survived, so calculating overall OR was not possible.
2. For the important outcome of quality of performance in actual resuscitations, no studies during cardiac arrest were found, but very low-certainty evidence for trauma resuscitation (1 randomized trial[200] and 3 observational studies[201–203]), downgraded for risk of bias, inconsistency, indirectness, and imprecision, was identified. These studies enrolled 5094 patients but reported quality of performance using different metrics, so calculating overall OR was not possible.

   Fitzgerald et al[200] reported fewer errors in teams who used a cognitive aid (incident rate ratio [RR], 0.889; 95% CI, 0.793–0.996; *P*=0.04) but found that compliance to trauma algorithms was not significantly improved with the use of a cognitive aid (incident RR, 1.020; 95% CI, 0.989–1.051; *P*=0.21).

   Lashosher et al[202] reported that almost all aspects of completing primary and secondary trauma surveys improved with using the cognitive aid and that ordering radiological investigations improved with using a cognitive aid (*P*<0.001), except when ordering abdominal computed tomography scans.

   Bernhard et al[201] reported that time to completion of required radiological investigations in trauma patients improved with using a cognitive aid except when ordering chest computed tomography scans in the most severely injured subset of patients. However, they found that teams performed more lifesaving interventions (laparotomy and decompressive craniectomy) when using a cognitive aid (19% preimplementation of cognitive aid versus 29% postimplementation; *P*<0.05).

Kelleher et al[203] reported that most primary and secondary survey tasks were completed more consistently when teams used a cognitive aid. Primary and secondary survey tasks overall were more likely to be completed (primary survey: adjusted OR, 2.66 [95% CI, 2.07–3.42]; secondary survey: adjusted OR, 2.46 [95% CI, 2.04–2.98]).[203] The average adjusted time to task completion was 9 seconds (–0.15 minutes; 95% CI, –0.23 to –0.08 minutes) faster in the post–checklist implementation period.[203]

3. For the important outcome of skill performance in simulated resuscitations, 1 year from course conclusion we identified no studies.
4. For the important outcome of time to starting CPR in simulated resuscitations between course conclusion and 1 year, we identified very low-certainty evidence in 1 randomized trial,[204] downgraded for indirectness and imprecision. This outcome was evaluated in only 4 resuscitation teams, and there was no difference (15 seconds without versus 14 seconds with cognitive aid).
5. For the important outcome of chest compression rate in simulated resuscitations between course conclusion and 1 year, we identified very low-certainty evidence in 2 randomized trials,[205,206] downgraded for risk of bias, inconsistency, indirectness, and imprecision. Ward et al[205] found no significant differences in the percentages of lay provider participants who performed the correct compression rate with no cognitive aid using either a short or long version of a checklist type of cognitive aid (43% control versus 34% short versus 54% long; not significant [NS]). Williamson et al[206] found a significantly higher chest compression rate in lay provider participants who used a cognitive aid (94.5/min control versus 99.0/min cognitive aid; $P<0.05$), but noted that neither group achieved a mean rate within the recommended rates of 100 to 120/min.
6. For the important outcome of chest compression depth in simulated resuscitations between course conclusion and 1 year, we identified very low-certainty evidence in 2 randomized trials,[205,206] downgraded for risk of bias, indirectness, and imprecision. Ward et al[205] found no significant differences in the percentage of compressions with proper depth performed by lay provider participants who had access to either a short or long version of a checklist type of cognitive aid (34% control versus 34% short versus 43% long, NS). Williamson et al[206] found no significant differences in the percentage of compressions with proper depth performed by lay provider participants who had access to a cognitive aid (36.6 mm control versus 42.2 mm cognitive aid, NS). Note that neither group achieved a mean depth in the recommended range of 50 to 60 mm.
7. For the important outcome of CCF/hands-off time (HOT) in simulated resuscitations, between course conclusion and 1 year we identified very low-certainty evidence in 1 randomized trial,[204] downgraded for risk of bias, indirectness, and imprecision. No significant differences in percentage HOT were found when resuscitation teams used a cognitive aid (18.9% when 4 teams did not versus 15.8% when 4 teams did use a cognitive aid, NS).
8. For the important outcome of ventilation in simulated resuscitations between course conclusion and 1 year, we identified very low-certainty evidence in 2 randomized trials,[205,206] downgraded for risk of bias, indirectness, and imprecision.
   Ward et al[205] found no significant differences in the percentage of ventilations with proper technique performed by lay provider participants who had access to either a short or long version of a checklist type of cognitive aid (50% control versus 47% short versus 56% long; NS).

   Williamson et al[206] found significant differences in the percentage of ventilations with proper tidal volume performed by lay provider participants who had access to a cognitive aid (audio prompts) (55.5% control versus 84.8% cognitive aid; $P<0.01$).
9. For the important outcome of time to start CPR in simulated resuscitations at course conclusion, we identified low-certainty evidence in 4 randomized trials[207–210] (downgraded for risk of bias, indirectness, and imprecision) and 1 observational study[204] (downgraded for risk of bias, indirectness, and imprecision). All studies demonstrated statistically significant and likely clinically significant delays in starting CPR for lay provider participants who used a cognitive aid compared with those who did not (Hunt: 78.2 seconds control versus 159.5 seconds cognitive aid, $P<0.001$[207]; Merchant: 18 seconds [95% CI, 15–21 seconds] control versus 48 seconds [95% CI, 47–49 seconds] cognitive aid[208]; Paal: 93.3 seconds control versus 165.3 seconds cognitive aid, $P<0.001$[209]; Rössler: 23 seconds control versus 63 seconds flowchart, $P<0.0001$[210]).
10. For the important outcome of chest compression rate in simulated resuscitations at course conclusion, we identified very low-certainty evidence from 6 randomized trials,[205–210] downgraded for risk of bias, inconsistency, indirectness, and imprecision. Hunt et al[207] reported no significant differences in mean chest compression rate between lay provider participants who used a cognitive aid and those who did not (117/min control versus 127.9/min with cognitive aid; NS).

Merchant et al[208] reported a higher mean chest compression rate by lay provider participants who used a cognitive aid compared with those who did not (compression rate: 100/min [95% CI, 97–103/min] versus 44/min [95% CI, 38–50/min]).

Paal et al[209] reported a higher percentage of lay provider participants who used the correct chest compression rate when using a cognitive aid compared with those who did not (14% control versus 44% cognitive aid; $P<0.001$).

Rössler et al[210] reported no significant differences in mean chest compression rate delivered by lay provider participants who used a cognitive aid compared with those who did not (76/min control versus 78/min flowchart; NS).

Ward et al[205] reported no significant differences in percentage of lay provider participants who used a correct chest compression rate when using either a short or long version of a checklist type of cognitive aid compared with those who did not use a cognitive aid (45% control versus 50% short versus 51% long; NS).

Williamson et al[206] reported a higher mean chest compression rate delivered by lay provider participants who used a cognitive aid compared with those who did not (52.3/min control versus 87.3/min cognitive aid; $P<0.01$).

11. For the important outcome of chest compression depth in simulated resuscitations at course conclusion, we found low-certainty evidence from 5 randomized trials,[205,206,208–210] downgraded for risk of bias, indirectness, and imprecision. Only 1 study found a difference in chest compression depth achieved by lay provider participants but not in the recommended range of depth: control 31 mm (95% CI, 38–44 mm) compared with cognitive aid 41 mm (95% CI, 28–34 mm).[208] All other studies showed no statistically significant difference in compression depth or percentage of compressions in the target range when using cognitive aids compared with not using cognitive aids.[205,206,209,210]
12. For the important outcome of CCF/HOT in simulated resuscitations at course conclusion, we found very low-certainty evidence from 4 randomized trials,[207,208,210,211] downgraded for risk of bias, inconsistency, and indirectness.

    Hawkes et al[211] reported similar HOT in lay providers with and without a cognitive aid. Hunt et al[207] showed no difference in CCF if lay provider participants did or did not use cognitive aids, but they included time to starting CPR (75.4% control versus 72.2% cognitive aid; NS). However, the time to starting CPR was significantly longer in the cognitive aid group, so it is possible that CCF was actually better in the cognitive aid group, if time to starting CPR was taken into consideration.

    Merchant et al[208] showed a difference in CCF between lay provider participants who did and did not use cognitive aids (50.6% control versus 58.9% cognitive aid), and the use of the cognitive aid was also accompanied by a delay in time to starting CPR.

    Rössler et al[210] showed that if delays in starting CPR were accounted for, lay provider participants had lower HOT when using a cognitive aid compared with not using a cognitive aid (146 seconds control versus 87 seconds cognitive aid; $P<0.0001$).
13. For the important outcome of ventilation in simulated resuscitations at course conclusion, we found low-certainty evidence from 3 randomized trials.[205,206,209] Paal et al[209] reported that there was no difference in the percentage of participants who performed the correct ventilation rate when using or not using cognitive aids (15% control versus 20% cognitive aid; NS). Ward et al[205] reported no differences in correct ventilations performed by lay provider participants using or not using a checklist type of cognitive aid (44% control versus 44% short versus 51% long; NS). Williamson et al[206] reported more ventilations performed with the correct technique by lay provider participants who used cognitive aids compared with those who did not (control 15% versus 51% cognitive aids; $P<0.01$).
14. For the important outcome of knowledge in simulated resuscitations at course conclusion, we found no studies.

Treatment Recommendations

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 healthcare 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 healthcare providers in resuscitation (weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-6. The EIT Task Force prioritized this topic because international resuscitation councils commonly provide cognitive aids to resuscitation course participants and healthcare organizations (algorithms, pocket cards, flowcharts, infographics, etc). However, it has not been determined if they are effective in

improving patient outcomes or provider performance during resuscitation.

Cognitive aids may improve performance and patient outcomes by doing the following:

- Decreasing cognitive load of individuals or team collectively[212]
- Assisting memory; enhancing automatic, fast, subconscious decision-making or cognitive processes; and reducing the impact of stress and distraction on rapid, accurate decision-making[213]
- Standardizing communication among resuscitation team members[214]
- Allowing for better situation awareness/shared mental model among team members[215]

However, cognitive aids may do the following:

- Promote fixation errors and groupthink[216]
- Impair communication among team members[217]
- Be distracting, especially when not developed well (flow, color, how easy to read, confusing to follow, etc), so they may worsen performance/patient outcomes

Our recommendation has been divided into different contexts, because we believe that the evidence for routine implantation of cognitive aids during resuscitation and training is conflicting. For lay providers, there is consistent evidence that there are potentially clinically important delays in initiating CPR; however, the evidence for impact on other CPR quality metrics (eg, rate, depth, CCF) is less consistent.

There is almost no evidence for the use of cognitive aids by trained healthcare providers during CPR. However, there is substantial evidence, albeit inconsistent, showing that trauma resuscitation teams generally adhere to resuscitation guidelines better, make fewer errors, and perform key clinical tasks more frequently if they use cognitive aids. We believe that the trauma resuscitation environment is sufficiently similar to the CPR environment to enable extrapolation to our recommendation; however, we appreciate that others may not agree with this.

When selecting our performance outcomes, we elected to include studies that measured data related to discrete tasks. There were many studies that used composite scores as their primary outcome (eg, score calculated based on completion of several clinical tasks). We excluded these studies for this SysRev, because it was very difficult to compare and consolidate the results.

None of the studies examined provided evidence to describe implementation concerns, eg, training or resource implications. However, it appears feasible to provide cognitive aids for resuscitation providers to use during training and actual resuscitation.

In the 2010 CoSTR, the use of checklists was described as reasonable during adult and pediatric ALS, provided that they do not delay the start of resuscitative efforts.[1,2] This 2020 treatment recommendation provides a more detailed insight into the limited evidence on cognitive aids during resuscitation.

Knowledge Gaps

- Actual cardiac arrest studies: Given that resuscitation councils are de facto endorsing the use of cognitive aids by providing pocket cards and algorithm posters, there is an urgent need to adequately study the impact of cognitive aids in the real-world cardiac arrest environment.
- Simulated cardiac arrest studies with healthcare providers using cognitive aids: The 1 study that examines healthcare provider performance[204] is a very small proof-of-concept pilot study and was not sufficiently powered to be able to demonstrate any effects of cognitive aids on performance in this population. Future, larger studies in this area will allow us to strengthen our recommendation for this provider group.
- Human factors: There is no standard format to the types of cognitive aids developed and examined in the studies included in this SysRev. It is likely that providers respond differently to different kinds of cognitive aids, so it is very difficult to consolidate findings from different studies to form a unified conclusion.
- There is much known about how human beings interact with cognitive aids in other clinical (eg, World Health Organization Safe Surgery Checklist) and nonclinical environments (eg, aviation, power plants, and large-scale industry). However, for the scientific community to develop the most effective, targeted cognitive aid for resuscitation, the focus of research should be the impact on human factors, specifically situational awareness (eg, attention/distraction), cognitive load, and communication. This may help us better understand why cognitive aids seem to help providers perform some clinical tasks more completely and efficiently (eg, trauma primary and secondary survey tasks) but seem to impair the ability of providers to perform some other clinical tasks (eg, initiating CPR).

Team and Leadership Training (EIT 631: SysRev)

Rationale for Review

This CoSTR for EIT is based on the 2015 CoSTR for team and leadership training[3,4] Evidence for the effect of team and leadership training on educational and clinical outcomes was sought for adult, pediatric, and neonatal courses. The search also included advanced trauma life support courses. *Leadership* was defined in terms of the attributes of a leader or the process of leadership,[218] and *teamwork* can be defined as the ability of team members to work together, communicate

effectively, anticipate and meet each other's demands, and inspire confidence, resulting in a coordinated collective action.[219]

Because teamwork and leadership are increasingly recognized factors contributing to patient safety and outcome in healthcare,[220] these human factors are expected to make a significant contribution to patient outcome in the context of ALS.

Because of the high degree of heterogeneity in context, intervention, and the way outcomes were measured, no meta-analyses could be performed. The results are summarized in a narrative form.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Students who are taking ALS courses in an educational setting
- Intervention: Inclusion of specific leadership or team training
- Comparator: No such specific training
- Outcome: Patient survival, skill performance in actual resuscitations, skill performance at 3 to 15 months (patient tasks, teamwork, leadership), skill performance at course conclusion (patient tasks, teamwork, leadership), and cognitive knowledge
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were eligible for inclusion. Studies evaluating scoring systems (no relevant outcome), studies with self-assessment as the only outcome, reviews, and abstracts without full articles were excluded.
- Time frame: Because this is an update of a CoSTR published in 2015, PubMed was searched from January 1, 2014; Embase was searched from January 1, 1999; and the Cochrane database was searched for all years. The literature search was updated to November 28, 2019.
- PROSPERO registration submitted January 3, 2020

Consensus on Science

For the critical outcome of patient survival, we found no randomized clinical trials, but we found very low-certainty evidence from 3 observational studies (downgraded for risk of bias, indirectness, and imprecision),[198,221,222] all showing improved patient survival. Andreatta et al[198] reported hospital survival from pediatric cardiac arrest over a period of 4 years after implementation of a hospital-wide mock code program, which included team training. These authors found an increase in survival from pediatric cardiac arrest at their hospital during the study period (from 33% to 48% within 1 year) in increments that correlated with the increasing number of mock code events. Neily et al[221] reported hospital mortality in surgical patients at 74 hospitals in the United States that had implemented a surgical team training program. The 74 hospitals in the training program experienced an 18% reduction in annual mortality (RR, 0.82; 95% CI, 0.76–0.91; *P*=0.01) compared with a 7% decrease among the 34 hospitals that had not yet undergone training (RR, 0.93; 95% CI, 0.80–1.06; *P*=0.59). Clarke et al[222] studied if establishing a specialist, second-tier paramedic response for OHCA was feasible and reported a rate of ROSC of 22.5% (the national average was 16%).

For the critical outcome of skill performance in actual resuscitations, we found very low-certainty evidence from a single RCT,[223] downgraded for risk of bias, indirectness, and imprecision. The study randomized 32 internal medicine residents to receive simulation training with a focus on the role of the resuscitation team leader compared with no additional training but did not find an effect on CPR quality during actual resuscitation of patients. We also found very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 4 observational studies[110,224–226] that reported improved CPR depth, rate, ratio, team communication, and improved deployment times of mechanical devices.

For the important outcome of skill performance at 3 to 15 months (patient tasks), we found very low-certainty evidence from 3 randomized trials (downgraded for risk of bias, inconsistency, and imprecision) that reported improvement in patient tasks.[227–229]

Hunziker et al[227] compared instructions on resuscitation technique with instructions on leadership and communication in medical students during simulated cardiac arrest. Hands-on time was significantly longer in the leadership instruction groups (120 seconds [IQR, 98–135] versus 87 seconds [IQR, 61–108]; *P*<0.001). The time elapsed until CPR was started was significantly shorter in the leadership instruction group (*P*<0.018).

Thomas et al[228] studied interns for pediatrics and combined pediatrics and internal medicine, family medicine, emergency medicine, and obstetrics and gynecology. They compared team training in neonatal resuscitation using high- and low-fidelity manikins. They found no evidence that trained participants maintained more vigilance (median: 100% [control participants] versus 100% [intervention]; *P*=0.951) or workload management (median: 100% [control participants] versus 100% [intervention]; *P*=0.549) than did control participants. The intervention groups had shorter-duration resuscitations compared with control groups immediately after training (mean: 9.3 minutes [control participants] versus 8.3 minutes [intervention]; *P*=0.314).

Blackwood et al[229] randomized pediatric residents to a 1-hour crisis resource management (CRM) instruction or no additional training. The overall Ottawa Global Rating Scale score (maximum=7) of the CRM group was 1.15 points (95% CI, 0.2–2.1; *P*=0.02) higher than the control group, and this increase was maintained at the 3-month retest scenario. The summative score of all 7 categories (out of 42) was 6.7 points (1.6–11.8;

P=0.01) higher in the CRM group, and this difference remained at 3 months.

For the important outcome of skill performance at 3 to 15 months (teamwork), we found low-certainty evidence from a single randomized trial,[228] downgraded for bias and imprecision. Thomas et al[228] studied interns for pediatrics and combined pediatrics and internal medicine, family medicine, emergency medicine, and obstetrics and gynecology. They compared team training in neonatal resuscitation using high- and low-fidelity manikins. Interns who received team training demonstrated more frequent teamwork behaviors in the 6-month follow-up megacodes than did control participants (mean, 11.8 versus 10.0 behaviors per minute; *P*=0.03).

We also found very low-certainty evidence (downgraded for risk of bias) from 2 observational studies that reported improved teamwork scores and faculty ratings after CPR team training.[230,231]

For the important outcome of skill performance at 3 to 15 months (leadership), we found moderate-certainty evidence from a single randomized trial,[227] downgraded for risk of bias. Hunziker et al[227] compared instructions on resuscitation technique with instructions on leadership and communication in medical students during simulated cardiac arrest. In the follow-up visit, more leadership utterances (7 [IQR, 4–10] versus 5 [IQR, 2–8]; *P*=0.02) were documented. We also found very low-certainty evidence from 2 observational studies (downgraded for risk of bias and imprecision) that reported improved checklist scores and self-reported surveys after CPR team training.[231,232]

For the important outcome of skill performance at course conclusion (patient tasks), we found low-certainty evidence from 12 randomized trials,[227–229,233–241] downgraded for risk of bias and imprecision. Eight of these 12 randomized trials[227–229,233,235–237,241] reported improvement in patient tasks, whereas 4 trials were neutral.[234,238–240]

Hunziker et al[233] compared the performance of teams of general practitioners and hospital physicians in simulated cardiac arrest with and without prior team training. Teams without prior teambuilding had less hands-on time during the first 180 seconds of the arrest (93±37 versus 124±33 seconds; *P*<0.0001), and they delayed their first defibrillation (67±42 versus 107±46 seconds; *P*<0.0001).

Thomas et al[228] studied interns for pediatrics and combined pediatrics and internal medicine, family medicine, emergency medicine, and obstetrics and gynecology. They compared team training in neonatal resuscitation using high- and low-fidelity manikins. Teams that had received team training completed the resuscitation an average of 2.6 minutes faster than did control participants, a time reduction of 24% (95% CI, 12% to 37%).

Hunziker et al[227] compared instructions on resuscitation technique with instructions on leadership and communication among medical students during simulated cardiac arrest. The leadership instruction group demonstrated a longer hands-on time (120 seconds [IQR, 98–135] versus 87 seconds [IQR, 61–108]; *P*<0.001) and a shorter median time to start CPR (44 seconds [IQR, 32–62] versus 67 seconds [IQR, 43–79]; *P*=0.018).

Chung et al[234] compared training using a didactic lecture and simulation with debriefing with training using a resuscitation script among doctors and nurses. After training, there were no differences between the 2 groups in the score for performance in a simulated setting (control, 5.5±11.4 versus script, 4.7±9.6; *P*=0.838).

Castelao et al[235] compared video-based CRM training embedded in an ALS course for final-year medical students with a control group receiving additional ALS training. HOT times were significantly lower in the CRM group (31.4±6.1% versus 36.3±6.6%; *P*=0.014).

Jankouskas et al[236] randomized nursing and medical students to BLS (using a bag-mask device and oxygen) plus CRM training or BLS only. CRM training predicted 13% of the variance in task management (*P*=0.05), and CRM training and situation awareness predicted 20% of the variance (*P*=0.04) in response time to chest compressions.

Fernandez et al[237] compared a 25-minute computer-based teamwork training with placebo training in medical students and emergency medicine residents. Teams in the computer-based training group demonstrated better patient care (F1, 42=4.66; *P*<0.05; η=10%) than did teams in the placebo group.

Blackwood et al[229] randomized pediatric residents to a 1-hour CRM instruction or no additional training. The CRM group placed monitor leads 24.6 seconds earlier (*P*=0.02), placed an intravenous catheter 47.1 seconds sooner (*P*=0.04), called for help 50.4 seconds faster (*P*=0.03), and checked for a pulse after noticing a rhythm change 84.9 seconds quicker (*P*=0.01). There was no difference in the time to initiation of CPR.

Semler et al[238] compared 3 teamwork teaching modalities for incoming internal medicine interns: didactic, demonstration-based, or simulation-based instruction. Clinical performance scores in a simulated setting were similar across the 3 groups and correlated only weakly with teamwork behavior (coefficient of determination [R_s^2]=0.267; *P*<0.001).

Castelao et al[239] randomized teams of medical students to CRM team leader training or additional ALS training. In a simulated environment, CRM-trained team leaders showed better adherence to the ALS algorithm (difference, –6.4; 95% CI -10.3,–2.4; *P*=0.002), but there was no improvement in no-flow time.

Couper et al[240] randomized healthcare providers with intermediate or advanced resuscitation training to receive standard mechanical chest compression device training or pit-crew device training (up to 1 hour). Regarding CCF in the minute preceding the first mechanical chest compression, pit-crew training was not superior to standard training (0.76 [95% CI, 0.73–0.79]

versus 0.77 [95% CI, 0.73–0.82]; mean difference, –0.01 [95% CI, -0.06 to 0.03; *P*=0.572]).

Haffner[241] randomized final-year medical students to receive a 10-minute computer-based CRM training or a control training on ethics. After the CRM training, team leaders corrected improper chest compressions (35.5%) significantly more often compared with controls (7.7%, *P*=0.03).

We also found very low-certainty evidence from 4 observational studies[242–245] (downgraded for risk of bias and indirectness) that showed improved resuscitation skills (time to initiation of chest compression, correct positioning of defibrillator electrodes, time to defibrillation, shorter preshock pauses etc) and improved simulated survival.

For the important outcome skill performance at course conclusion (teamwork), we found low-certainty evidence from 10 randomized trials,[228,229,234,236–238,240,246–248] downgraded for risk of bias and imprecision. Seven out of these 10 randomized trials showed improved teamwork whereas 3 trials were neutral.[234,238,247]

Thomas[246] randomized interns to receive a neonatal resuscitation course with team training or a standard course. The interns with team training exhibited more frequent team behaviors (number of episodes per minute [95% CI]) than interns in the control group: information sharing 1.06 (0.24, 1.17) versus 0.13 (0.00, 0.43); inquiry 0.35 (0.11, 0.42) versus 0.09 (0.00, 0.10); assertion 1.80 (1.21, 2.25) versus 0.64 (0.26, 0.91); and any team behavior 3.34 (2.26, 4.11) versus 1.03 (0.48, 1.30) (*P*<0.008 for all comparisons).

Thomas[228] studied interns for pediatrics, combined pediatrics and internal medicine, family medicine, emergency medicine, and obstetrics and gynecology. They compared team training in neonatal resuscitation using high and low fidelity manikins. The high-fidelity team training resulted in more teamwork than control participants (12.8 versus 9.0 behaviors per minute; *P*<0.001). Team training groups had better workload management (control participants: 89.3%; low-fidelity training group: 98.0% [*P*<0.001]; high-fidelity training group: 98.8%; high-fidelity training group compared with control participants [*P*<0.001)].

Chung[234] compared training using a didactic lecture, simulation, and debriefing with training using a resuscitation script in doctors and nurses. There were no differences in the score improvement after training between the 2 groups in dynamics (C: 9.16±12.6 versus S: 7.4±13.7, *P*=0.715), performance (C: 5.5±11.4 versus S: 4.7±9.6, *P*=0.838) and total scores (C: 14.6±20.1 versus S: 12.2±19.5, *P*=0.726).

Jankouskas[236] randomized nursing and medical students to BLS (using a bag-mask device and oxygen) plus CRM training or BLS only. CRM training predicted 13% in task management (*P*=0.05), 15% of the variance in teamworking (*P*=0.04), and 18% of the variance in situation awareness (*P*=0.03).

Fernandez[237] studied a 25-minute computer-based teamwork training versus placebo training among medical students and emergency medicine residents. Teams in the training group demonstrated better teamwork (F[1, 42]=4.81, *P*<0.05; η=10%).

Blackwood[229] randomized pediatric residents to a 1-hour CRM instruction or no additional training. The intervention group had overall CRM performance scores 1.15 points higher (Ottawa Global Rating Scale) out of 7 (*P*=0.02).

Semler[238] compared 3 teamwork teaching modalities for incoming internal medicine interns: didactic, demonstration-based, or simulation-based instruction. The average overall Teamwork Behavioral Rater score for those who received demonstration-based training was similar to simulation participation (4.40±1.15 versus4.10±0.95, *P*=0.917) and significantly higher than didactic instruction (4.40±1.15 versus 3.10±0.51, *P*=0.045).

Rovamo[247] evaluated the impact of CRM and anesthesia nontechnical skills instruction on teamwork during simulated newborn emergencies performed by doctors and nurses. They could not show that the CRM instruction improved teamwork performance.

Lorello[248] studied mental rehearsal of advanced trauma life support by residents in anesthesiology, emergency medicine, and surgery. The mental practice group engaged in 20 minutes of mental practice, and the control group received 20 minutes of advanced trauma life support training. The mental practice group showed improved teamwork behavior as assessed by the Mayo High Performance Teamwork Scale (*r*=0.67, *P*<0.01).

Couper[240] randomized healthcare providers with intermediate or advanced resuscitation training to receive standard mechanical chest compression device training or pit-crew device training (up to 1 hour). PIT-crew training did not result in improvement of the global Team Emergency Assessment Tool score (out of 10): PIT-crew training 8.1 (7.2–8.9) versus standard training 7.9 (7.3–8.6); mean difference, 0.15 (95% CI, -0.87 to 1.17), *P*=0.760.

We also found very low-certainty evidence from 3 observational studies[230,231,243] (downgraded for risk of bias, inconsistency, indirectness, and imprecision) that found improved teamwork scores and faculty ratings after CPR team training.

For the important outcome skill performance at course conclusion (leadership) we found low-certainty evidence from 6 randomized trials,[227,233,235,239,241,249] downgraded for risk of bias and imprecision. Of these trials, 5 out of 6 showed improved leadership, whereas 1 trial was neutral.[235]

Cooper[249] studied the effect of a 75-minute leadership seminar during an ALS course for doctors, nurses and technicians. The leadership training program improved the leadership performance in a simulated setting.

Hunziker[233] compared the performance of teams of general practitioners and hospital physicians in

simulated cardiac arrest with and without prior team training. Teams without prior team training made less leadership statements during simulated cardiac arrest (15±5 versus 21±6, *P*<0.0001).

Hunziker[227] compared instructions on resuscitation technique with instructions on leadership and communication in medical students during simulated cardiac arrest. The leadership instruction group demonstrated more leadership utterances compared with the control group (7 [IQR, 4–10] versus 5 [IQR, 2–8]; *P*=0.02).

Castelao[235] compared video-based CRM training embedded in an ALS course for final year medical students with a control group receiving additional ALS training. They could not show an association between team leader verbalization of instructions and no-flow time.

Castelao et al[239] randomized teams of medical students to CRM team leader training or additional ALS training. Significantly higher team leader verbalization proportions were found for the team leader training group: direct orders (difference, –1.82; 95% CI –2.4,–1.2; *P*<0.001), undirected orders (difference, –1.82; 95% CI, –2.8, –0.9), *P*<0.001), planning (difference, –0.27; 95% CI, –0.5,–0.05; *P*=0.018), and task assignments (difference, –0.09 (95% CI, –0.2, –0.01; *P*=0.023).

Haffner et al[241] randomized final-year medical students to receive a 10-minute computer-based CRM or a control training on ethics. Communication quality assessed by the Leader Behavior Description Questionnaire significantly increased in the intervention group by a mean of 4.5 compared with 2.0 (*P*=0.01) in the control group.

We also found very low-certainty evidence from 3 observational studies[231,232,244] (downgraded for risk of bias, indirectness, and imprecision) that showed improved checklist scores and self-reported surveys after CPR team training.

For the important outcome of cognitive knowledge, we found no evidence.

Treatment Recommendations

We suggest that specific team and leadership training be included as part of ALS training for healthcare providers (weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-7. The relevance of this review is further supported by the observations in 1999 by Cooper, who reported that leadership during resuscitation is associated with team performance and that, therefore, leadership training should be provided.[250]

In 2015, the EIT Task Force recommended team and leadership training in ALS courses (weak recommendation, low-quality evidence).[3,4] The current review supports this statement.

Although our current review identified many new studies since the 2015 CoSTR, no RCT addressed the most critical outcome of patient survival. On the other hand, we found 3 observational studies[198,221,222] for this critical outcome of patient survival, but they suffer from risk of bias, indirectness, and imprecision.

In making our recommendation about team and leadership training in ALS courses, we have placed emphasis on the potential benefit, lack of harm, and high level of acceptance of team and leadership training and lesser value on associated costs.

In the studies, many different methods to train leadership and team behavior were reported: through eLearning, video-based training, instruction, demonstration, low-fidelity simulation, or high-fidelity simulation. Team and leadership training may be delivered as an add-on training module to an ALS course, or as an integral part of an ALS course. As such, there was considerable heterogeneity in the studies analyzed. The EIT Task Force was of the opinion that the integration of team and leadership training in ALS courses may promote its sustainability. In addition to team and leadership training, sufficient exposure to resuscitation may be required to achieve improved patient outcome.

This update of the 2015 treatment recommendation[3,4] still favors leadership training during advanced resuscitation education.

Knowledge Gaps

- What is the most effective/efficient method of team and leadership training (eLearning, instruction, demonstration, simulation training, other) and assessment?
- How do team training and leadership training interact, and what is their relative importance? Is training of the leader more efficient than training of the team?
- What is the effect of team and leadership training on patient outcome (there are no RCTs)?
- How do team/leadership training and provider experience/exposure to resuscitation interact?
- Are there any downsides of leadership training on resuscitation performance (eg, delay of initiating CPR, stress for the leader or the team)?

Learning Formats Preceding Face-to-Face Training in Advanced Courses (formerly: Precourse Preparation for Advanced Courses (EIT 637: SysRev)

Rationale for Review

This review is a follow-up to the CoSTR published in 2015[3,4] (Precourse preparation for advanced life support [ALS] courses), which was based on 1 study. The task force concluded in 2015 that a specific recommendation was too speculative. Since then, blended learning

approaches have been developed for ALS courses. As the term *blended learning* is highly context specific, a clear definition is not possible.[251] From a broad perspective, any type of learning format preceding face-to-face training may be regarded as part of the course. This topic was prioritized by the EIT Task Force because of the recent dynamic development of online learning (blended learning) with the aim of reducing face-to-face training time. To account for the different learning formats, we report the results of the search separately for studies (a) comparing the distribution of precourse learning material with no distribution, and (b) comparing any kind of blended learning format that reduces face-to-face training with traditional courses.

Because of the high degree of heterogeneity with context, intervention, and the way outcomes were measured, no meta-analyses could be performed. The results are summarized in a narrative form.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Students who are taking ALS courses in an educational setting
- Intervention: Precourse preparation for advanced courses (eg, eLearning or pretesting combined with face-to-face training)
- Comparator: Traditional course (face-to-face training)
- Outcome: Cognitive knowledge, skill performance at course conclusion, skill performance at 1 year, skill performance in actual resuscitations, increased survival rates, and skill performance at time between course conclusion and 1 year
- Study design: All comparative, human studies (prospective and retrospective) examining the use of precourse preparation for ALS training and reporting knowledge/skills outcomes. Also, patient outcomes and performance in actual resuscitation situations. 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 updated to November 20, 2019.
- PROSPERO registration submitted [160799] December 2, 2019

Consensus on Science

The question of providing learning resources before a face-to-face course was addressed by two RCTs.[252,253] One study compared the 2-week access to an online ACLS simulator with no access to such a simulator,[252] and the other study provided a Microsim CD as precourse material and compared it with no CD distribution.[253] The heterogeneous nature of the studies prevented pooling of data for any outcome; therefore, no meta-analysis was performed.

Neither study addressed the critical educational outcomes of skill performance 1 year after course conclusion and skill performance between course conclusion and 1 year. Furthermore, neither study addressed the important educational outcomes of quality of performance in actual resuscitations or patient survival with favorable neurological outcome.

For the important educational outcome of skill performance at course conclusion, we found low-certainty evidence (downgraded for risk of bias and imprecision) from the 2 RCTs. The first study,[252] with 65 medical students, found no influence on time to initiate chest compressions but significant decreases in the intervention group for the time to defibrillate ventricular fibrillation (112 seconds versus 140 seconds; $P<0.05$) and pacing of symptomatic bradycardia (95 seconds versus 155 seconds; $P<0.05$). The second RCT, with 572 participants of ALS courses[253] distributing a Microsim CD before the course to the intervention group, found no significant differences in performance between intervention and control during a standardized cardiac arrest scenario test at course conclusion (I: 93.6% versus C: 91.8%; $P=0.4$).

For the important educational outcome of knowledge at course conclusion, we found low-certainty evidence (downgraded for risk of bias and imprecision) reported by 1 RCT.[254] The 1 RCT, with 572 participants of ALS courses,[253] that distributed a Microsim CD to the intervention group before the face-to-face ALS course found no significant differences of postcourse MCQ scores between the groups (C: 101.9 [SD 13.8] versus I: 101.4 [SD 13.9]; $P=0.7$).

The question of analyzing blended-learning formats to reduce face-to-face time in ALS courses compared with traditional courses was addressed by 1 RCT[254] and 2 non-RCTs.[255,256] The heterogeneous nature of the studies prevented pooling of data for any outcome; therefore, no meta-analysis was performed.

None of the studies addressed the critical educational outcomes of skill performance 1 year after course conclusion and skill performance between course conclusion and 1 year. Furthermore, no studies addressed the important educational outcomes of quality of performance in actual resuscitations or patient survival with favorable neurological outcome.

For the important educational outcome of skill performance at course conclusion, we found low-certainty evidence (downgraded for risk of bias and imprecision) from 1 RCT[254] and 2 non-RCTs.[255,256] The 1 RCT randomizing 3732 participants of ALS courses to either 6 to 8 hours of eLearning plus 1 day of face to face training or to a traditional 2-day face-to-face ALS course.[254] This study was inconclusive in demonstrating noninferiority in the intervention group (C: 80.2% versus I: 74.5%; mean difference, –5.7%; 95% CI, –8.8% to –2.7%). The first non-RCT, with 96 ACLS course participants,[255]

comparing 6 hours of online lectures plus a 1-day face-to-face training with a traditional 2-day face-to-face course, showed that cardiac arrest scenario test pass rates did not differ statistically (C: 87.5% versus I: 95.8%; *P*=0.13). The second non-RCT compared 27170 participants of ALS courses[256] who underwent either 6 to 8 hours of eLearning plus 1 day of face-to-face training or a traditional 2-day face-to-face ALS course. In this study, the first-attempt cardiac arrest scenario test pass rate was significantly higher in the intervention group (84.6% versus 83.6%; *P*=0.035); however, the absolute educational effect was very low (difference: 1.0% first-attempt cardiac arrest scenario test pass rate).

For the important outcome of knowledge at course conclusion, we also found very low-certainty evidence (downgraded for risk of bias and imprecision) reported by 1 RCT[254] and 2 non-RCTs.[255,256] The RCT, randomizing 3732 participants of ALS courses to either 6 to 8 hours of eLearning plus 1 day of face-to-face training or to a traditional 2-day ALS course,[254] reported no statistical difference for end-of-course MCQ test scores (I: 88.96% versus C: 89.54%; adjusted difference, 0.55%; CI, –1.11% to 0.02%; *P*=0.054). The first non-RCT, with 96 ACLS course participants[255] comparing 6 hours of online lectures plus a 1-day face-to-face course with a traditional 2-day face-to-face course, showed that MCQ pass rates at course conclusion did not differ statistically (C: 85.4% versus I: 95.8%; *P*=0.08). The second study, including 27170 participants of ALS courses,[256] compared 6 to 8 hours of eLearning plus 1 day of face-to-face training with a traditional 2-day face-to-face ALS training. The intervention group scored significantly higher (I: 87.9% versus C: 87.4%; *P*<0.001); however, the absolute difference of 0.5% was not found to represent educational significance.

Treatment Recommendations

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 ALS courses (strong recommendation, very low- to low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-8. Given the higher flexibility for learners and the savings of resources, the EIT Task Force strongly recommends providing the option of such formats for ALS courses (eg, a 1 day's equivalent of eLearning plus 1 day of a face-to-face course). In making this recommendation, the task force takes into account that learning styles may differ substantially and that face-to-face courses may be more effective for some groups of learners.

By implementing such programs, the return of investment in eLearning will be more pronounced if materials can be used by larger groups of learners. Programs should therefore consider developing materials collectively among several providers to save resources (ie, on a national level). However, it should also be taken into account that learners will profit most if the material is produced in the learners' native cultural context. The EIT Task Force emphasizes that close monitoring and evaluation within accredited courses is recommended and appears feasible. The EIT Task Force considers the inclusion of eLearning as a substitute for a part of the ALS course, but the PICOST question left the amount and format of the precourse preparation open. This decision was based on the consideration that the final goal of providing precourse material was to realize an increase of learner flexibility and savings of resources.

For the case of learning formats as a preparation for a traditional course, desirable consequences probably outweigh undesirable consequences in most settings, whereas in the case of eLearning formats as part of a blended learning, the desirable consequences clearly outweigh undesirable consequences.

In 2015, the EIT Task Force estimated the effect so low that a specific recommendation for or against precourse preparation in ALS courses was too speculative.[3,4] In 2020, the evidence for an effect of precourse preparation is still limited. The task force nonetheless recommends providing learning formats as precourse preparation for advanced courses, even though the certainty of the evidence found was very low to low. The task force takes into account that for nearly all ALS courses worldwide, course organizers provide learning formats preceding face-to-face training as precourse preparation, mostly in the form of reading or eLearning. Furthermore, the task force strongly recommends providing the option of eLearning as part of a blended-learning approach to reduce face-to-face training.

Knowledge Gaps

- No studies were identified evaluating effects of learning formats preceding face-to-face training on long-term retention or on outcomes related to actual resuscitations (performance in resuscitations, patient survival).
- Also, no studies addressed different formats of delivery (eg, invested time for preparation, educational involvement of learners, linkage to face-to-face training) or the content covered by the learning formats preceding face-to-face training.
- Evidence is needed for other formats of resuscitation courses (eg, BLS, pediatric ALS).

Rapid Response Systems in Adults (EIT 638: SysRev)

Rationale for Review

Unwell patients admitted to hospital are at risk of deterioration that may progress to cardiorespiratory arrest. Patients commonly show signs and symptoms of deterioration for hours or days before cardiorespiratory arrest.[257] RRSs are programs that are designed to improve the safety of hospitalized patients whose condition is deteriorating quickly.[258] A successful RRS may be defined as a hospital-wide system that ensures observations, detection of deterioration, and tailored response to ward patients that may include RRT, also called a MET.[259] There is uncertainty as to whether these systems are effective in improving patient outcomes (eg, improving patient survival, reducing the number of cardiac arrests).

There was high heterogeneity among studies. The overall certainty of evidence was rated as very low to low for all outcomes primarily because of a very serious risk of bias. The individual studies were all at a serious to critical risk of bias. Because of this and a high degree of heterogeneity, no meta-analyses were performed and, instead, we have conducted a narrative synthesis of the findings.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults who are at risk of cardiac or respiratory arrest in hospital
- Intervention: Introduction of an RRS (includes RRT or MET)
- Comparator: No RRS
- Outcome: Survival to hospital discharge with good neurological outcome, survival to hospital discharge, and in-hospital incidence of cardiac/respiratory arrest
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) were included. All languages were included if there was an English abstract available.
- Time frame: The literature search of the 2015 CoSTR was updated to December 10, 2019.
- PROSPERO registration CRD42019160097

Consensus on Science

For the critical outcome of hospital discharge with favorable neurological outcome, we did not find any study.

For the critical outcome of survival to hospital discharge, we have found low-certainty evidence (downgraded for risk of bias and inconsistency) from 2 RCTs[260,261] and very low-certainty evidence (downgraded for risk of bias, inconsistency, and indirectness) from 37 non-RCTs.[262–298]

Of the 2 RCTs, 1 demonstrated no significant difference between control hospitals (functioned as usual) and intervention hospitals (introduced a MET team) for both unadjusted (P=0.564; Diff, –0.093; 95% CI, -0.423 to 0.237) and adjusted (P=0.752; OR, 1.03; 95% CI, 0.84–1.28) survival.[261] The other study demonstrated a significant difference between control wards and intervention wards (introduction of a critical care outreach service) with all patients (OR, 0.70; 95% CI, 0.50–0.97) and matched randomized patients (OR, 0.52; 95% CI, 0.32–0.85).[260]

Of the nonrandomized studies reporting mortality, no studies reported statistically significant worse outcomes for the intervention. For studies not reporting adjusted outcomes:

- Sixteen studies with no adjustment demonstrated no significant improvement.[265,266,268,270–272,277,278,280,282,284,286–288,293,296]
- Ten studies with no adjustment demonstrated significant improvement.[263,264,279,281,289,292,294,295,297,298]
- One study with no adjustment reported on rates, which improved with MET but did not report on significance.[267]
- One study with no adjustment demonstrated significant improvement for medical patients but not surgical patients (combined significance not reported).[283]

For studies reporting adjusted outcomes:

- Three studies with adjustment demonstrated significant improvement both before and after adjustment.[273,276,290]
- Three studies with adjustment demonstrated significant improvement before adjustment but not after adjustment.[274,291,299]
- Two studies with adjustment demonstrated no significant improvement both before and after adjustment.[262,269]
- One study that reported on both unexpected mortality and overall mortality showed significant improvement both before and after adjustment for unexpected mortality but no significant improvement both before and after adjustment for overall mortality.[275]
- One before-and-after study that presented "after" data for unexpected mortality in 3 separate time bands demonstrated significant improvement in time band 3 before adjustment and in time bands 2 and 3 after adjustment.[285]

The heterogeneous nature of the studies prevents pooling of data; however, there is a suggestion of improved hospital survival in those hospitals that introduced an RRS and a suggestion of a dose-response effect, with higher-intensity systems (eg, higher RRS activation rates, senior medical staff on RRS teams) being more effective.

For the critical outcome of in-hospital incidence of cardiac arrest, we found low-certainty evidence (downgraded for risk of bias and indirectness) from 1 RCT[261] and very low-certainty evidence (downgraded for risk of bias, inconsistency, and indirectness) from 33 further non-RCTs.[262–268,270,272–276,279–281,283,284,286–290,292,294,300–304]

For the 1 RCT,[261] there was no significant difference between control hospitals and intervention hospitals, for both unadjusted (*P*=0.306; Diff, –0.208; 95% CI, –0.620 to 0.204) and adjusted (*P*=0.736; OR, 0.94; 95% CI, 0.79–1.13) analyses.

Of the 32 observational studies reporting on cardiac arrest rates:

- Seventeen studies with no adjustment demonstrated significant improvement in cardiac arrest rates after the introduction of a MET system.[264,267,268,273,274,276,279,281,283,286,289,296,298,301–303,305]
- Seven studies with no adjustment demonstrated no significant improvement in cardiac arrest rates after the introduction of a MET system[266,270,272,280,284,287,288]
- One before-and-after study using an aggregated weighted scoring system (Modified Early Warning Score) reported significantly higher cardiac arrest rates in Modified Early Warning Score bands 3 to 4 after intervention but not in Modified Early Warning Score bands 0 to 2 or 5 to 15, and overall cardiac arrest rate significance was not reported.[265]
- Three studies with adjustment demonstrated significant improvement in cardiac arrest rates after the introduction of an RRS both before and after adjustment.[263,290,300]
- One study with contemporaneous controls demonstrated no significant improvement in cardiac arrest rates after the introduction of an RRS both before and after adjustment.[262]
- One study with contemporaneous controls demonstrated significant improvement in cardiac arrest rates after the introduction of an RRS both before and after adjustment.[290]
- One study with adjustment demonstrated significant improvement before adjustment for whole of hospital and non–intensive care unit cardiac arrest rates, but only for non–intensive care unit cardiac arrest rates after adjustment.[269]
- One before-and-after study that presented "after" unadjusted data for cardiac arrest in 3 separate time bands demonstrated significant improvement in time bands 2 and 3.[275]

The heterogeneous nature of the studies prevents pooling of data. However, there is a suggestion of a reduced incidence of cardiac arrest in those hospitals that introduce an RRS and a suggestion of a dose-response effect, with higher-intensity systems (eg, higher RRS activation rates, senior medical staff on RRS teams) being more effective.

Treatment Recommendations

This recommendation (below) is unchanged from 2015.[3,4] We suggest that hospitals consider the introduction of an RRS (RRT/MET) to reduce the incidence of IHCA and in-hospital mortality (weak recommendation, low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-9. The task force places a high value on the outcomes—the prevention of IHCA and death—relative to the likely substantial cost of the system. RRSs have been successfully implemented in many healthcare settings worldwide.[306]

RRS is recommended by the Institute for Healthcare Improvement[307] and other national patient safety initiatives around the world.

There may be a role for an RRS in patients with end-of-life care[308] and also in reduction of medical errors.[309]

Careful consideration needs to be given to the elements of such systems. Effective afferent (detection and activation) and efferent limbs (RRS/MET response) may need the support of administrative and quality improvement strategies.[310]

Adequate resources should be dedicated to such systems to include (a) staff education about the signs of patient deterioration; (b) appropriate and regular vital signs monitoring of patients; (c) clear guidance (eg, alert systems or early warning scores) to assist staff in the early detection of patient deterioration; (d) a clear, uniform system of tiered clinical response; and (e) a clinical response to calls for assistance. The optimal method of patient monitoring and delivery of these components remains unclear.[1,2,311]

The performance of RRSs should be monitored and used as part of a quality improvement program of healthcare organizations. The "Recommended Guidelines for Monitoring, Reporting, and Conducting Research on Medical Emergency Team, Outreach, and Rapid Response Systems: An Utstein-Style Scientific Statement"[312] should be used by hospitals to collect the most meaningful data to optimize system interventions and improve clinical outcomes. This update of the 2015 CoSTR[3,4] confirms the recommendation to implement RRSs.

Knowledge Gaps

- There is lack of evidence on long-term survival with favorable neurological outcomes.
- What is the role of technology in RRSs (eg, remote monitoring, wearable devices)?
- What are the ideal components of the afferent limb of an RRS, eg, which vital signs, observations, and/or laboratory parameters, and with what frequency?

- What are the ideal components of an education program in the recognition of a deteriorating patient?
- What is the ideal mechanism for escalation for assistance (eg, conventional escalation versus automated electronic escalation)?
- What is the ideal makeup of the efferent limb (the response team)?
- What are the causes of failure to rescue or underutilization of RRSs?
- What is the cost-effectiveness of an RRS?

End-of-Course Testing Versus Continuous Assessment (EIT 643: SysRev)

Rationale for Review

This PICOST was prioritized by the EIT Task Force on the basis of the ongoing discussion about developing more appropriate assessment methods in resuscitation courses. Current educational literature reports positive educational effects of end-of-course testing.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Participants undergoing BLS/ALS courses
- Intervention: End of course testing
- Comparator: Continuous assessment and feedback
- Outcome: Cognitive knowledge and/or skill performance at course conclusion, skill performance at time between course conclusion and 1 year, skill performance at 1 year, skill performance in actual resuscitations, and increased survival rates
- Study design: All comparative, human studies (prospective and retrospective) in ALS training and reporting knowledge/skills outcomes; also, patient outcomes and performance in actual resuscitation situations
- Time frame: All years and all languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. Literature search was updated to November 28, 2019.
- PROSPERO registration submitted December 3, 2019

Consensus on Science

No studies were found that addressed the PICOST question.

We identified 3 studies[313–315] that analyzed the educational effect of end-of-course testing (without comparing it with continuous assessment).

Treatment Recommendations

Given that no evidence was identified, we are unable to make a recommendation.

Knowledge Gaps

- Evidence is needed for the most appropriate way to assess competence of candidates attending resuscitation courses (eg, continuous assessment versus end-of-course testing).

Virtual Reality, Augmented Reality, and Gamified Learning (EIT 4005: EvUp)

An EvUp was performed (Supplement Appendix C-5) with several studies identified that suggest the need for consideration of a SysRev, especially because no former assessment of the training of laypersons was done by ILCOR and no treatment recommendation was issued as of January 31, 2020.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Learners (ie, lay responders and/or healthcare providers) who are taking BLS or ALS training
- Intervention: Use of virtual reality/augmented reality/gamified learning
- Comparator: None of these
- Outcome: Skill performance at course conclusion, skill retention beyond course conclusion, performance in actual resuscitations, or patient outcomes
- Study design: All comparative, human studies (prospective and retrospective)
- Time frame: All languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. Literature search was from January 1, 2013, to September 30, 2019.

No ILCOR review of this topic has been done previously. An EvUp was conducted for 2020. A search conducted in PubMed, Scopius, and Embase yielded 180 studies, and a total of 13 articles were reviewed exploring gamified learning (9) and virtual reality (4). The complete EvUp is included in Supplement Appendix C-5.

Treatment Recommendation

This EvUp does not enable a treatment recommendation to be made.

In Situ Training (EIT 4007: EvUp)

An EvUp was performed (Supplement Appendix C-6) with several studies identified that suggest the need for consideration of a SysRev. No previous review on the training of laypersons has been done by ILCOR, and there was no treatment recommendation as of January 31, 2020.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Healthcare providers

- Intervention: In situ (workplace-based) simulation-based resuscitation training
- Comparator: No in situ (workplace-based) simulation-based resuscitation training
- Outcome: Learning, performance, and patient outcomes
- Study design: All comparative, human studies (prospective and retrospective) with all different designs examining the effect of in situ simulation relative to conventional training or no intervention on learning outcome of learners, clinical performance, and patient outcomes
- Time frame: All languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. Literature search was from January 1, 2013, to October 20, 2019.

An EvUp was conducted for 2020. A search conducted in PubMed yielded 791 studies and 15 were identified as relevant. The complete EvUp is included in Supplement Appendix C-6.

Treatment Recommendation

This EvUp does not enable a treatment recommendation to be made.

High-Fidelity Manikins for ALS Training (EIT 623: EvUp)

The topic of high-fidelity training in advanced life support courses was last reviewed in 2015.[3,4] An EvUp was performed (Supplement Appendix C-7) with several studies identified that suggest the need for consideration of a SysRev.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Participants undertaking ALS training in an education setting
- Intervention: Use of high-fidelity manikins
- Comparator: Use of low-fidelity manikins
- Outcome: Patient outcomes, skill performance in actual resuscitations, skill performance at 1 year, skill performance at time between course conclusion and 1 year, skill performance at course conclusion, and cognitive knowledge
- Study design: All comparative, human studies (prospective and retrospective) examining the use high versus low fidelity manikins for ALS training and reporting knowledge/skills outcomes. Also, patient outcomes and performance in actual resuscitation situations.
- Time frame: All years and all languages were included if there was an English abstract; unpublished studies (eg, conference abstracts, trial protocols) were excluded. Literature search was from January 1, 2013, to October 2, 2019.

An EvUp was conducted for 2020. A search conducted in PubMed, Scopus, and Embase yielded 109 studies, and 3 were identified as relevant. The complete EvUp is included in Supplement Appendix C-7.

Treatment Recommendation

This treatment recommendation (below) is unchanged from 2015.[3,4]

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).

MEASURING CPR PERFORMANCE, FEEDBACK DEVICES, AND DEBRIEFING

Debriefing of Resuscitation Performance (EIT 645: SysRev)

Rationale for Review

This PICOST was an update of the 2015 CoSTR,[3,4] which was based on only 2 studies. For the purpose of this review, *briefing* was defined as a process of reviewing and communicating pertinent facts about the resuscitation before the event,[316] and *debriefing* was defined as a postevent discussion between 2 or more individuals in which aspects of performance are analyzed, with the aim of improving future performance.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Rescuers who are caring for patients in cardiac arrest in any setting
- Intervention: Briefing or debriefing
- Comparator: No briefing or debriefing
- Outcome: Survival, skill performance in actual resuscitations, quality of resuscitation (eg, reduce hands-off time, allowing for continuous compressions), and cognitive knowledge
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) of healthcare providers, IHCA or OHCA, and debriefing intervention were included. Exclusion criteria were debriefing as part of quality intervention bundle and debriefing after simulated cardiac arrest. All languages were included if there was an English abstract available.
- Time frame: Because this is an update of the 2015 CoSTR, the literature search was from January 1, 2014, to September 30, 2019.
- PROSPERO registration submitted December 1, 2019

Consensus on Science

There were no studies comparing briefing as an intervention. For debriefing, data from 3 in-hospital observational before-and-after studies (2 in adults[112,317] and 1 in pediatrics[100]), involving a total of 591 patients, and data from 1 out-of-hospital observational before-and-after study in adults,[318] involving a total of 124 patients, was analyzed. All studies included data-driven debriefing interventions using CPR quality metrics such as chest compression depth, chest compression rate, or CCF.

For the critical outcome of survival with favorable neurological outcome, we identified very low-certainty evidence (downgraded for inconsistency, indirectness, and imprecision) from 2 observational studies[100,317] including 367 patients. One study[100] demonstrated significantly increased survival with favorable neurological outcome from the use of the intervention compared with no debriefing, while the other[317] demonstrated no significant improvement from the use of the intervention compared with no debriefing. Meta-analysis demonstrates no significant effect from the use of debriefing compared with no debriefing on this outcome (RR, 1.41; 95% CI, 0.86–2.32; *P*=0.18; I^2=28%).

For the critical outcome of survival to discharge, we identified very low-certainty evidence (downgraded for indirectness and imprecision) from 4 observational studies[100,112,317,318] including 715 patients. One study[100] reported a trend toward improved survival to hospital discharge from the use of the intervention compared with no debriefing, while 3 other studies[112,317,318] demonstrated no improvement in survival to hospital discharge from the use of the intervention compared with no debriefing. Meta-analysis demonstrates a significant effect from the use of debriefing compared with no debriefing on this outcome (RR, 1.41; 95% CI, 1.03–1.93; *P*=0.03; I^2=0%).

For the critical outcome of ROSC, we identified very low-certainty evidence (downgraded for inconsistency, indirectness, and imprecision) from 3 observational studies[100,112,317] including 591 patients. One study[112] reported improved ROSC from the use of the intervention compared with no debriefing, while the other 2 studies[100,317] reported no improvement in ROSC from the use of the intervention compared with no debriefing. Meta-analysis demonstrates a significant effect from the use of debriefing compared with no debriefing on this outcome (RR, 1.18; 95% CI, 1.03–1.44; *P*=0.02; I^2=0%).

For the critical outcome of chest compression depth (mean depth), we identified very low-certainty evidence (downgraded for inconsistency and indirectness) from 3 observational studies[100,112,317] including 591 patients. One study[112] reported improved mean chest compression depth from the use of the intervention compared with no debriefing, and a second study[317] demonstrated no improvement in mean chest compression depth from the use of the intervention compared with no debriefing. A third study[100] that reported improved compliance with chest compression depth targets from the use of the intervention compared with no debriefing was not included in the meta-analysis because of differing outcome measures. Meta-analysis of 2 studies[112,317] demonstrated a significant effect from the use of debriefing compared with no debriefing on this outcome (mean difference, 4.00 mm; 95% CI, 0.18–7.82; I^2=79%).

For the critical outcome of chest compression rate (mean rate), we identified very low-certainty evidence (downgraded for inconsistency and indirectness) from 4 observational studies[100,112,317,318] including 715 patients. Two studies[112,318] reported improved mean chest compression rate from the use of the interventions compared with no debriefing, while a third study[317] demonstrated no improvement in mean chest compression rate from the use of the intervention compared with no debriefing. The last study[100] reported improved compliance with chest compression rate targets from the use of the intervention compared with no debriefing but was not included in meta-analysis because of differing outcome measures. Meta-analysis of 3 studies[112,317,318] demonstrates no significant effect from the use of the intervention compared with no debriefing on this outcome (mean difference, 5.81 bpm; 95% CI, –0.08 to 11.70; I^2, 91%).

For the critical outcome of CCF, we identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 2 observational studies[317,318] including 397 patients. Whereas one study[318] demonstrated improved CCF from the use of debriefing compared with no debriefing, the other[317] did not. Meta-analysis of these studies demonstrates no significant effect from the use of the intervention compared with no debriefing on this outcome (mean difference, 4.11%; 95% CI, –1.17 to 9.39; I^2, 89%). For this reason, the task force reduced the strength of recommendation regarding debriefing for IHCA.

Treatment Recommendations

We suggest data-driven, performance-focused debriefing of rescuers after IHCA for both adults and children (weak recommendation, very low-certainty evidence).

We suggest data-driven, performance-focused debriefing of rescuers after OHCA in both adults and children (weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-10. Although the certainty of evidence is very low, our recommendations are based on the suggested positive effects of debriefing on patient and process-related outcomes for cardiac arrest.

One limitation is that our analysis revealed high inconsistency (heterogeneity) across studies, reflecting variation in instructional design, provider type, and outcome measures. We have not identified any undesirable effects

(eg, emotional trauma) related to debriefing after cardiac arrest in the reviewed studies. Hence, we justify that the reported positive effects outweigh any possible undesirable effects. However, defusing emotions of rescuers after stressful or traumatic events has to be taken into account when assessing any potential risks related to debriefing.

While the certainty of evidence is very low, the associated costs to implement debriefing are likely to be low in many institutions. However, the reviewed studies did not explore the cost-effectiveness of debriefing. This is also applicable, when referring to the required resources for debriefing.

We also consider the high likelihood that this intervention is both acceptable to stakeholders (because of potential benefits, such as improved teamwork, improved communication, or identification of latent safety threats) and feasible in most institutions. This 2020 treatment recommendation supports the treatment recommendation made in 2015.[3,4]

Knowledge Gaps

- No studies addressed comparisons related to various specifications of debriefing, such as the format (individual feedback versus group debriefings), the timing (hot [immediate] versus cold [delayed] debriefings), use of CPR-quality metrics (data-driven versus non data-driven debriefings), or facilitation (facilitated versus nonfacilitated debriefings).
- No study was adequately powered to investigate effects on patient outcome, such as ROSC, survival to discharge, or favorable neurological outcome at discharge. One study was aimed at assessing the feasibility of intervention delivery rather than effectiveness.[317] Thus, future study design should aim at quantitative and qualitative endpoints related to process measures, such as CPR-quality metrics, and patient outcomes.
- Future research questions may include training of facilitators and impact on debriefings, type of data to be included to improve effectiveness of debriefing, and determination of the optimal length of debriefing, as well as exploration of any possible emotional side effects and their incidence and nature. Related to briefing, future studies may explore effects on rescuers and patients.

CPR Feedback Devices During Training (EIT 648: SysRev)

Rationale for Review

CPR quality is a key component in outcome of both OHCA and IHCA. Optimal methods of training both healthcare providers and laypersons are key to improving cardiac arrest outcomes. We searched for studies investigating the use of CPR feedback or guidance device in CPR training published since the last search in 2015.[3,4] We excluded studies that examined the use of CPR feedback devices in performance of CPR (either on patients or in the simulated environment). We considered both true feedback devices (systems that assess participant performance and provide corrective information) and guidance devices (systems that only provide prompts not based on participant performance, such as a metronome for CPR rate).

There was high heterogeneity among the studies in type of device used, learner demographics, and outcomes. We were unable to perform a meta-analysis, and present the data narratively.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Students who are receiving resuscitation training
- Intervention: Use of a CPR feedback/guidance device
- Comparator: No use of a CPR feedback/guidance device
- Outcome:
  - Patient survival
  - Quality of performance in actual resuscitations
  - Skill performance 1 year after course conclusion
  - Skill performance between course conclusion and 1 year
  - Skill performance at course conclusion
  - Knowledge at course conclusion
- Study design: RCTs and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, cohort studies) are eligible for inclusion. Unpublished studies (eg, conference abstracts, trial protocols) were excluded.
- Time frame: New SysRev search strategy: all years and all languages were included if there was an English abstract; rerunning existing search strategy: January 1, 2014, to November 1, 2019
- PROSPERO registration submitted November 9, 2019

Consensus on Science

We identified 13 randomized studies[319–331] and 1 nonrandomized study[332] examining the effects of CPR feedback/guidance devices on learning CPR skills. All studies were simulation-based studies, and none examined any patient outcomes or performance of teams in actual resuscitations. As a result, all studies were downgraded for indirectness.

CPR Performance at 1 Year After Training

We identified low-certainty evidence (downgraded for risk of bias and indirectness) from 2 RCTs. The first[331] reported no difference in CPR performance between a group of laypeople trained with a CPR feedback device compared with a control group at 1 year after training. In the second study of CPR training of healthcare providers,[319] both control and feedback groups improved

from baseline at 1 year after training, but there was no difference between the control and feedback groups.

CPR Performance From Training Conclusion to 1 Year After Training

We identified 5 RCTs[324,327,329,331,332] that addressed this outcome. We identified low-certainty evidence (downgraded for risk of bias and indirectness) from 4 RCTs that used true feedback devices.[324,327,329,331] All of these studies were in laypeople or junior healthcare providers, and they reported improvements in retention of CPR skills at 7 days to 3 months after training.

We identified moderate-certainty evidence (downgraded for indirectness) for 1 study[332] that examined the use of a guidance device (a song for compression rate). This study reported an improved compression rate (RR of compression rate between 100 and 120/min, 1.72; 1.17–2.55) compared with learners with no access to a guidance device. We identified 5 RCTs[324,327,329,331,332] that addressed this outcome.

We identified low-certainty evidence (downgraded for risk of bias and indirectness) from 4 RCTs that used true feedback devices.[324,327,329,331] All of these studies were in laypeople or junior healthcare providers, and they reported improvements in retention of CPR skills at 7 days to 3 months after training.

CPR Performance at End of Training

We identified 8 RCTs[319–323,326,328,330] with moderate to low certainty of evidence downgraded for risk of bias (because of confounding interventions, indirectness, and unclear outcomes) and 1 observational study (very low-certainty evidence, downgraded for indirectness).[325] Five studies showed improvement in CPR skills at the end of training with the use of feedback devices compared with no feedback device.[319,320,323,328,330] Two studies showed no difference in performance.[322,326] One study showed worse CPR performance at the conclusion of training, although this study has a high risk of bias because of unclear outcome definitions and the use of the audiovisual feedback system to replace an instructor.[321] One observational study found improvements in delivered chest compression rate (118.61 +/10.74 compressions/min versus 137.72±11.14 compressions/min; $P<0.001$), with the use of a feedback device during training of student teachers.[325]

Treatment Recommendations

These treatment recommendations (below) are unchanged from 2015.[3,4] We suggest the use of feedback devices that provide directive feedback on compression rate, depth, release, and hand position during CPR training (weak recommendation, low-certainty evidence).

If feedback devices are not available, we suggest the use of tonal guidance (examples include music or metronome) during training to improve compression rate only (weak recommendation, low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-11. In making this recommendation, the EIT Task Force noted that there have been a number of RCTs examining this topic in simulated settings but none examining patient-related outcomes. These studies have shown positive effects on retention of CPR skills, at least in the short-term, with 1 very low-certainty study suggesting harm. We recognize that effective feedback devices are only part of an efficient CPR educational strategy. This update confirms the 2015 ILCOR treatment recommendation to use feedback devices during resuscitation training.

Knowledge Gaps

- Although there are several simulation studies that demonstrate improved CPR performance both immediately after training with a feedback device and short-term retention of CPR skills after training, only 2 studies examined the effect of feedback devices on long-term retention, and none evaluated patient outcomes.
- The use of feedback devices is likely an important component of CPR training, and how it should be integrated with other instructional design elements such as mastery learning and distributive practice needs to be better defined.
- It remains unclear how best to use these devices, how they interact with instructors, and how timing of feedback may impact learning and retention. The use of a team member as a CPR coach who is dedicated to analyzing feedback data from the device and provides real-time coaching to team members providing CPR may improve the efficacy of these devices.[333]

Patient Outcomes as a Result of a Member of the Resuscitation Team Attending an ALS Course (EIT 4000: SysRev)

Rationale for Review

Attendance of participants on an ALS course comes at a cost—both financial and time—to stakeholders, including participants themselves and their institutions. It is therefore important to show whether this participation has any meaningful impact on patient outcomes. There is likely to be a lack of recent data addressing this question because ALS training is generally widespread. This ILCOR EIT Task Force review is an "adolopment" of an existing publication,[334] which was a SysRev and meta-analysis of 8 observational studies.[335–342] The literature search was repeated on October 31, 2019, and

no additional studies have been identified, making the published work contemporary.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adult in-hospital patients who have a cardiac arrest
- Intervention: Prior participation of 1 or more members of the resuscitation team in an accredited ALS course
- Comparator: No such participation
- Outcome: ROSC, survival to hospital discharge or to 30 days, and survival to 1 year
- Study design: Inclusion: any language, specifically looking at ALS or ACLS, RCTs, and observational; exclusion: other types of life support courses (eg, neonatal life support, advanced trauma life support, BLS), studies looking at impact of individual components (eg, airway, drug therapy, defibrillation)
- Time frame: The search dates for the Systematic Review published in Resuscitation extended through May 2018.[334] The search strategy was rerun July 29, 2019, covering May 2018 onward. No additional papers were identified.

Consensus on Science

For the critical outcome of ROSC, we identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 6 observational studies[335–337,339,341,342] enrolling 1461 patients showing benefit for ALS training (OR, 1.64; 95% CI, 1.12–2.41).

For the critical outcome of survival to hospital discharge or survival to 30 days, we identified very low-certainty evidence (downgraded for risk of bias, inconsistency, indirectness, and imprecision) from 7 observational studies[335,336,338–342] enrolling 1507 patients showing benefit for ALS training (OR, 2.43; 95% CI, 1.04–5.70)

For the critical outcome of survival to 1 year, we identified very low-certainty evidence (downgraded for risk of bias, inconsistency, and imprecision) from 2 observational studies[339,341] enrolling 455 patients showing no benefit for ALS (OR, 3.61; 95% CI, 0.11–119.42).

Treatment Recommendations

We recommend the provision of accredited adult ALS training for healthcare providers (weak recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-12. Adult ALS training improves resuscitation knowledge and skills and is likely to ensure best practice is applied in these emergency situations. We recognize that the evidence in support of this recommendation comes from observational studies of very low certainty. However, pooling of the available evidence consistently favors ALS training, and having ALS-trained staff present during an attempted adult resuscitation has been found to reduce treatment errors such as incorrect rhythm assessment[337] and time to ROSC.[341] We recognize that the provision of accredited adult ACLS training may not be feasible or appropriate in low-resource settings.

Knowledge Gaps

- Impact on patient outcomes of prior participation of 1 or more members of the cardiac arrest team for other life support courses (eg, pediatrics, newborns)

USE OF SOCIAL MEDIA

First Responder Engaged by Technology (EIT 878: SysRev)

Rationale for Review

Bystander CPR/defibrillation improves survival from OHCA, but rates of bystander CPR and performance quality remain low. Engaging volunteer citizens through different social media/technologies could potentially increase rates of bystander CPR/defibrillation and survival. Therefore, this PICOST searched for the role of citizen as first responder, defined as all individuals who were engaged/notified by a smartphone app with mobile positioning system (MPS) or text message (TM)–alert system to attend OHCA events and initiate early CPR and early defibrillation.

Population, Intervention, Comparator, Outcome, Study Design, and Time Frame

- Population: Adults and children with OHCA
- Intervention: Having a citizen CPR responder notified of the event via technology or social media
- Comparators: No such notification
- Outcome: Survival to hospital discharge with good neurological outcome, survival to hospital discharge/30-day survival, hospital admission, ROSC, bystander CPR rate, and time to first compression/shock
- 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), animal studies, case series, and simulation studies were excluded.
- Time frame: All years and all languages were included if there was an English abstract. The search strategy was performed on the same day (October 25, 2019) for the 3 databases.

- PROSPERO registration submitted to PROSPERO on November 12, 2019

Consensus on Science

Three of the included studies[344–346] assessed the role of a TM-alert system, 3 studies[347–349] assessed the role of a smartphone app with MPS, and 1 study[350] assessed both.

Most studies' outcomes were compared between the intervention and the control period, while 2 studies[347,349] compared the time to compression/shock in the intervention group with that of the EMS.

Studies covered different search radiuses (ie, 500 m, 1000 m). When it was possible, we extracted only adjusted outcomes from the studies.

The most important confounders (eg, primary rhythm, etiology, witnessed status, location of arrest, gender, age, comorbidities response time, time of the arrest) were controlled for in the multivariable analysis.

However, some studies did not report adjusted data or did so only for certain outcomes (mainly primary outcomes). In these cases, we reported unadjusted RR with 95% CI. In the case of studies assessing the same outcomes, a pooled RR was calculated and reported along with the 95% CI.

For the critical outcome of survival with favorable neurological outcome at discharge, we identified very low-certainty evidence from 2 observational studies (downgraded for serious risk of bias) enrolling 2149 OHCAs showing no benefit for having a citizen CPR responder notified of the event via technology or social media (adjusted pooled RR, 1.4; 95% CI, 0.6–3.4).[344,349]

For the critical outcome of survival to hospital discharge/30-day survival, we identified moderate-certainty evidence from 1 RCT (downgraded for serious risk of bias)[348] and very low-certainty evidence (downgraded for serious risk of bias and serious inconsistency) from 4 observational studies.[344,346,349,350] The RCT reported no benefit in 1-month survival between the intervention and the control group (unadjusted RR, 1.3; 95% CI, 0.8–2.1). The meta-analysis of adjusted data included 2905 OHCAs (4 studies) and showed benefit in survival to hospital discharge when a citizen CPR responder was notified of the event by a smartphone app with MPS or TM-alert system (adjusted pooled RR, 1.70; 95% CI, 1.16–2.48; I^2=69%; *P*=0.02); 98/1000 more patients benefitted with the intervention (95% CI, 22 more patients/1000 to 208 more patients/1000 when compared with notification by a smartphone app with MPS or TM-alert system not being offered). These results are confirmed by RRs reported separately in 3 of the 4 studies, showing benefit in survival to hospital discharge when a citizen CPR responder was notified by technology (RR, 1.7 [95% CI, 1.17–2.5][350]; RR, 2.23 [95% CI, 1.41–3.23][346]; RR, 2.37 [95% CI, 1.07–4.55][349]). One of the studies did not report any significant benefit (RR, 1.06; 95% CI, 0.72–1.51).[344]

For the critical outcome of survival to hospital admission, we identified no studies.

For the important outcome of ROSC, we identified moderate-certainty evidence (downgraded for serious risk of bias) from 1 RCT enrolling 667 OHCAs showing no significant benefit for having a citizen CPR responder notified of the event via technology or social media (0.3 percentage points higher for the intervention group; 95% CI, 6.5 lower–7.3 higher; unadjusted RR, 1.01; 95% CI, 0.79–1.28).[348] We also identified very low-certainty evidence (downgraded for serious risk of bias) from 3 observational cohort studies enrolling 2571 OHCAs showing no benefit for having a citizen CPR responder notified of the event via technology or social media (unadjusted pooled RR, 0.97; 95% CI, 0.60–1.57).[344,346,349]

For the important outcome of bystander CPR, we identified high-certainty evidence from 1 RCT.[348] This RCT enrolled 667 OHCAs, showing an absolute difference for intervention versus control of 14 percentage points (6 higher to 21 higher; adjusted RR, 1.27; 95% CI, 1.10–1.46); 129/1000 more patients benefitted with the intervention (95% CI, 48 more patients/1000 to 219 more patients/1000 when compared with notification by a smartphone app with MPS or TM-alert system not being offered).[348]

We also identified low-certainty evidence from 1 before-and-after study.[344] This study enrolled 1696 OHCAs, showing benefits for having a citizen CPR responder notified of the event via technology or social media (adjusted RR, 1.29; 95% CI, 1.20–1.37); 160/1000 more patients benefitted with the intervention (95% CI, 110 more patients/1000 to 204 more patients/1000 when compared with no intervention).[344]

For the important outcome of time to first compression/shock delivery, we identified very low-certainty evidence (downgraded for serious risk of bias and inconsistency) from 4 observational studies enrolling 1833 OHCAs showing that having a citizen CPR responder notified of the event via technology or social media led to significantly lower response times compared with no technology, ie, median response time (minutes:seconds) 6:17 (IQR, 4:49– 7:57) versus 9:38 (IQR, 7:14–12:51), Z=–14.498, *P*<0.0001[347] and median time for defibrillation delivery (minutes:seconds) 8:00 (IQR, 6:35–9:49) versus 10:39 (IQR, 8:18–13:23; *P*<0.001).[345] Another study showed a significant difference in median response time between mobile rescuers (4 minutes; IQR, 3–6) and EMS teams (7 minutes; IQR, 6–10]), *P*<0.001.[349] In a comparison of an application-based system with a TM-based system, benefit was found in using the app: responders' median response time 3.5 minutes (IQR, 2.8–5.2) compared with the TM-based system 5.6 minutes (IQR, 4:2–8:5; *P*=0.0001).[350]

Treatment Recommendations

We recommend that citizen/individuals who are in close proximity to a suspected OHCA event and willing to be

engaged/notified by a smartphone app with an MPS or TM-alert system should be notified (strong recommendation, very low-certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The evidence-to-decision table is included in Supplement Appendix A-13. Notifying a citizen CPR responder by a smartphone app with an MPS or TM-alert system to attend OHCA events can lead to an increase in early CPR and defibrillation, improving survival. We considered the improved outcomes in OHCA patients when a citizen CPR responder was notified by a smartphone app or TM for the event and started CPR or delivered defibrillation across most studies.

Even though the certainty of the evidence is very low/low among the observational cohort studies, there was 1 RCT and 1 before-and-after study, reporting improved outcomes when first responders were notified by a smartphone app with MPS or TM-alert system for the OHCA event and started CPR or delivered defibrillation.

Pooled RRs were estimated using a random effect model, because it takes into account the between-studies variability. Heterogeneity between studies was assessed by using the I^2 statistics and was evaluated to be moderate (I^2=69%, P=0.021) for the outcome of survival to hospital discharge. Sensitivity analyses were conducted to investigate the impact each study had on the overall estimate. The presence of statistical heterogeneity suggests the presence of variability among the clinical characteristics of the studies' populations (ie, comorbidities, cause of cardiac arrest, time and location of the arrest, arrival time of laypersons or first responders at the location) as well as methodological heterogeneity (ie, study design, data collection).

In 2015, the EIT Task Force suggested that individuals in close proximity to a suspected OHCA, and who are willing and able to perform CPR, be notified of the event via technology or social media.[3,4] In 2020, we have made a clear recommendation that a smartphone app with an MPS or TM-alert system should be used to notify potential rescuers.

Knowledge Gaps

- There is a need for more high-certainty prospective studies including the critical outcome of long-term survival. Risk of bias is a common issue, with studies controlling for confounding factors only for a few outcomes. More RCT studies are needed for more robust evidence.
- There is no evidence of the cost-effectiveness of notifying laypersons through a smartphone app with an MPS or TM-alert system in the case of OHCAs.
- There was only 1 study assessing which of these technologies most improved outcome after OHCA (app versus text message). There is the need for more high-certainty evidence to determine the best technology to use in terms of OHCA outcomes.
- There is a need for the extension of these studies in different social, cultural, ethnic, and geographical contexts.
- The results of the included studies apply only to OHCAs of cardiac origin; there is a need for more evidence in cases of OHCA caused by trauma, drowning, intoxication, or suicide.
- There is a need for more consistent high-certainty evidence on the impact of engaged/notified versus unnotified bystander responses on survival with favorable neurological outcome at hospital discharge, ROSC, and survival to hospital admission.
- The impact of engaged/notified versus unnotified bystander responses on bystander CPR rates and time to first compressions/shock delivery
- Safety of notifying CPR responders by a smartphone app with an MPS or TM-alert system to attend OHCA events
- The psychological or emotional impact imposed on responders by potential or actual engagement in a call to rescue

TOPICS NOT REVIEWED IN 2020

BLS Including AED Training

- CPR instruction methods (self-instruction versus traditional) (EIT 647)
- Skills testing for resuscitation (EIT 632)
- BLS training for high-risk populations (EIT 649)
- First aid training (EIT 773)
- Chest compression CPR training (EIT 881)
- Duration of BLS courses (EIT 644)

ALS Training Including Team and Leadership Training, and METs and RRTs

- Timing for advanced resuscitation retraining (EIT 633)

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Disclosures

Appendix 1. Writing Group Disclosures

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Adam Cheng	Alberta Children's Hospital (Canada)	None	None	None	None	None	None	None
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Elaine Gilfoyle	Alberta Children's Hospital (Canada)	None	None	None	None	None	None	None
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Kasper G. Lauridsen	Aarhus University Hospital (Denmark)	Laerdal Foundation (Unrestricted research project grant)*	None	None	None	None	None	None
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Appendix 1. Continued

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Deems Okamoto	Self-employed	None	None	None	None	None	None	None
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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.

Appendix 2. Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Expert Witness	Ownership Interest	Consultant/ Advisory Board	Other
Jeffrey M. Berman	UNC Hospitals	None	None	None	None	None	None	None
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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.

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