CoSTR

2025 International Liaison Committee on Resuscitation Consensus on Science With Treatment Recommendations

Neonatal Life Support

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ABSTRACT

The International Liaison Committee on Resuscitation continually reviews new, peer-reviewed cardiopulmonary resuscitation science and publishes comprehensive reviews every 5 years. The Neonatal Life Support chapter of the *2025 International Liaison Committee on Resuscitation Consensus on Science With Treatment Recommendations* addresses all published resuscitation evidence reviewed by the Neonatal Life Support Task Force science experts since 2020. This summary addresses 40 questions on population, intervention, comparator, and outcomes, addressing all parts of the Neonatal Resuscitation Algorithm. The summary includes 4 new systematic reviews, 2 new scoping reviews, and evidence updates for other topics. Members of the Neonatal Life Support Task Force have assessed, discussed, and debated the quality of the evidence on the basis of Grading of Recommendations Assessment, Development, and Evaluation criteria, and their statements include consensus treatment recommendations. Insights into the deliberations of the task force are provided in the Justification and Evidence-to-Decision Framework Highlights sections. In addition, the task force lists priority knowledge gaps for further research.

Key words: ILCOR**,** infant, newborn, neonatal resuscitation

INTRODUCTION

Resuscitation of the Newborn Infant

The physiological adaptations that take place during and immediately after birth are interdependent and critical to survival and good health. They include the establishment of air breathing, closure of fetal cardiovascular shunts, and functional adaptations to increase pulmonary blood flow while maintaining or increasing systemic flows and pressures. Additional adaptations that are critical to survival of the immediate newborn period include the maintenance of body temperature and of a consistent supply of glucose and substrates for metabolism of vital organs. The majority of newborns adapt to extrauterine life without resuscitation, but interventions to support or achieve these adaptations can be critical to achieving survival and preventing morbidity.

National data from 2022 to 2023 from Australia indicated that among over 600 000 live-born infants, 10.3% received continuous positive airway pressure, 4.5% received positive-pressure ventilation, 0.8% were intubated, and 0.2% received chest compressions.[1] However, although these results are from a country where neonatal resuscitation training is widely accessible and the neonatal mortality rate is low (2.3/1000), the data reflect those who received various resuscitation interventions and do not define the optimal proportions who would benefit. The need for resuscitation interventions may be affected by various factors including maternal health, the quality of antenatal and intrapartum care, rates of prematurity, and other risk factors. Higher intervention rates may be needed to optimize survival without major morbidity when high-quality pregnancy and birth care are unavailable.

As consistently recommended by the Neonatal Life Support (NLS) Task Force,[2,3] newborn infants who are breathing or crying and have good tone and an adequate heart rate may undergo delayed cord clamping and should be placed skin-to-skin with their mothers, using

methods to maintain a normal body temperature. Ongoing observation is needed because the low oxygen saturations that are normal in the first few minutes after birth can persist or recur, and secondary apnea and breathing difficulties are common. When respiratory effort is inadequate, escalation should be undertaken by using the steps of the Neonatal Resuscitation Algorithm (Figure 1), which is unchanged from 2015 and 2020.[4,5]

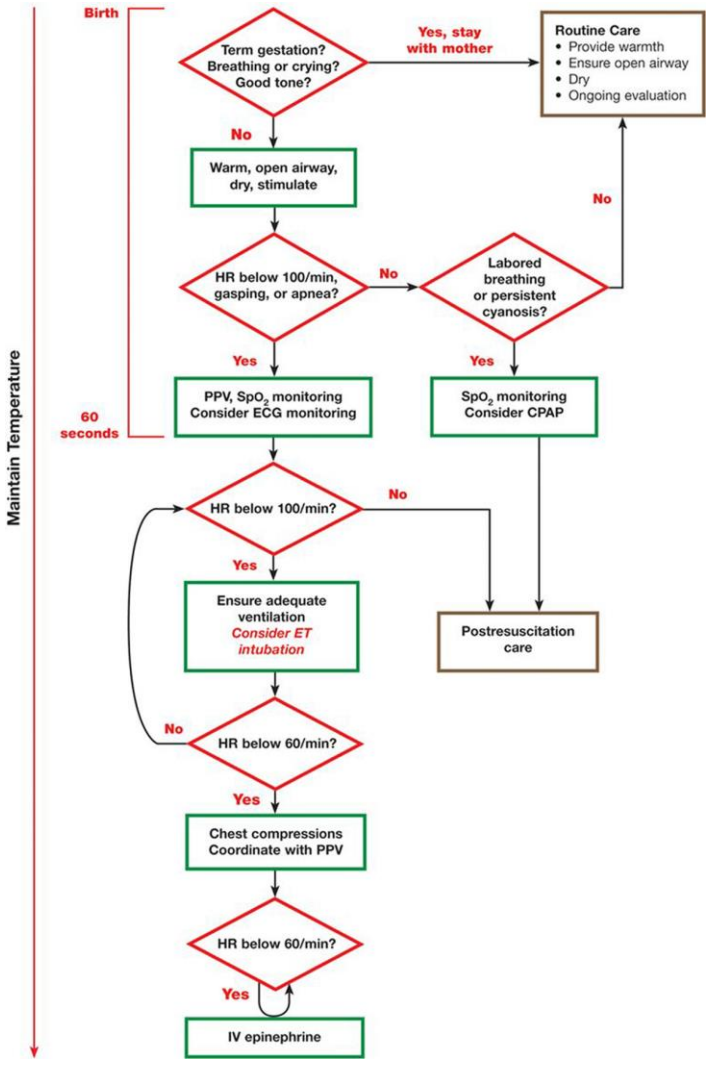

Figure 1. Neonatal Resuscitation Algorithm. CPAP indicates continuous positive airway pressure; ECG, electrocardiographic; ET, endotracheal; HR, heart rate; IV, intravenous; and PPV, positive-pressure ventilation.

This NLS Task Force chapter of the International Liaison Committee on Resuscitation (ILCOR) *2025 International Liaison Committee on Resuscitation Consensus on Science With Treatment Recommendations* (CoSTR) includes 4 systematic reviews (SysRevs) and 2 scoping reviews (ScopRevs) conducted by the NLS Task Force in the previous year. Another 22 reviews conducted and published[6-9] since the 2020 publication are also summarized to provide a single reference document for readers, along with evidence updates (EvUps) for these reviews and for 12 reviews conducted in 2020 or earlier. Thus, the NLS Task Force work presented here encompasses 40 PICOST (population, intervention, comparator, outcome, study design, time frame) questions. Draft CoSTRs for all topics evaluated with SysRevs were posted on a rolling basis on the ILCOR website,[10] with public comments accepted for at least 2 weeks after posting and considered before final versions were posted.

Although only SysRevs can generate a full CoSTR and new treatment recommendations, many other topics were evaluated with more streamlined processes, including ScopRevs and EvUps. Good practice statements, which represent the opinion of task force experts in light of very limited or no direct evidence, can be generated after ScopRevs and occasionally after EvUps in cases where the task force thinks providing guidance is especially important. A separate article in this issue includes the full details of the evidence evaluation process.[11]

This summary statement contains the final wording of the treatment recommendations and good practice statements as approved by the ILCOR NLS Task Force. SysRevs include evidence-to-decision highlights and knowledge gaps, and ScopRevs summarize task force insights on specific topics. Links to the published reviews and full online CoSTRs are provided in the corresponding sections. Evidence-to-decision tables for SysRevs are provided in Appendix A, and the complete EvUp worksheets are provided in Appendix B.

Topics are presented using the PICOST format. To minimize redundancy, PICOST wording has been removed from EvUps and reviews published previously, and the study designs have been removed from all reviews except in cases where the designs differed from the NLS standard criteria. The standard study designs included were randomized controlled trials (RCTs) and nonrandomized studies (non-RCTs, interrupted time series, controlled before-and-after studies, and cohort studies). Case series, case reports, animal studies, and unpublished studies (conference abstracts, trial protocols) were excluded. All languages were included provided they had an English abstract.

The following topics are addressed in this NLS Task Force CoSTR summary. The order reflects the steps in the Neonatal Resuscitation Algorithm. Importance of all outcomes was in accord with Strand et al[12] and (where stated) Webbe et al,[13] or by consensus of the task force for outcomes specific to each review.

Anticipation and Preparation

- Effect of briefing before neonatal resuscitation **(**NLS 5002: EvUp 2025)

Umbilical Cord Management

- Umbilical cord management at birth for nonvigorous term and late preterm infants **(**NLS 5050[a]: SysRev 2025)
- Umbilical cord management at birth for vigorous term and late preterm infants (NLS 5050[b]: SysRev 2021, EvUp 2025)
- Umbilical cord management at birth for preterm infants (NLS 5051: SysRev 2024, EvUp 2025)

Initial Steps

- Maintaining normal temperature immediately after birth in term and late preterm infants (NLS 5100: SysRev 2022, EvUp 2025)

- Maintaining normal temperature immediately after birth in preterm infants (NLS 5101: SysRev 2023, EvUp 2025)
- Suctioning of clear amniotic fluid at birth (NLS 5120: SysRev 2022, EvUp 2025)
- Tracheal suctioning of meconium-stained amniotic fluid (NLS 5130: SysRev 2022, EvUp 2025)
- Tactile stimulation (NLS 5140: SysRev 2022, EvUp 2025)

Assessment of Heart Rate

- Heart rate assessment methods in the delivery room—diagnostic characteristics (NLS 5200: SysRev 2023, EvUp 2025)
- Heart rate assessment methods in the delivery room—clinical outcomes (NLS 5201: SysRev 2022, EvUp 2025)

Ventilation and Oxygenation

- Devices for administering positive-pressure ventilation (NLS 5300: SysRev 2021, EvUp 2025)
- Continuous positive airway pressure versus positive-pressure ventilation for preterm infants (NLS 5310: SysRev 2015, EvUp 2025)
- Continuous positive airway pressure for term and late preterm infants with respiratory distress (NLS 5312: SysRev 2022, EvUp 2025)
- Sustained inflations during newborn resuscitation (NLS 5320: EvUp 2025)
- Supraglottic airway device versus face mask (NLS 5340: SysRev 2022, EvUp 2025)
- Supraglottic airway device versus tracheal tube (NLS 5341: EvUp 2025)
- Use of a supraglottic airway device during chest compressions (NLS 5342: ScopRev 2025)
- Exhaled CO_2 monitoring to guide noninvasive ventilation (NLS 5350: SysRev 2023, EvUp 2025)

- Video versus traditional laryngoscope (NLS 5351: SysRev 2025)
- Respiratory function monitoring during resuscitation at birth (NLS 5360: SysRev 2022, EvUp 2025)
- Near-infrared spectroscopy during positive-pressure ventilation (NLS 5362: SysRev 2025)
- Oxygen concentration for initiating resuscitation in preterm infants (NLS 5400: SysRev 2025)
- Oxygen concentration for initiating resuscitation in late preterm and term infants (NLS 5401: EvUp 2025)

Circulatory Support

- Heart rate for commencing chest compressions (NLS 5500: ScopRev 2023, EvUp 2025)
- Chest compressions with 2 thumbs versus other techniques (NLS 5501: ScopRev 2023, EvUp 2025)
- Supplemental oxygen during chest compressions (NLS 5503: ScopRev 2023, EvUp 2025)
- Compression-to-ventilation ratio (NLS 5504: ScopRev 2023, EvUp 2025)
- Use of feedback cardiopulmonary resuscitation (CPR) devices for neonatal cardiac arrest (NLS 5505: ScopRev 2023, EvUp 2025)
- Depth of chest compressions (NLS 5506: ScopRev 2023, EvUp 2025)
- Chest compression location on sternum (NLS 5507: EvUp 2025)

Drug and Fluid Administration

- Epinephrine (adrenaline) for neonatal resuscitation (NLS 5600: SysRev 2020, EvUp 2025)
- Sodium bicarbonate during neonatal resuscitation (NLS 5601: EvUp 2020, EvUp 2025)
- Glucose management during or immediately after resuscitation (NLS 5602: ScopRev 2025)
- Blood volume expansion during neonatal resuscitation (NLS 5650: EvUp 2020, EvUp 2025)

- Intraosseous versus intravenous cannulation for emergency access (NLS 5652: SysRev 2020, EvUp 2025)

Postresuscitation Care

- Rate of rewarming hypothermic newborns (NLS 5700: EvUp 2025)
- Therapeutic hypothermia in limited-resource settings (NLS 5701: EvUp 2025)

Prognostication During CPR

- Impact of duration of intensive resuscitation (NLS 5800: SysRev 2020, EvUp 2025)

Family Presence

- Family presence during neonatal resuscitation (NLS 5900: SysRev 2019, EvUp 2025)

Readers are encouraged to monitor the ILCOR website[10] to provide feedback on planned SysRevs and to provide comments when additional draft reviews are posted.

ANTICIPATION AND PREPARATION

Effect of Briefing Before Neonatal Resuscitation (NLS 5002: EvUp 2025)

Rationale for Review

A ScopRev addressed both briefing and debriefing to determine whether they improve outcomes for infants, families, and healthcare professionals for the 2020 CoSTR and concluded that there was insufficient evidence to make a treatment recommendation.[5,14] This EvUp only assessed briefing because debriefing has been addressed in a recent SysRev by the Education, Implementation, and Teams Task Force.[15] The complete EvUp, including the full PICOST, can be found in Appendix B.

Time frame: December 1, 2019, to December 30, 2025

Summary of Evidence

Four new studies including observational data from before and after implementation of an intervention to increase or improve aspects of briefing before newborn resuscitation were

identified.[16-19] The studies were generally supportive of the use of briefing, but there is insufficient new evidence to justify a new SysRev.

Treatment Recommendation (2025)

There was no previous treatment recommendation on the topic. The task force considered that the following statement was justified:

Whenever the need for resuscitation of a newborn is anticipated, there should be a briefing of the neonatal team that includes communication with the obstetric and/or midwifery team to inform the neonatal management plan (good practice statement).

UMBILICAL CORD MANAGEMENT

For umbilical cord management, the previous reviews for preterm and term infants used definitions that do not adequately reflect more recent research studies and routine definitions used in clinical practice. These terms have been replaced, as noted in Table 1, in the following 3 summaries of reviews of umbilical cord management. There is also some variation in how individual clinical trialists or previous reviews have used these terms. Where essential to interpretation of results, we will point this out. Adherence to the intended intervention may also vary between the arms of different studies.

Table 1. Abbreviations and Definitions of Terms Related to Umbilical Cord Management

Time-based decisions	Physiology-based decisions	Cord milking
ICC: Immediate cord clamping (usually ≤15 s) without initiation of respiratory support **ECC:** Early cord clamping (usually <60 s) without initiation of respiratory support; may include infants who had ICC	**Intact cord resuscitation:** Any time to cord clamping (usually ≥60 s) but when respiratory support (high-flow, CPAP, PPV) is provided before cord clamping **PBCC:** Physiologically based cord clamping; cord clamping not based	**I-UCM:** Intact umbilical cord milking; repeated compression of the cord from the placental side toward the baby with the connection to the placenta intact **C-UCM:** Cut umbilical cord milking; drainage of the cord by

Time-based decisions	Physiology-based decisions	Cord milking
DCC: Deferred cord clamping (usually ≥60 s), before respiratory support	on a specific time but on physiological observations such as a defined duration of breathing or effective PPV	compression from the cut end toward the baby after clamping and cutting a long segment

CPAP indicates continuous positive airway pressure; C-UCM, cut umbilical cord milking; DCC, deferred cord clamping; ECC, early cord clamping; ICC, immediate cord clamping; I-UCM, intact umbilical cord milking; PBCC, physiologically based cord clamping; and PPV, positive-pressure ventilation.

Umbilical Cord Management at Birth for Nonvigorous Term and Late Preterm Infants (NLS 5050[a]: SysRev 2025)

Rationale for Review

Clamping the umbilical cord at birth is a key event affecting adaptation to extrauterine life, particularly in the seconds and minutes immediately after birth. If cord clamping is deferred, umbilical venous return contributes to hemodynamic stability for several minutes after birth.[20,21] Placental transfusion also reduces later need for red cell transfusion in preterm infants and helps to prevent anemia and iron deficiency in term infants.[9]

A 2021 SysRev conducted for ILCOR with the Cochrane Collaboration found substantial evidence to support a recommendation suggesting deferred cord clamping for ≥60 seconds.[9,22] Because of a paucity of evidence at the time, this recommendation excluded the important subgroup of infants who are not vigorous at birth. Their treatment has traditionally involved immediate clamping of the umbilical cord and transfer to a resuscitation trolley for the commencement of assisted ventilation. Alternative strategies to enable placental transfusion before or during resuscitation have since been investigated. The task force updated the previous SysRev for term and late preterm infants for the specific subgroup of infants who are not

vigorous at birth. The review was registered before initiation (PROSPERO 2024 CRD42024562012). The full online CoSTR can be found on the ILCOR website.[23]

Population, Intervention, Comparator, Outcome, and Time Frame

- ***Population:*** Term and late preterm infants (≥34 weeks' gestation) who are not vigorous at birth
- ***Intervention:*** Any cord management strategy designed to improve fetal to neonatal cardiorespiratory transition, including deferred cord clamping, intact cord resuscitation, intact umbilical cord milking, and cut umbilical cord milking
- ***Comparator:*** Immediate cord clamping, early cord clamping, or between-intervention comparisons (eg, deferred cord clamping versus intact umbilical cord milking or cut umbilical cord milking)
- ***Outcome:***
  - Infant
  - Neonatal mortality (critical)
  - Moderate to severe neurodevelopmental impairment at 18 to 24 months (critical)
  - Any component of neurodevelopmental impairment at 18 to 24 months (critical) (cerebral palsy, significant mental developmental delay, blindness as defined by the World Health Organization [<20/200 visual acuity] or the author's definition, hearing deficit [aided or <60 dB on audiometric testing])
  - Moderate to severe hypoxic ischemic encephalopathy (Sarnat 2 or 3[24]) (critical)
  - Proportion of infants receiving chest compressions in the delivery room (important)
  - Admission to a neonatal intensive care unit (NICU) (important)
  - Jaundice: treated with exchange transfusion (critical) or phototherapy (important)

- Hematologic outcomes including peak hemoglobin or hematocrit concentration during hospital admission (important) and anemia or iron deficiency at 4 to 6 months (important)
- Unintended hypothermia within the first hour of life (important)
- Mother
- Postpartum hemorrhage, estimated as at least 1000 mL (critical), postpartum infection (critical), death or severe morbidity (composite), major surgery, organ failure, intensive care unit admission (critical)

- ***Time frame:*** January 1, 2019, to July 10, 2024

Consensus on Science

Intact Umbilical Cord Milking Compared With Early Cord Clamping

One eligible cluster-randomized multicenter crossover trial including 1730 infants,[25] of whom 971 were followed up to 2 years of age,[26] was identified. Infants were eligible if they had poor tone, pallor, or were not breathing despite stimulation. For those in the intact umbilical cord milking arm, the infant was held below the level of the incision (for caesarean births) or on the mother's abdomen (for vaginal births) while a 20 cm length of umbilical cord was milked for 2 seconds per time a total of 4 times before cord clamping. For those in the early cord clamping arm, the cord was clamped within 60 seconds after birth (median interquartile range, 20 [10–30] s). Key outcomes are summarized in Table 2. For additional outcomes, see the full online CoSTR.[23] Statistical results are reported conforming to analytical methods that were used in the study because of the cluster randomization (eg, modified odds ratio instead of relative risk).

Table 2. Milking of the Intact Umbilical Cord Compared With Early Cord Clamping: Critical and Important Outcomes

Outcome (importance*)	Participants (studies), n	Certainty of evidence, GRADE	Relative effect (95% CI)	Anticipated absolute effect (95% CI)	
				Risk with ECC	Risk difference with I-UCM
Mortality (critical)	1730 (1 RCT)[25] (follow-up to hospital discharge)	Low	RR 0.11 (0.01–2.03)	5/1000	4 fewer per 1000 (5 fewer to 5 more)
Moderate or severe HIE (critical)	1634 (1 RCT)[25]	Moderate	RR 0.49 (0.25–0.97)	30/1000	15 fewer per 1000 (22 fewer to 1 fewer)
Admission to NICU (important)	1730 (1 RCT)[25]	Moderate	mOR† 0.69 (0.41–1.14)	279/1000	68 fewer per 1000 (142 fewer to 27 more)
Hemoglobin (g/dL) (important)	1730 (1 RCT)[25]	Moderate	–	Median hemoglobin (g/dL) was 17.3 g/L	mMD† 0.7 g/L higher (0.3 higher to 1.1 higher)
Survival with typical development (ASQ domains normal range)	971 (1 RCT)[26] (follow-up to 2 years of age)	Low	mOR† 0.76 (0.54–1.08)	829/1000	42 fewer per 1000 (105 fewer to 11 more)

*Outcome importance according to Strand et al.[12]

[†]Modeled odds ratios or modeled mean differences were as reported by study authors (modeling to account for the cluster-randomized study design).

ASQ indicates Ages & Stages Questionnaires; ECC, early cord clamping; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; HIE, hypoxic ischemic encephalopathy; I-UCM, intact cord milking; mMD, modelled mean difference; mOR, modeled odds ratio; NICU, neonatal intensive care unit; RCT, randomized controlled trial; and RR, relative risk.

Intact Cord Resuscitation Compared With Early Cord Clamping or Immediate Cord Clamping

Three studies were included,[27-29] and 2-year follow-up data[30] were available for one.[28] In all 3 studies, the intervention group received respiratory support, if required, using a T-piece resuscitator[27,29] or self-inflating bag[28] with the umbilical cord intact. Two studies aimed for at least 180 seconds before cord clamping[27,28] and the other at least 2 minutes and until ≥60 seconds after change in color of a CO_2 detector placed between the face mask and T-piece.[29] Timing of clamping of the umbilical cord in the control arm of each study was generally within 1 minute. Clinical benefit or harm could not be excluded for any of the critical or important short- and long-term outcomes.

Two other small single-arm studies examining resuscitation with an intact cord concluded that intact cord resuscitation was feasible in 12 nonvigorous infants ≥32 weeks' gestation[31] and 20 infants with congenital diaphragmatic hernia.[32]

Prior Treatment Recommendations (2021; see NLS 5050[b])

There are none for this subgroup of nonvigorous term and late preterm infants.

Treatment Recommendations (2025)

Intact Umbilical Cord Milking Compared With Early Cord Clamping

In term and late preterm infants who remain nonvigorous despite stimulation, we suggest intact cord milking in preference to early cord clamping (weak recommendation, low-certainty evidence).

Intact Cord Resuscitation Compared With Early Cord Clamping or Immediate Cord Clamping

There is currently insufficient evidence to recommend either for or against intact cord resuscitation for term and late preterm infants who are nonvigorous at birth.

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision table is provided in Appendix A.

Intact Umbilical Cord Milking Compared With Early Cord Clamping

The use of intact umbilical cord milking in preference to early cord clamping in infants who remain nonvigorous despite stimulation is justified by the reduction in moderate or severe hypoxic ischemic encephalopathy and improvement in early hemoglobin, given that there was no evidence of adverse effects. It also allows a uniform suggestion for intact cord milking as an alternative to early cord clamping for all infants ≥28 weeks' gestation,[9] bearing in mind that deferred cord clamping is still the preferred option for all vigorous infants. The rationale differs depending on gestation, but the certainty of evidence and strength of recommendation are similar.[9] The strategy is simple, requires no expensive equipment, and appears safe and feasible. Although no formal cost-benefit analysis has been performed, any reduction in moderate or severe hypoxic ischemic encephalopathy is likely to result in cost savings both in relation to the costs of NICU care and the lifetime costs of adverse outcomes of this condition.

An additional observational study reported that in newborn infants who were not yet crying, providing tactile stimulation while the cord remained intact (deferred cord clamping) was associated with a higher proportion who breathed spontaneously, a decrease in use of bag-mask ventilation, fewer Apgar scores ≤3, and increased odds of spontaneous breathing than providing stimulation after early cord clamping,[33] supporting the role of tactile stimulation during deferred cord clamping and indicating that the task force treatment recommendation for tactile stimulation to stimulate breathing should apply regardless of the method of umbilical cord management.[34]

Intact Cord Resuscitation Compared With Early Cord Clamping or Immediate Cord Clamping

The task force considered that because clinical benefit or harm cannot be excluded for any outcome, and certainty of evidence was low, no general or conditional treatment recommendation can be made at this time. Resuscitation of infants still attached to the umbilical cord can be accomplished by using a variety of strategies and devices. These include purpose-built resuscitation tables that may include equipment to provide an external heat source, assisted ventilation, and monitoring. Given that in many cases, the finding that an infant is not vigorous at birth is unexpected, these devices may only be available for a small proportion of high-risk births, and potentially not in locations where resources are limited.

No studies were found to inform a treatment recommendation about any other form of umbilical cord management in late preterm and term infants who are not vigorous at birth, or to compare intact umbilical cord milking to intact cord resuscitation.

Knowledge Gaps

- The need for large multicenter RCTs evaluating both intact umbilical cord milking and intact cord resuscitation, including high-quality follow-up with formal assessment of cognition, motor development, hearing, and vision
- The safety, useability, and cost-effectiveness of different devices to support resuscitation with an intact cord
- The effect of other techniques to facilitate placental transfusion including milking of a long segment of clamped-and-cut umbilical cord

Umbilical Cord Management for Vigorous Term and Late Preterm Infants (NLS 5050(b): SysRev 2021, EvUp 2025)

Various methods of umbilical cord management for all term and late preterm infants were addressed by a 2021 SysRev and included in the 2021 CoSTR summary, although the studies

found for inclusion included few infants who were nonvigorous.[9,22] An EvUp was conducted for 2025 to determine whether, in vigorous infants, any of these methods compared with early cord clamping (or any other method) improved neonatal or infant outcomes without causing any harm to mothers. The complete EvUp, including the full PICOST, can be found in Appendix B.

- **Time frame:** July 26, 2019, to July 10, 2024

Summary of Evidence

Forty-six eligible RCTs since the last SysRev were identified. Four focused on risk of postpartum hemorrhage in the setting of deferred cord clamping.[35-38] Eight trials compared intact umbilical cord milking with deferred cord clamping for infant hematologic outcomes for different durations of deferred cord clamping.[39-46] Four trials examined neurodevelopmental or brain-imaging outcomes.[47-50] One trial assessed breastfeeding scores.[51] Nine trials compared longer durations of deferred cord clamping with shorter durations of deferred cord clamping.[52-60] Six trials compared deferred cord clamping (60 s) with immediate cord clamping.[61-66] Two trials compared physiologically based cord clamping with deferred cord clamping or umbilical cord milking,[67,68] and 1 compared intact umbilical cord milking performed twice with cut umbilical cord milking performed 2 to 4 times.[69] Eight trials examined specific subgroups of infants, including those at risk of Rh hemolytic disease,[70] infants of mothers with diabetes or large-for-gestational age infants,[71-74] and infants who were small for gestational age, had fetal growth restriction, or whose mothers had preeclampsia.[75-77] Three trials reported other comparisons or outcomes,[78-80] and additional results of one trial[65] were reported in a second paper.[81]

Based on the amount of evidence, the task force will prioritize an updated SysRev.

Treatment Recommendation (2021)

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

Umbilical Cord Management at Birth for Preterm Infants (NLS 5051: SysRev 2023, EvUp 2025)

Umbilical cord management for preterm infants was addressed by a 2021 SysRev,[9,82] which was updated for the 2024 CoSTR summary[7] by adolopment of a large, individual patient data pairwise meta-analysis[83] and network meta-analysis[84]—the iCOMP (Cord Management of Preterm Birth) study. An EvUp was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Study design:*** The iCOMP individual patient data meta-analysis and network meta-analysis included RCTs comparing umbilical cord management strategies for which individual patient data were available but excluded trials with missing data, integrity issues, those not fitting intervention categories, and cluster- and quasi-randomized trials.[85] The updated search included RCTs whether or not individual patient data were available.
- ***Time frame:*** June 6, 2023, to June 6, 2024

Summary of Evidence

The search found 8 eligible RCTs[75,86-92] and 1 SysRev.[93] Most of the clinical trials had insufficient sample size for critical and important outcomes, but overall, they supported the use of deferred cord clamping or umbilical cord milking compared with early cord clamping or immediate cord clamping, with no new adverse effects reported. The task force concluded that

they would not change the current treatment recommendations or justify updating the SysRev at this time.

Treatment Recommendations (2024)

In preterm infants born at <37 weeks' gestation who are deemed not to require immediate resuscitation at birth, we recommend deferring clamping of the umbilical cord for at least 60 seconds (strong recommendation, moderate-certainty evidence).

In preterm infants born at 28+0 to 36+6 weeks' gestation who do not receive deferred cord clamping, we suggest umbilical cord milking as a reasonable alternative to immediate cord clamping to improve infant hematologic outcomes. Individual maternal and infant circumstances should be taken into account (conditional recommendation, low-certainty evidence).

We suggest against intact cord milking for infants born at <28 weeks' gestation (weak recommendation, low-certainty evidence). There is insufficient evidence to make a recommendation regarding cut-cord milking in this gestational age group.

In preterm infants born at <37 weeks' gestation who are deemed to require immediate resuscitation at birth, there is insufficient evidence to make a recommendation with respect to cord management (weak recommendation, low-certainty evidence).

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

Whenever circumstances allow, the plan for umbilical cord management should be discussed between maternity and neonatal providers and parents before delivery and should take into account individual maternal and infant circumstances (good practice statement).

INITIAL STEPS

Maintaining Normal Temperature Immediately After Birth in Term and Late Preterm Infants (NLS 5100: SysRev 2022, EvUp 2025)

A previous ILCOR SysRev reported a dose-responsive association between hypothermia and increased risk of mortality and other adverse outcomes,[2] and another SysRev found that hypothermia was very common in infants born in hospitals and homes, even in tropical environments.[94] Hence, the effect of various interventions to maintain normal temperature immediately after birth on survival, on the response to resuscitation, and on temperature outcomes was addressed in a 2022 SysRev,[95] details of which can be found in the 2022 CoSTR summary.[8] An EvUp was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** July 20, 2022, to July 20, 2024

Summary of Evidence

The update found 1 SysRev establishing a national guideline that had extensive overlap with the previous ILCOR SysRev,[96] 3 RCTs, 2 observational studies, and 1 quality improvement study. There was insufficient new evidence for most interventions to justify an updated SysRev. However, 1 cluster RCT comparing different ambient temperatures in the operating room was thought to justify an updated SysRev for this specific intervention, which the task force will prioritize.[97]

Treatment Recommendations (2022)

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

In late preterm and term newborn infants (≥34 weeks' gestation) at low risk of needing resuscitation, we suggest the use of skin-to-skin care with a parent immediately after birth rather than no skin-to-skin care to maintain normal temperature (weak recommendation, very low–certainty evidence).

In some situations where skin-to-skin care is not possible, it is reasonable to consider the use of a plastic bag or wrap, among other measures, to maintain normal temperature (weak recommendation, very low–certainty evidence).

In late preterm and term newborn infants ≥34 weeks' gestation, for routine use of a plastic bag or wrap in addition to skin-to-skin care immediately after birth compared with skin-to-skin care alone, the balance of desirable and undesirable effects was uncertain. Furthermore, the values, preferences, and cost implications of the routine use of a plastic bag or wrap in addition to skin-to-skin care are not known; therefore, no treatment recommendation can be formulated.

Maintaining Normal Temperature Immediately After Birth in Preterm Infants (NLS 5101: SysRev 2023, EvUp 2025)

Recent observational studies[98-101] confirm the association between hypothermia on admission to a neonatal unit and increased mortality and other adverse outcomes,[2] and also suggest there is potential harm from hyperthermia on admission. Therefore, a SysRev on the effect of various methods for maintaining normal temperature immediately after birth on critical and import neonatal outcomes was conducted[102] and included in the 2023 CoSTR summary,[6] and

an EvUp was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** The literature search was updated from July 20, 2022, to July 20, 2024.

Summary of Evidence

One SysRev[96] that addressed the PICOST had extensive overlap in included studies with the ILCOR SysRev[102] and similar conclusions. In addition, 1 cluster RCT addressed ambient operating room temperature (24 °C versus 20 °C) at birth[97] and 2 RCTs assessed aspects of plastic bag or wrap versus no plastic bag or wrap.[103,104] These studies do not warrant an updated SysRev.

Some additional studies provided evidence on admission temperatures in relation to skin-to-skin care after delivery room resuscitation.[105-108] These may justify a ScopRev or SysRev to consider the role of skin-to-skin care during transfer from delivery room to NICU after resuscitation.

Treatment Recommendations (2023)

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

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

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

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

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

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

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

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

Suctioning of Clear Amniotic Fluid at Birth (NLS 5120: SysRev 2022, EvUp 2025)

Since 2010, ILCOR treatment recommendations and many guidelines have advised selective rather than routine oropharyngeal or nasopharyngeal upper airway suctioning, with use only if the airway appears obstructed or when positive-pressure ventilation is required.[109] To update the assessment of evidence using Grading of Recommendations Assessment,

Development, and Evaluation methods, the topic was prioritized for a SysRev,[110] details of which can be found in the 2022 CoSTR summary.[8] An EvUp was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** September 21, 2021, to June 23, 2024

Summary of Evidence

A new quality improvement study that focused on reducing unnecessary suctioning of clear amniotic fluid in the delivery room included 999 infants, of whom 12% received oropharyngeal suctioning in the first phase of the study and 4% in the second.[111] The study found no disadvantages of the more selective suctioning approach. An updated SysRev is not justified at this time.

Treatment Recommendations (2022)

We suggest that suctioning of clear amniotic fluid from the nose and mouth should not be used as a routine step for newborn infants at birth (weak recommendation, very low–certainty evidence).

Airway positioning and suctioning should be considered if airway obstruction is suspected (good practice statement).

Tracheal Intubation and Suctioning of Meconium-Stained Amniotic Fluid (NLS 5130: EvUp 2025)

ILCOR guidance has progressively changed for infants exposed to meconium-stained amniotic fluid, from recommending routine tracheal suctioning in all infants with depressed respirations and decreased muscle tone to prevent meconium aspiration syndrome and reduce risk of death,[112] to concluding that there was insufficient evidence for this practice,[4] to suggesting against it as a result of a 2020 ILCOR SysRev.[8,113] An EvUp was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** November 1, 2018, to June 3, 2024

Summary of Evidence

A meta-analysis of RCTs[114] included the same studies as the previous ILCOR SysRev[113] and supported its conclusions, as did a meta-analysis of observational studies.[115] Eight single-center observational studies were identified.[116-123] All were retrospective or prospective with historical controls and were considered unlikely to change the existing treatment recommendation or to justify a new SysRev at this time.

Treatment Recommendations (2020)

For nonvigorous newborn infants delivered through meconium-stained amniotic fluid, we suggest against routine immediate direct laryngoscopy with or without tracheal suctioning when 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 (good practice statement).

Tactile Stimulation (NLS 5140: SysRev 2022, EvUp 2025)

Tactile stimulation as an initial step in resuscitation immediately after birth was included in ILCOR neonatal resuscitation treatment recommendations since 1999, largely based on expert opinion.[124-127] A SysRev[128] was conducted for 2022 examining whether—in infants with absent, intermittent, or shallow breathing immediately after birth—tactile stimulation improved survival or other critical and important outcomes, including response to resuscitation. Details can be found in the 2022 CoSTR summary.[8] An EvUp was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** September 17, 2021, to June 30, 2024

Summary of Evidence

One narrative review[129] and 4 observational studies[33,130-132] were identified. All the observational studies supported use of tactile stimulation to promote spontaneous breathing, but none specifically addressed the PICOST. There is insufficient new evidence to justify updating the SysRev.

Treatment Recommendations (2022)

We suggest it is reasonable to apply tactile stimulation in addition to routine handling with measures to maintain temperature in newborn infants with absent, intermittent, or shallow respirations during resuscitation immediately after birth (weak recommendation, very low–certainty evidence).

Tactile stimulation should not delay the initiation of positive-pressure ventilation for newborn infants who continue to have absent, intermittent, or shallow respirations after birth (good practice statement).

ASSESSMENT OF HEART RATE AT BIRTH

Heart Rate Assessment Methods in the Delivery Room—Diagnostic Characteristics (NLS 5200: SysRev 2023, EvUp 2025)

The diagnostic characteristics of methods to assess heart rate were addressed in a SysRev[133] that was included in the 2023 CoSTR summary.[6] A companion review (NLS 5201) examined the effects of different methods of heart rate measurement on survival and other critical and important outcomes.[134] For this review of diagnostic characteristics, heart rate measured by electrocardiography (ECG) was considered the gold standard against which the relative accuracy and precision of other methods were assessed. The time to first heart rate assessment from the device placement and from birth was also compared. An EvUp was

conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** August 16, 2023, to June 30, 2024

Summary of Evidence

No new studies were identified.

Treatment Recommendations (2023)

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

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

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

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

Heart Rate Assessment Methods in the Delivery Room—Clinical Outcomes (NLS 5201: SysRev 2022, EvUp 2025)

Because heart rate is considered a critical indicator of both the need for and the response to resuscitation in newborn infants, fast and accurate measurement is desirable.[133] However, heart rate should be considered in the context of other characteristics, such as tone and breathing effort, and with an awareness of the time it takes for the heart rate to improve after any intervention. Fixation on heart rate alone could lead to too many or too few resuscitation

interventions. Because evaluation of test characteristics and the effects on clinical outcomes required different methods, clinical outcomes were addressed by a separate SysRev[134] included in the 2022 CoSTR summary,[8] and an EvUp was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** August 16, 2023, to June 30, 2024

Summary of Evidence

One new retrospective observational study compared the frequency of resuscitation interventions before and after implementation of ECG in the delivery room and reported an initial increase in the use of chest compressions at birth and a decrease in frequency of tracheal intubation. These changes were reversed by a focused educational intervention highlighting the importance of achieving effective ventilation.[135] This study was not deemed to justify a new SysRev.

Treatment Recommendations (2022, Superseded)

Recommendations for NLS 5201 were superseded in 2023 by those for heart rate assessment methods—diagnostic characteristics (NLS 5200), which reflect conclusions of both reviews.

VENTILATION AND OXYGENATION

Devices for Administering Positive-Pressure Ventilation (NLS 5300: SysRev 2021, EvUp 2025)

Establishing lung aeration and tidal ventilation is essential in newborn infants who remain apneic or are not breathing effectively. A 2021 ILCOR ScopRev identified possible differences in the effectiveness and safety of T-piece resuscitators versus self-inflating bags for administering positive-pressure ventilation.[136] A subsequent SysRev in the same year addressed this question.[137] Details of this review can be found in the 2021 CoSTR summary.[9] An EvUp was

conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** December 30, 2020, to July 1, 2024

Summary of Evidence

Two new SysRevs were identified that included RCTs and cohort studies mostly already included in the 2021 ILCOR review,[138,139] and which, in general, concurred with the previous ILCOR SysRev.[137] Two additional small RCTs[140,141] provide insufficient new evidence to justify a new SysRev.

Treatment Recommendations (2021)

Where resources permit, we suggest the use of a T-piece resuscitator over the use of a self-inflating bag in infants receiving positive-pressure ventilation at birth (weak recommendation, very low–certainty evidence).

However, a self-inflating bag should be available as a backup device for the T-piece resuscitator in case of gas-supply failure (technical remark).

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

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

The confidence in effect estimates is so low that the task force concluded that any recommendation for the use of a positive end-expiratory pressure valve with a self-inflating bag versus a self-inflating bag without a positive end-expiratory pressure valve is too speculative.

Continuous Positive Airway Pressure Versus Positive-Pressure Ventilation for Preterm Infants (NLS 5310: EvUp 2025)

Continuous positive airway pressure is a well-established method of respiratory support during NICU care for preterm infants whose breathing is spontaneous but labored because of lung immaturity, or as part of treatment for apnea of prematurity. A 2015 SysRev[2] addressed the use of continuous positive airway pressure compared with tracheal intubation and positive-pressure ventilation immediately after birth for mortality and critical and important neonatal morbidity outcomes. An EvUp was undertaken for the 2020 CoSTR[5] and again in 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** November 1, 2019, to September 30, 2024

Summary of Evidence

No new studies were identified. A new SysRev concluded that in spontaneously breathing, very preterm infants, nasal continuous positive airway pressure (within the first 15 minutes) compared with mechanical ventilation reduces the incidence of bronchopulmonary dysplasia, the combined outcome of death and bronchopulmonary dysplasia, and mechanical ventilation but does not affect neurodevelopmental impairment at 18 to 22 months of age.[142] In the absence of new evidence, there is no justification for an updated SysRev.

Treatment Recommendation (2015)

For spontaneously breathing preterm infants with respiratory distress requiring respiratory support in the delivery room, we suggest initial use of continuous positive airway pressure rather than tracheal intubation and positive-pressure ventilation (weak recommendation, moderate-certainty evidence).

Continuous Positive Airway Pressure for Term and Late Preterm Infants With Respiratory Distress (NLS 5312: SysRev 2022, EvUp 2025)

Although it has become increasingly common to use continuous positive airway pressure for respiratory distress immediately after birth in late preterm and term infants, the evidence for it is not as well established as for preterm infants. The effect of continuous positive airway pressure for late preterm and term infants with respiratory distress on mortality, major neonatal morbidity, and response to resuscitation was addressed in a SysRev[143] included in the 2022 CoSTR summary.[8] An EvUp was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** October 8, 2021, to August 28, 2024

Summary of Evidence

One new retrospective observational study compared outcomes before and after introduction of local guidelines to avoid the use of continuous positive airway pressure in certain late preterm and term infants. It suggested no harm and a possible benefit from reducing the use of continuous positive airway pressure for term and late preterm infants immediately after birth who have signs of respiratory distress (eg, grunting, retractions or tachypnea) but whose blood oxygen saturations are reaching target ranges.[144] Given the limited new evidence, there is no justification for an updated SysRev.

Treatment Recommendation (2022)

For spontaneously breathing late preterm and term newborn infants in the delivery room with respiratory distress, there is insufficient evidence to suggest for or against routine use of continuous positive airway pressure compared with no continuous positive airway pressure.

Sustained Inflations During Newborn Resuscitation (NLS 5320: EvUp 2025)

Whether initial sustained inflations, with longer inspiratory times than those used for subsequent positive-pressure ventilation, improve critical or important outcomes from resuscitation of newborn infants was addressed with a SysRev included in the 2020 CoSTR.[5,145] An EvUp was undertaken for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** January 1, 2020, to July 2, 2024

Summary of Evidence

One RCT including 160 participants found no differences in outcomes.[146] The task force concluded that this single new study did not justify updating the SysRev at this time.

Treatment Recommendation (2020)

For preterm newborn infants who receive positive-pressure ventilation due to bradycardia or ineffective respirations at birth, we suggest against the routine use of initial sustained inflation(s) >5 seconds (weak recommendation, low-certainty evidence). A sustained inflation may be considered in research settings.[5]

Supraglottic Airway Device Versus Face Mask (NLS 5340: SysRev 2022, EvUp 2025)

Positive-pressure ventilation administered via a face mask is commonly ineffective because of mask leak or failure to achieve airway patency. The effect of the use of supraglottic airway devices compared with face masks for administering positive-pressure ventilation on mortality, morbidity, and response to resuscitation was assessed by a SysRev[147] included in the 2022 CoSTR summary.[8] An EvUp was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** December 9, 2021, to July 2, 2024

Summary of Evidence

One new quasi-RCT (67 participants) was found,[148] which provided insufficient evidence to justify updating the SysRev at this time.

Treatment Recommendation (2022)

Where resources and training permit, we suggest that a supraglottic airway device may be used in place of a face mask for newborn infants ≥34 weeks' gestation receiving intermittent positive-pressure ventilation during resuscitation immediately after birth (weak recommendation, low-certainty evidence).

Supraglottic Airway Device Versus Tracheal Tube (NLS 5341: EvUp 2025)

Tracheal intubation can be a lifesaving intervention during resuscitation of newborn infants, but it is a difficult, complex task. There are limited opportunities and a lack of well-defined pathways for care providers to consolidate simulation-based training with guided clinical practice.[149] Supraglottic airway devices do not require laryngoscopy and are used in resuscitation in other age groups, albeit with low certainty of evidence.[150,151] Until recently, devices small enough for infants <34 weeks' gestation were not available. The effect of the use of supraglottic airway devices in newborns as an alternative to tracheal intubation on mortality, major morbidity, and response to resuscitation was last assessed by the NLS Task Force in 2015.[2] An EvUp was undertaken for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** January 1, 2014, to November 4, 2024

Summary of Evidence

Two SysRevs,[152,153] 3 new RCTs (2 of which were included in the SysRevs, together enrolling 223 participants),[154-156] and 1 observational study of 86 infants[157] addressed the comparison for this PICOST.

The evidence was considered unlikely to change the current treatment recommendation but may justify updating the SysRev to reevaluate the certainty of evidence. The terms *laryngeal mask* and *low-quality evidence* have been updated to reflect current terminology (*supraglottic airway device* and *low-certainty evidence*, respectively).

Treatment Recommendations (2015, Updated to Reflect Current Terminology)

We suggest using a supraglottic airway device as an alternative to tracheal intubation during resuscitation of the late preterm and term newborn (≥34 weeks) if face mask ventilation is unsuccessful (weak recommendation, low-certainty evidence).

A supraglottic airway device should be considered during newborn resuscitation if face mask ventilation is unsuccessful and tracheal intubation is unsuccessful or not feasible (good practice statement).

Use of a Supraglottic Airway Device During Chest Compressions (NLS 5342: ScopRev 2025)

Rationale for Review

Despite being one of the most common neonatal resuscitation interventions, positive-pressure ventilation via a face mask can be compromised by leaks around the mask or upper airway obstruction leading to inadequate tidal volume.[158] Reduced tidal volume and minute volume with positive-pressure ventilation via a face mask during chest compressions have been reported.[159] Because immediate availability of a clinician with skills to intubate the trachea cannot be assured in all locations where advanced resuscitation is needed, the task force prioritized a new ScopRev addressing whether a supraglottic airway device would provide an effective alternative to face mask positive-pressure ventilation during chest compressions. The full review is available on the ILCOR CoSTR website.[23]

Population, Intervention, Comparator, Outcome, and Time Frame

- ***Population:*** Newborn infants of ≥34 weeks' gestation receiving chest compressions despite optimized positive-pressure ventilation
- ***Intervention:*** Positive-pressure ventilation with a supraglottic airway device
- ***Comparator:*** Positive-pressure ventilation with a face mask or tracheal tube
- ***Outcome:***
  - Delivery room outcomes:
    - Death in the delivery room (critical)
    - Time to heart rate ≥60 beats per minute (bpm) and time to heart rate ≥100 bpm (important)
    - Duration of advanced airway placement attempt and duration of interruption of CPR (important)
    - Number of attempts to insert advanced airway (important)
    - Epinephrine (adrenaline) administration (important)
    - Team preference (important)
    - Failure of primary device (important)
    - Physiologic pulmonary outcomes (eg, tidal volume, peak inspiratory pressure) (important)
  - NICU outcomes:
    - Survival to hospital discharge (critical)
    - Incidence of hypoxic ischemic encephalopathy (critical)
    - Air leak (eg, pneumothorax, pneumomediastinum) during first 48 hours of life (important)
    - Airway injury (important)

- Length of hospital stay (important)
  - Long-term outcomes:
    - Neurodevelopmental impairment at ≥18 months (critical)
- ***Time frame:*** All years to July 15, 2024

Summary of Evidence

Neonatal or Infant Studies

No studies addressed the PICOST in human infants in the delivery room or during the neonatal period. Indirect evidence was available from 2 studies that addressed the use of supraglottic airway devices during chest compressions in newborn animals,[160,161] 2 in adult animals,[162,163] and 1 assessing resuscitator performance in a neonatal manikin study.[164]

In lambs that were asphyxiated before the transition from intrauterine to extrauterine life, similar rates of return of spontaneous circulation (ROSC) were achieved within similar time frames with a supraglottic airway device and a tracheal tube.[160] No differences in peak inspiratory pressure, positive end-expiratory pressure, tidal volume, or mean airway pressure were found, leading the authors to conclude that use of the supraglottic airway device is noninferior to the use of a tracheal tube during chest compressions. In piglets asphyxiated after the transition to air breathing, similar tidal volumes and peak inspiratory pressures were achieved during ventilation with a supraglottic airway device or tracheal tube during neonatal chest compressions.[161]

A crossover manikin study evaluating single-rescuer CPR found that peak inspiratory pressures much closer to the pressure that was set for the T-piece resuscitator were achieved with the supraglottic airway compared with a face mask.[164] The time taken to complete 30 compression-to-ventilation cycles was shorter with the supraglottic airway device than with a

face mask (60.6±3.4 s versus 66.2±6.1 s; [mean±SD] $P<0.0001$), which enabled better adherence to recommendations for completing 120 events in 60 seconds.[165]

Because of the paucity of human infant evidence, indirect evidence from other age groups was also evaluated.

Indirect Evidence From Studies in Children or Adolescents

A registry study reported improved 30-day survival when a supraglottic airway device was used compared with a tracheal tube.[166] Other pediatric studies have also reported worse outcomes with tracheal intubation during CPR.[167,168]

Indirect Evidence From Studies in Adults

A 2020 SysRev and network meta-analysis (of 11 studies including 8 RCTs) compared effectiveness of different airway interventions for out-of-hospital cardiac arrest.[169] The study reported increased ROSC with the use of a supraglottic airway device compared with a tracheal tube (odds ratio, 1.11; 95% CI, 1.03–1.20) or compared with bag-mask ventilation (odds ratio, 1.35; 95% CI, 1.11–1.63). No differences in survival or long-term neurological outcomes were found. A later SysRev and meta-analysis comparing the use of a supraglottic airway with tracheal intubation in adults with out-of-hospital cardiac arrest concluded that it took less time to place a supraglottic airway device (mean difference 2.5 min less; 95% CI, 1.6–3.4 min less; high certainty), and the use of a supraglottic airway device likely led to more ROSC (relative risk, 1.09; 95% CI, 1.02–1.15; moderate certainty).[170]

Epinephrine Administration During CPR

For the outcome of epinephrine administration, no studies addressed whether epinephrine use was reduced by using a supraglottic airway device during chest compressions. For efficacy of epinephrine via supraglottic airway devices, 2 studies in adult pigs (not in cardiac arrest) concluded that epinephrine administration via a catheter passed through the supraglottic airway

device had similar effects to epinephrine administration via tracheal tube. But if administering epinephrine from the top of the supraglottic airway devices, higher doses would be needed.

In the same model, 5 different routes and doses of epinephrine were compared.[163] The authors again concluded that higher doses of epinephrine may be needed if administering the epinephrine at the top of the supraglottic airway device to produce an equivalent effect to epinephrine administered via tracheal tube.

Task Force Insights

The task force noted the lack of studies in newborn infants but concluded that the few animal studies suggest that the use of a supraglottic airway device compared with a tracheal tube achieves similar rates of ROSC and that ventilation of the lungs is not compromised. The pediatric and adult (human) studies suggest benefits including reduced time to airway placement and increased rates of ROSC, without evidence of any adverse effects attributable to supraglottic airway devices. The animal studies of epinephrine administration suggest that doses given via a catheter down a supraglottic airway device may be as effective as administration via a tracheal tube. However, no human infant studies are available, and the task force noted that intravascular administration remains the preferred route for epinephrine.[5,171] The task force concluded that there was insufficient evidence to justify a SysRev but that it was reasonable to generate a new good practice statement based on the results of this ScopRev.

Treatment Recommendations (2025)

In newborn infants ≥34 weeks' gestation who are receiving chest compressions despite optimized positive-pressure ventilation, if placement of a tracheal tube is not possible or is unsuccessful, ventilation via a supraglottic airway device during compressions is reasonable (good practice statement).

Exhaled CO_2 Monitoring to Guide Noninvasive Ventilation (NLS 5350: SysRev 2023, EvUp 2025)

The effectiveness of noninvasive positive-pressure ventilation can be difficult to judge objectively. There may be a delay in improvement in heart rate and blood oxygen saturation, even after positive-pressure ventilation is established.[172] Therefore, the effect of exhaled CO_2 monitoring to guide noninvasive positive-pressure ventilation on survival, major morbidity, and response to resuscitation was addressed by a SysRev[173] included in the 2023 CoSTR summary.[6] An EvUp was undertaken for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** August 1, 2022, to July 3, 2024

Summary of Evidence

One small pilot RCT addressed the PICOST, providing insufficient evidence to justify updating the SysRev.

Treatment Recommendation (2023)

There is insufficient evidence to suggest for or against the use of exhaled CO_2 to guide noninvasive intermittent positive-pressure ventilation using interfaces, such as face masks, supraglottic airways, and nasal cannulas in infants immediately after birth.

Video Versus Traditional Laryngoscope (NLS 5351: SysRev 2025)

Rationale for Review

Aspects of neonatal anatomy (including the small mouth and airway, the large tongue, epiglottis, and arytenoids, and appearance of the glottis) make tracheal intubation difficult, especially in preterm infants. Delivery room intubation for resuscitation is a time-critical procedure with a relatively low first-attempt success rate.[174] Video laryngoscopes provide indirect visualization of the glottis using a screen that (depending on the device) may also be

visible to an instructor or assistant, and they may also enable direct visualization. In contrast, traditional laryngoscopes enable only a direct view, which may be impeded by airway anatomy. Performance of and training in neonatal intubation may be improved by using video laryngoscopes instead of traditional laryngoscopes.[149,175] Therefore, the NLS Task Force prioritized a SysRev, of which full details are available on the CoSTR website.[23] The protocol was registered on PROSPERO CRD42023467940.

- ***Population:*** Infants receiving tracheal intubation at birth or on a neonatal unit
- ***Intervention:*** Tracheal intubation using video laryngoscopy
- ***Comparator:*** Tracheal intubation using traditional laryngoscopy
- ***Outcome:***
  - Mortality in-hospital (critical)
  - Successful tracheal intubation (important)
  - Successful tracheal intubation at the first attempt (important)
  - Number of attempts to achieve successful tracheal intubation (important)
  - Time taken to successfully intubate (important)
  - Adverse events around the time of laryngoscopy, eg, airway trauma, bradycardia, desaturation, esophageal intubation, pneumothorax (important)
  - Perception of intubating clinician, eg, intubation difficulty (as defined by the author) (important)
  - Any intraventricular hemorrhage (IVH) (preterm only) (important)
- ***Time frame:*** All years to August 22, 2024

Consensus on Science

The SysRev identified 6 RCTs including 817 infants and 862 tracheal intubations,[176-181] as well as 4 observational studies involving 3289 infants who received 3342 tracheal

intubations.[178-180,182] The evidence was considered indirect because approximately 80% of the infants were intubated in the NICU, not the delivery room. Outcomes were described by intubation, not by infant.

Key results from RCTs are summarized in Table 3. The full online CoSTR can be found on the ILCOR website.[23]

Table 3. Video Laryngoscopy Compared With Traditional Laryngoscopy for Tracheal Intubation at Birth or in a Neonatal Unit: RCTs

Outcomes (importance*)	Intubations, n (studies)	Certainty of evidence, GRADE	Relative effect (95% CI)	Anticipated absolute effect (95% CI)	
				Risk with traditional laryngoscopy	Risk difference with video laryngoscopy
Successful intubation—overall (%) (important)	567 (4 RCTs)[176-178,181]	Moderate	RR 1.43 (1.15–1.77)	513/1000	220 more intubations per 1000 (77 more to 395 more)
Successful intubation—first attempt (%) (important)	610 (4 RCTs)[178-181]	High	RR 1.57 (1.33–1.85)	394/1000	225 more intubations per 1000 (130 more to 335 more)

*Outcome importance according to task force consensus.

GRADE indicates Grading of Recommendations Assessment, Development, and Evaluation; RCT, randomized controlled trial; and RR; relative risk.

For the number of attempts to intubate and time to successful intubation, meta-analysis was not performed because of heterogeneity in how these results were reported. For other critical and important outcomes for which data were available, clinical benefit or harm could not be excluded.

Treatment Recommendations (2025)

Where resources and training allow, in infants being intubated at birth or on a neonatal unit, we suggest the use of video laryngoscopy in comparison to traditional laryngoscopy, especially in settings where less-experienced clinicians are intubating (conditional recommendation, moderate-certainty evidence).

Traditional laryngoscopy remains a reasonable option, as no increased harm was shown compared with video laryngoscopy (weak recommendation, very low–certainty evidence).

A traditional laryngoscope should always be available as a backup device (good practice statement).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision table is provided in Appendix A.

The task force noted the high-certainty evidence for successful intubation overall and for first attempts. Although the RCT evidence was used to formulate the treatment recommendations, the observational studies were broadly consistent. For adverse effects, there were either no data or clinical benefit or harm could not be excluded. Of note, for the critical outcomes of mortality and IVH, the combined sample size was well below the optimal information size to detect clinical benefit or harm. The RCTs mainly included infants without airway anomalies, and they were intubated by trainees or other relatively inexperienced clinicians. In previous studies, success rates using traditional laryngoscopes were proportional to experience.[183-186] So, for clinicians who are already very experienced, benefits may be smaller. The cost of video laryngoscopes is higher than for traditional laryngoscopes (although no studies have assessed cost-effectiveness), and they are unlikely to be available in all locations where infants needing resuscitation are born. So there is a potential to decrease health equity.

Knowledge Gaps

- Efficacy, effectiveness, and safety of video laryngoscopy compared with traditional laryngoscopy in different gestational ages, in emergency intubation (including for infants immediately after birth), and in the delivery room compared with other settings
- The usability, feasibility, comparative effectiveness, and cost-effectiveness of different types of video laryngoscopes
- Effect of video laryngoscopy in those who are already experienced in intubation, compared with the effect in less-experienced practitioners and in training settings

Respiratory Function Monitoring During Resuscitation at Birth (NLS 5360: SysRev 2022, EvUp 2025)

Respiratory function monitors have the potential to help resuscitation teams to recognize problems that cause insufficient or excessive tidal volumes during resuscitation, such as airway obstruction or ventilation pressures that are too high or too low for the respiratory mechanics of the infant's lungs. Therefore, the effect of the use of respiratory function monitors during neonatal resuscitation on mortality, neonatal morbidity, and response to resuscitation was addressed by a SysRev[187] included in the 2022 CoSTR summary.[8] An EvUp was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** December 31, 2021, to September 30, 2024

Summary of Evidence

No new studies were found to alter the current treatment recommendation or to justify a new SysRev. The task force is currently undertaking a SysRev of the use of respiratory function monitors during simulation-based training.

Treatment Recommendation (2022)

There is insufficient evidence to make a recommendation for or against the use of a respiratory function monitor in newborn infants receiving respiratory support at birth (low-certainty evidence).

Near-Infrared Spectroscopy During Positive-Pressure Ventilation (NLS 5362: SysRev 2025)

Rationale for Review

Oxygenation is a determinant of morbidity and mortality in preterm infants. Evidence suggests that even when preterm infants reach early peripheral oxygen saturation targets, cerebral regional oxygen saturation ($crSO_2$) measured with near-infrared spectroscopy may remain low. A low $crSO_2$ may be a risk factor for IVH.[188] Recent studies have addressed whether the use of near-infrared spectroscopy accompanied by a treatment guideline that suggests adjustments to inspired oxygen or positive-pressure ventilation for out-of-range $crSO_2$ values, compared with standard care, improves outcomes for infants receiving positive-pressure ventilation for resuscitation in the delivery room. This SysRev was registered on PROSPERO 2024 CRD42024511496. The full online CoSTR can be found on the ILCOR website.[10]

Population, Intervention, Comparator, Outcome, and Time Frame

- ***Population:*** Newborn infants receiving continuous positive airway pressure, positive-pressure ventilation, or both (any interface) during stabilization or resuscitation at birth
- ***Intervention:*** Delivery room monitoring of $crSO_2$ with a dedicated treatment guideline in addition to clinical assessment, pulse oximetry, or ECG
- ***Comparator:*** Clinical assessment, pulse oximetry, or ECG only
- ***Outcome:***
  - Survival without neurodevelopmental impairment (critical)

- Survival (critical)
- Neurodevelopmental impairment (critical)
- Response to resuscitation (important): $crSO_2$ <10th or >90th centile, maximum fraction of inspired oxygen (FIO_2) used, total oxygen exposure
- Morbidity outcomes in infants <34 weeks (critical): Severe IVH (Papile grade III or IV),[189] periventricular leukomalacia

- ***Time frame:*** All years to November 5, 2024
  - Potential subgroups were defined a priori: methods of near-infrared spectroscopy (including brand, manufacturer); continuous positive airway pressure versus positive-pressure ventilation; cord management strategy, ie, immediate or delayed cord clamping or cord milking; sex, gestation at birth: <28 weeks; 28 to 33 weeks; and ≥34 weeks' gestation.

Consensus on Science

Two RCTs[190,191] reporting outcomes for a total of 667 infants were included, and additional follow-up data were available for one.[192] The studies examined a similar intervention, but there were some differences in which outcomes were reported. Key results from included RCTs are summarized in Table 4. Additional details can be found on the ILCOR website.[23]

Table 4. Comparison of the Use of Near Infrared Spectroscopy With a Dedicated Treatment Guideline Versus Standard Care During PPV in the Delivery Room: RCTs

Outcomes (importance*)	Participants, n (studies) Follow-up	Certainty of evidence, GRADE	Relative effect (95% CI)	Anticipated absolute effect (95% CI)	
				Risk with clinical assessment	Risk difference with NIRS plus a dedicated treatment guideline
Survival (critical)	667 (2 RCTs)[190,191]	Low	RR 1.02 (0.99–1.05)	946/1000	19 more infants per 1000 (9 fewer to 47 more)
In infants <34 weeks—severe IVH (critical)	667 (2 RCTs)[190,191]	Very low	RR 0.76 (0.3–1.54)	51/1000	12 fewer infants per 1000 (32 fewer to 28 more)
In infants <34 weeks—periventricular leukomalacia (critical)	667 (2 RCTs)[190,191]	Very low	RR 1.93 (0.66–5.70	15/1000	14 more infants per 1000 (5 fewer to 71 more)
Regional cerebral tissue oxygenation ($crSO_2$ <10th centile) (important)	60 (1 RCT)[190]	Very low	RR 1.00 (0.78–1.29)	800/1000	0 fewer infants per 1000 (176 fewer to 232 more)

*Outcome importance according to Strand et al[12] or task force consensus.

$crSO_2$ indicates cerebral regional oxygen saturation; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; IVH, intraventricular hemorrhage; NIRS, near-infrared spectroscopy; PPV, positive-pressure ventilation; RCT, randomized controlled trial; and RR, relative risk.

For all other critical and important outcomes, there were either no data or clinical benefit or harm could not be excluded. For the preplanned subgroup analysis by gestation, there were no significant differences in effect size by gestation groups <28 weeks versus 28+0 to 32+6 weeks gestation for the outcomes of survival, severe IVH, or periventricular leukomalacia. There were insufficient data for other preplanned subgroup analyses.

Treatment Recommendation (2025)

In newborn infants receiving continuous positive airway pressure and/or positive-pressure ventilation immediately after birth, there is insufficient evidence to recommend for or against use of delivery room monitoring of regional cerebral oxygen saturation with a dedicated treatment guideline in addition to (and compared with) clinical assessment and pulse oximetry with or without ECG (very low–certainty evidence).

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision table is provided in Appendix A.

Concerns about clinical effectiveness, resources, equity, acceptability, and feasibility led the task force to conclude that in the absence of evidence of benefit or harm, delivery room monitoring of $crSO_2$ with a dedicated treatment guideline should only be considered where resources permit and ideally in the context of a research trial to close knowledge gaps.

Knowledge Gaps

- The effectiveness of interventions in response to out-of-range $crSO_2$ values
- Prioritized research that includes human factors, opportunities to reduce inequity, and cost-benefit analysis
- The training requirements needed to achieve and maintain competency in interpretation of and response to monitoring of $crSO_2$ during neonatal resuscitation

- Cost-benefit analysis of monitoring of $crSO_2$, taking into account both critical short-term outcomes and also long-term neurodevelopmental disability

Oxygen Concentration for Initiating Resuscitation in Preterm Infants (NLS 5400: SysRev 2025)

Rationale for Review

A 2019 ILCOR SysRev reviewed 10 RCTs and 4 cohort studies including 5697 participants and concluded that there were no clear benefits or harms from starting with lower compared with higher FIO_2 for short-term mortality, long-term mortality, neurodevelopmental impairment, or key preterm morbidities.[193] As a result of these findings, the task force suggested starting with a lower oxygen concentration (FIO_2 0.21–0.30) compared with a higher concentration (0.60–1.00) for preterm infants <35 weeks' gestation, with subsequent titration of oxygen concentration using pulse oximetry.[194]

Recently, an individual patient data network meta-analysis (NetMotion)[195] obtained individual patient data for 1055 infants included in 8[196-203] of the 12 RCTs included in the previous ILCOR SysRev[193] and 4 additional trials.[204-207] The authors concluded that "high initial FIO_2 (≥0.90) may be associated with reduced mortality in preterm infants born at <32 weeks' gestation compared to low initial FIO_2 (low certainty). High initial FIO_2 is possibly associated with reduced mortality compared to intermediate initial FIO_2 (very low certainty), but more evidence is required."

Given the discordance between the conclusions of these 2 SysRevs, the task force concluded that an updated ILCOR SysRev was required to consider the following:

- Evidence from study-level meta-analysis of eligible RCTs, including those in the previous SysRev[193] plus any published since the last search date

- Evidence from large observational studies judged to provide similar or higher certainty of evidence to the RCTs
- Results of the NetMotion individual patient data network meta-analysis,[195] by adolopment.

Key results from NetMotion and of the study-level meta-analysis of RCTs are described in text. The full online CoSTR can be found on the ILCOR website.[23] The review was registered on PROSPERO (CRD42024589330).

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

- ***Population:*** Newborn infants <35 weeks' estimated gestational age who receive respiratory support at delivery
- ***Intervention:*** Lower initial oxygen concentration ($F_{IO_2} \leq 0.5$)
- ***Comparator:*** Higher initial oxygen concentration ($F_{IO_2} > 0.5$)
- ***Outcome:***
  - All-cause mortality in-hospital or by 28 days (critical)
  - All-cause mortality before 1 to 3 years (critical)
  - Neurodevelopmental impairment at 1 to 3 years of age (critical)
  - Major IVH (grade III or IV)[189] (critical)
  - Retinopathy of prematurity (important)
  - Necrotizing enterocolitis (Bell's stage II or III[208]) (important)
  - Bronchopulmonary dysplasia (chronic neonatal lung disease) (important)
  - Number with heart rate >100 bpm at 5 minutes; time from birth to peripheral oxygen saturation ≥80% (important)
  - Advanced resuscitation (chest compressions with or without epinephrine [adrenaline]) (important)

- ***Study design****:* In addition to standard criteria, individual patient data SysRevs were eligible for inclusion.
- ***Time frame:*** August 10, 2018, to August 7, 2024. Articles included in the previous review were assumed to be eligible for inclusion in meta-analyses.[193]

A priori subgroups included those based on gestational age, level of initial supplemental oxygen delivered, whether there was oxygen saturation targeting, and method of umbilical cord management as well as sensitivity analysis by high versus low risk of bias.

Consensus on Science

The NetMotion individual patient data network meta-analysis[195] evaluated 1055 infants from 12 of 13 eligible studies[200-205,207,209-212] and was deemed suitable for adolopment by using the AMSTAR2 checklist.[213] It included only infants <32 weeks' gestation, whereas the ILCOR PICOST and the previous SysRev includes infants <35 weeks' gestation. NetMotion used individual patient data, which enabled adjustment for various important modifiers such as gestation at birth and birthweight.[214] So they should have greater precision of estimates than the study-level meta-analysis.

The study-level meta-analysis (new search plus studies included in the previous SysRev[193]) identified 18 articles,[131,196-204,206,207,209,210,212,215-217] reporting results from 14 RCTs. There were also 4 observational studies[211,218-220] (all included in the previous SysRev) that included 4437 infants.

The updated study-level meta-analysis included 3 RCTs published after the previous ILCOR SysRev[193] (all included in NetMotion[195]) and 1 additional cluster-RCT[216] (excluded from NetMotion). The study-level meta-analysis, therefore, included 1289 infants (compared with the 1007 included in the previous ILCOR meta-analysis).[221] It was thought unlikely that any

differences in the results of the NetMotion and the task force study-level meta-analyses are accounted for by study exclusions.

Results of the Individual Patient Network Meta-Analysis

For the critical outcome of mortality, 8 RCTs[197,199-203,206] enrolling 833 infants provided low-certainty evidence of lower mortality with high initial F_{IO_2} compared with low initial F_{IO_2} (aOR 0.45 [95% CI, 0.23–0.86]). Very low–certainty evidence from 4 RCTs[204,205,208,211] enrolling 652 infants found no difference in mortality with intermediate initial F_{IO_2} compared with low initial F_{IO_2} (aOR 1.33 [95% CI, 0.54–3.15]). An indirect comparison of 519 infants found very low–certainty evidence of lower mortality with high initial F_{IO_2} compared with intermediate initial F_{IO_2} (aOR 0.34 [95% CI, 0.11–0.99]).The prediction intervals (ie, range between results of a future study would be expected to fall) crossed the line of no effect for the high versus low comparison (prediction interval, 0.44; 95% credible interval, 0.15–1.34) and high versus intermediate comparison (prediction interval, 0.33; 95% credible interval, 0.08–1.40), which was considered to be evidence of inconsistency and, thereby, reduced certainty of evidence.[195]

For the critical outcomes of severe IVH and the important outcomes of chronic neonatal lung disease and retinopathy of prematurity, the comparison between high (>0.90) and low (≤0.30) F_{IO_2} could not exclude benefit or harm. In each case, the evidence was of very low certainty. For these outcomes, the comparisons between high (>0.90) and intermediate (0.50–0.65) F_{IO_2} have even greater imprecision because fewer infants were included. So they are not presented.[195]

For subgroup analyses, the NetMotion authors reported that “there was no evidence of differential effects of treatment across gestational ages or according to infant sex (post hoc, primary outcome only) when examining treatment-covariate interactions” and that there was limited statistical power to detect such interactions.[195] The authors also reported that there were

too few participants from low-or middle-income countries to perform prespecified subgroup analysis according to country income classification, and they considered that oxygen concentration titration strategies were too heterogenous to explore faster versus slower titration.[195]

Other critical and important outcomes of the PICOST were not reported.

From the Study-Level Meta-Analysis

Clinical benefit or harm could not be excluded for the comparison of lower initial oxygen concentration ($F_{IO_2} \leq 0.5$) with higher initial oxygen concentration ($F_{IO_2} > 0.5$) for any of the following critical or important outcomes: all-cause mortality (in-hospital or by 28 days),[196,198-204,206,207,209,212,215,216] long-term all-cause mortality,[197,217] neurodevelopmental impairment (at 1–3 years),[197,217] major IVH (grade III or IV),[197-200,202-204,206,207,215,216] severe retinopathy of prematurity,[197-200,202,206,207,215,216] necrotizing enterocolitis,[197-200,202,206,207,215,216] bronchopulmonary dysplasia,[197-200,202,206,215,216] or advanced resuscitation.[198,200,201,203,206,207,210] All comparisons yielded evidence of very low certainty, and tests for subgroup differences were not significant for any comparison.

Observational Studies

There were no new observational studies found for inclusion in this updated review; hence, the evidence is the same as that from the previous ILCOR SysRev, which included 4 observational studies. For long-term mortality, 2 observational cohort studies including 1225 preterm newborns receiving respiratory support at birth indicated possible benefit of starting with lower compared with higher F_{IO_2} (relative risk, 0.77; 95% CI, 0.59–0.99; I^2, 6%; very low–certainty evidence).[193] For the outcome of neurodevelopmental impairment, 2 studies including 930 infants could not exclude benefit or harm from starting with lower compared with higher F_{IO_2} (relative risk, 0.89; 95% CI, 0.66–1.20; I^2, 59%; very low–certainty evidence).[193]

Prior Treatment Recommendation (2018)

For preterm newborn infants (<35 weeks' gestation) who receive respiratory support at birth with subsequent titration of oxygen concentration using pulse oximetry, we suggest starting with a lower oxygen concentration (21%–30%) rather than higher oxygen concentration (60%–100%) (weak recommendation, very low–certainty evidence).

Treatment Recommendations (2025)

Among newborn infants <32 weeks' gestation, it is reasonable to begin resuscitation with ≥30% oxygen (weak recommendation, low-certainty evidence).

For infants born at 32 to 34+6 weeks' gestation, there is insufficient evidence to make a recommendation.

Justification and Evidence-to-Decision Framework Highlights

The complete evidence-to-decision table is provided in Appendix A. Evidence from NetMotion, which was included by adolopment, suggested benefit from higher concentrations of oxygen and that a high F_{IO_2} (0.90–1.00) may result in the lowest mortality.[195] However, the task force concluded that the overall certainty of evidence was very low, mainly because of concerns that the total sample for each comparison was substantially below the optimal information size for all outcomes. The updated study-level meta-analysis found that benefit or harm could not be excluded for any outcome for lower versus higher concentrations of oxygen for commencing resuscitation, with low to very low certainty of evidence for all outcomes.

There are still concerns about unmeasured adverse effects of hyperoxia and hypoxia. As a result, 2 pending multicenter trials are using F_{IO_2} of 0.30 versus 0.60 for their treatment arms (clinical trial registration ACTRN12618000879268 and NCT03825835[222]).

Whichever initial oxygen concentration was used, oxygen saturation monitoring and individualized adjustments of inspired oxygen concentration were used in most of the clinical trials and are likely to be needed to optimize outcomes.

Knowledge Gaps

- Comparison of oxygen saturation target levels and strategies to achieve them by adjusting inspired oxygen concentrations or other aspects of respiratory support in the first 10 to 20 minutes after birth in preterm infants
- Optimal oxygen concentration for commencing resuscitation in preterm newborn infants
- Human factor aspects of resuscitation performance depending on initial oxygen concentration for commencing resuscitation
- Effect of initial oxygen concentrations and titration targets and strategies on biomarkers of both hypoxic and hyperoxic injury to organs including the brain, lungs, and retinas

The task force concluded that the uncertainty over the optimal initial oxygen concentration means that it is reasonable to study a full range of oxygen concentrations (21%–100%) within a research protocol.

Oxygen Concentration for Initiating Resuscitation in Late Preterm and Term Infants (NLS 5401: EvUp 2025)

The oxygen concentration for commencing resuscitation in late preterm and term infants was reviewed in 2010 and 2019.[109,194,221] Both reviews concluded that there was improvement in survival and other outcomes from commencing resuscitation with F_{IO_2} 0.21 compared with F_{IO_2} 1.0. An EvUp was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame****:* July 1, 2018, to August 7, 2024

A priori subgroup analyses: gestational age (≥35 weeks, ≥37 weeks); grouped lower and higher oxygen concentrations; explicit oxygen saturation targeting versus no oxygen saturation targeting

Summary of Evidence

One retrospective observational study that included 68 infants with congenital diaphragmatic hernia, who were resuscitated with an initial F_{IO_2} of 0.5 and compared with historical controls who received F_{IO_2} 1.0, reported similar outcomes for both groups.[223] Although the limited new evidence is insufficient to justify an updated SysRev, the task force will prioritize updating the SysRev. We have concerns that the certainty of evidence would now be judged insufficient to make the previous strong recommendation against commencing resuscitation for term and late preterm infants with 100% oxygen.[194] We, therefore, withdraw this recommendation in the interim. The task force strongly encourages additional research on this important topic.

Treatment Recommendation (2019)

For newborn infants at ≥35 weeks' gestation receiving respiratory support at birth, we suggest starting with 21% oxygen (weak recommendation, low-certainty evidence).

CIRCULATORY SUPPORT

Chest Compressions in Newborn Infants (NLS 5500–5507: ScopRev 2023, EvUp 2025)

Chest compressions are used in only a few newborn infants in every thousand but can be lifesaving for infants who are asystolic or severely bradycardic and who are not responding to effective positive-pressure ventilation. Various aspects of chest compressions for newborn infants were addressed in 2023 using ScopRev methods because prior surveillance of the literature indicated that there was very little available human infant evidence; hence, a broad search would be needed to evaluate indirect evidence.[224] Details of this review can be found in

the 2023 CoSTR summary.[6] An EvUp was conducted for 2025. The results are summarized here by individual PICO questions. The complete EvUp, including the full PICOST, for each of the questions can be found in Appendix B.

Heart Rate for Commencing Chest Compressions (NLS 5500: ScopRev 2023, EvUp 2025)

This question addresses neonates who are being resuscitated who have a slow heart rate and compares the effect of starting chest compressions when the heart rate is <60 bpm with any other heart rate on survival, neurologic outcomes, and ROSC.

- ***Time frame:*** November 22, 2021, to June 16, 2024

Summary of Evidence

No further studies addressing this PICOST were identified in the EvUp. The task force considered that (despite the lack of evidence for any specific threshold), given the need to provide resuscitation teams with a standardized approach to clinical practice, formulation of a good practice statement was justified.

Treatment Recommendation (2023)

ILCOR has not developed an evidence-based treatment recommendation on heart rate threshold to initiate chest compressions previously. However, ILCOR guidance since 1999 has been to initiate chest compressions if the heart rate is <60 bpm despite adequate assisted ventilation for 60 seconds.

Treatment Recommendations (2025)

In neonates being resuscitated who have a slow heart rate even after optimizing ventilation, initiating cardiac compressions when the heart rate is <60 bpm is reasonable (good practice statement).

Chest Compressions With 2 Thumbs Versus Other Techniques (NLS 5501: ScopRev 2023, EvUp 2025)

This question compares the effect of using 2 thumbs with hands encircling the chest with using any other method on survival, neurologic outcomes, and ROSC.

- ***Time frame:*** November 22, 2021, to June 16, 2024

Summary of Evidence

Ten simulation studies,[225-232] 1 RCT in piglets,[233] and 1 prospective observational study in children in cardiac arrest, of whom 16 were <1 year of age[234] overall, supported the findings of the ScopRev. This ScopRev found that the 2-thumb technique resulted in greater chest compression depth, less fatigue, and higher proportion of correct hand placement compared with the 2-finger technique.[224] The new studies identified in the 2025 EvUp do not provide sufficient evidence to justify a new SysRev.

Treatment Recommendation (2015)

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

Supplemental Oxygen During Chest Compressions (NLS 5503: ScopRev 2023, EvUp 2025)

This question compares the effect of using an F_{IO_2} of 1.0 once chest compressions have been commenced with using any lower oxygen concentration on survival, neurologic outcomes, and ROSC.

- ***Time frame:*** November 22, 2021, to June 16, 2024

Summary of Evidence

Two animal studies compared F_{IO_2} 0.21 with F_{IO_2} 1.0 during chest compression after asphyxial cardiac arrest.[235,236] One was in older piglets[235] rather than in neonatal animals. The new evidence does not justify a new SysRev.

Treatment Recommendation (2015 Updated to Reflect Current Terminology)

By the time resuscitation of a newborn infant has reached the stage of chest compressions, the steps of trying to achieve ROSC using effective ventilation should have been completed. It is reasonable to increase the supplementary oxygen concentration (good practice statement). Once the heart rate has recovered, supplementary oxygen should be titrated to oxygen saturation targets (good practice statement).

Compression-to-Ventilation Ratio (NLS 5504: ScopRev 2023, EvUp 2025)

This question compares the effect of using a compression-to-ventilation ratio of 3:1 with using any other ratio, including chest compressions during sustained lung inflation, on survival, neurologic outcomes, ROSC hemodynamic measures, and compressor fatigue.

- ***Time frame:*** November 22, 2021, to June 16, 2024

Summary of Evidence

The updated EvUp search identified 1 clinical and 7 animal studies comparing various ratios. The new evidence does not justify a new SysRev at this time.

Treatment Recommendation (2015, Updated in 2023 CoSTR summary)

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

Use of Feedback CPR Devices for Neonatal Cardiac Arrest (NLS 5505: ScopRev 2023, EvUp 2025)

This question compares the effect of using any type of feedback device, including end-tidal CO_2 monitoring, pulse oximeters, or automated compression feedback devices on survival, neurologic outcomes, ROSC and hands-off time, and measures of perfusion.

- ***Time frame:*** November 22, 2021, to June 16, 2024

Summary of Evidence

Three studies in animals[237] or manikins[238,239] assessed the use of chest compression feedback devices including a chest compression machine,[237] real-time visual feedback,[239] and a new smart ring–based chest compression–depth feedback device.[238] While each suggested potential benefits, no studies assessed improvements in resuscitation practice or outcomes in human infants. The studies do not justify a new SysRev.

Treatment Recommendation (2023)

In newborn infants with asystole or bradycardia, we suggest against the routine reliance on any single feedback device such as end-tidal CO_2 monitors or pulse oximeters for detection of ROSC until more evidence becomes available (weak recommendation, very low–certainty evidence).

Depth of Chest Compressions (NLS 5506: EvUp 2025)

This EvUp adds to information published in the ILCOR ScopRev[224] but not reported in the 2023 CoSTR summary on whether the use of any other chest compression depth than one third the anteroposterior diameter of the chest improves survival, neurologic outcomes, or time to ROSC.[6] The results from all years were described in the EvUp worksheet.

- ***Time frame:*** All years to June 16, 2024

Summary of Evidence

Two animal physiology studies[240,241] and 3 human infant studies that used computed tomography scans[242,243] or laser distance meters[244] to estimate chest compression depths in infants were identified. The 2023 ILCOR ScopRev included some of these studies.[224] No studies were found that addressed survival rates or other critical or important outcomes in newborn infants. A new SysRev was not thought to be warranted.

Treatment Recommendation (2010, Now Worded as a Good Practice Statement)

Compress the chest one third the anterior-posterior diameter (good practice statement).

Chest Compression Location on Sternum (NLS 5507: EvUp 2025)

This question has not been addressed since 2010[109]; hence, a literature search was used for the EvUp that included contemporary search terms and was conducted without a start-date restriction. In infants receiving chest compressions, the PICOST compared whether any other location on the sternum than the lower one third improved survival, neurologic outcomes, or time to ROSC.

- ***Time frame:*** All years to June 16, 2024

Summary of Evidence

Studies considered before 2010 included observational studies in small numbers of human infants,[245,246] cadavers,[247] or predictions from chest radiographs.[246-249] More recent studies using chest radiographs[250] or chest computed tomography[251] have largely confirmed their results. The task force concluded that, because these studies had not been evaluated using Grading of Recommendations Assessment, Development, and Evaluation assessment of certainty of evidence, the 2010 treatment recommendation should be reworded as a good practice statement.

Treatment Recommendation (2025)

Neonatal chest compressions should be centered over the lower third of the sternum but above the xiphoid (good practice statement).

DRUG AND FLUID ADMINISTRATION

Epinephrine (Adrenaline) for Neonatal Resuscitation (NLS 5600: EvUp 2025)

In the 2020 ILCOR SysRev, studies of epinephrine in human infants were mostly observational cohort studies or case series.[171] Therefore, studies in asphyxiated newborn animals receiving effective positive-pressure ventilation and chest compressions that showed that epinephrine (especially when given intravenously) can achieve ROSC more effectively and sooner than control treatments contributed to the 2020 ILCOR treatment recommendations about epinephrine dose, route, and timing.[5,171] A 2025 EvUp was performed and also included relevant animal studies. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** March 6, 2019, to August 20, 2024

Summary of Evidence

The only new human infant evidence was from observational studies.[252-255] Eight animal studies (and an additional one published just after the search completion date[256]) examined various comparisons, including epinephrine versus no epinephrine as well as dose and route.[257-264] The task force concluded that the PICOST question deserves an updated SysRev, mainly to assess new indirect evidence from animal studies that refines understanding of dose, route, and potential harms of epinephrine, particularly when given in high cumulative doses.

Treatment Recommendations (2020)

If the heart rate has not increased to ≥60/min after optimizing ventilation and chest compressions, we suggest the administration of intravascular epinephrine (0.01–0.03 mg/kg) (weak recommendation, very low–certainty evidence).

If intravascular access is not yet available, we suggest administering endotracheal epinephrine at a larger dose (0.05–0.1 mg/kg) than the dose used for intravascular administration (weak recommendation, very low-certainty of evidence). The administration of endotracheal epinephrine should not delay attempts to establish vascular access (weak recommendation, very low–certainty evidence).

We suggest the administration of further doses of epinephrine every 3 to 5 minutes, preferably intravascularly, if the heart rate remains <60 bpm (weak recommendation, very low–certainty evidence).

If the response to endotracheal epinephrine 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).

Sodium Bicarbonate During Neonatal Resuscitation (NLS 5601: EvUp 2025)

In infants (newborn or in the neonatal period) requiring resuscitation, the question of whether sodium bicarbonate administration compared with no sodium bicarbonate improves survival, ROSC, or critical or important neonatal morbidity outcomes was last reviewed in 2005.[124] An EvUp was done in 2020.[5] The complete 2025 EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** January 1, 2020, to June 17, 2024

Summary of Evidence

No new evidence was found to support the use of sodium bicarbonate in neonatal resuscitation. One study in 2- to 5-day-old anesthetized, nonasphyxiated piglets suggested a potential mechanism of harm, particularly when vasoconstrictors were also administered.[265] One study of sodium bicarbonate treatment for acidosis in pediatric intensive care units suggested sodium bicarbonate treatment was beneficial in the setting of hyperchloremia but harmful if

chloride values were normal (as will usually be the case in newborn infants).[266] The overall evidence from the current and the previous EvUp (2019) is insufficient to justify a new SysRev.

The previous treatment recommendation (2005) was not supported by a SysRev using contemporary ILCOR methods of evidence appraisal. The conditions suggested in the previous treatment recommendation for the use of sodium bicarbonate (after adequate ventilation is established and there is no response to other therapies) are rare and unexpected in human infants needing resuscitation immediately after birth, meaning that human infant trials would be difficult to conduct and might take many years to complete. The animal studies assessed in previous ILCOR worksheets have not addressed these circumstances.

Prior Treatment Recommendation (2005, Withdrawn)

Sodium bicarbonate is discouraged during brief CPR, but it may be useful during prolonged arrests after adequate ventilation is established and there is no response to other therapies.[267]

Although this treatment recommendation was included in previous consensus statements (2005–2020), it can no longer be supported. Based on current methods of evaluating the certainty of evidence, the task force has concluded there is neither direct nor indirect evidence to inform a treatment recommendation. As a result, this treatment recommendation has been withdrawn and will be reconsidered if new evidence becomes available.

Glucose Management During or Immediately After Resuscitation (NLS 5602: ScopRev 2025)

Rationale for Review

Glucose management in neonatal resuscitation was last addressed for the 2010 CoSTR, which concluded that newborns who had hypoglycemia in the setting of hypoxic ischemic encephalopathy had worse outcomes than those who were normoglycemic, and that

hyperglycemia might be protective, although a specific target blood glucose concentration range could not be identified at that time.[109] An EvUp in 2020 prompted the task force to conduct this ScopRev. Complete details are available on the ILCOR website.[23]

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

- ***Population:*** Newborn infants (preterm and term) who receive resuscitation at birth in all healthcare settings that provide birthing services
  - *Question 1.* When and how should blood glucose be monitored in newborn infants receiving resuscitation?
- ***Intervention:*** Strategy of monitoring glucose or metabolites (lactate, ketones, insulin) or postresuscitation care bundles that include such monitoring
- ***Comparator:*** No monitoring or no defined strategy or alternative monitoring strategy
  - *Question 2.* When and how should glucose (or other treatments to control blood glucose concentration) be used during and after neonatal resuscitation?
- ***Intervention:*** Glucose (administered via intravenous, intraosseous, or buccal route) or glucagon or postresuscitation care bundles to control blood glucose concentration
- ***Comparator:*** No glucose (or other treatment to control blood glucose concentrations) or an alternative strategy
  - *Question 3.* What is the optimal blood glucose concentration range for newborn infants during and after resuscitation?
- ***Exposure:*** Dysglycemia or defined blood glucose target range
- ***Comparator:*** Normoglycemia or alternative target range
- ***Outcome:***
  - *All Questions*
    - Success of resuscitation (critical)

- Neonatal brain injury (critical)
- Long-term neurological function (critical)
- Neonatal morbidity (important)

– *Questions 1 and 2*

- Dysglycemia: referring to episode(s) of either hypoglycemia (blood glucose concentration ≤2.5 mmol/L [≤45 mg/dL]) and hyperglycemia (blood glucose concentration ≥7 mmol/L [≥126 mg/dL]), or both, for the purposes of this review (important)
- Metabolite levels: blood lactate, ketone, and insulin concentrations (important)
- Feasibility (important)

- ***Study design:*** Because this was a ScopRev, animal trials, human trials (randomized, nonrandomized, historically controlled), and human observational studies (cohort, before-and-after, case-control, case series if ≥6 participants) were eligible for inclusion. Studies were considered eligible for inclusion if they directly or indirectly addressed the review questions but were excluded if they had not been peer reviewed or published in full text. All years and all languages were included provided there was an English abstract.
- ***Time frame:*** All years to October 6, 2024

Summary of Evidence

Question 1. When and how should blood glucose be monitored in newborn infants receiving resuscitation?

Twenty-five articles reporting 24 observational studies described serial monitoring of blood glucose concentrations, commencing at NICU admission or at ≤2 hours of age to assess the frequency of neonatal dysglycemia.[268-292] Apart from 1 study in which 35% of infants were

born at ≤32 weeks' gestation,[269] all other studies included only infants born at ≥34 weeks' gestation.

Two studies used continuous glucose monitoring,[284,287] and all others used intermittent blood glucose sampling, with variation in whether the sampling site or analytic method was specified. The definitions of hypoglycemia and hyperglycemia also varied. *Hypoglycemia* was most often defined as blood glucose values <2.2 mmol/L (<40 mg/dL) or <2.6 mmol/L (<46 mg/dL). *Hyperglycemia* was most often defined as ≥1 blood glucose values >8.3 mmol/L (>150 mg/dL).

Only 9 studies provided information about specific resuscitation interventions received by infants that might be associated with increased risk of dysglycemia.[269,270,275,277,285,288,290,291,293] Three studies suggested a lower risk of hypoglycemia or higher blood glucose levels in infants who had received epinephrine compared with those who had not.[252,270,291]

In studies assessing the risk of hypoglycemia at different times after resuscitation, 1 study including 60 term infants with Apgar scores ≤6 at 5 minutes (of whom 73% had subsequent hypoxic ischemic encephalopathy) reported that 92% of the 12 patients with blood glucose measurement recorded in the delivery room were hypoglycemic.[271] In studies reporting glucose measurements on NICU admission, the proportions of infants with hypoglycemia ranged from 8% to 23%.[270,275-277,281,288] The proportions with hyperglycemia ranged from 19% to 53%.[276,277,281] In 6 studies reporting results in the first 6 hours after birth, the proportion of infants with hypoglycemia ranged from 7% to 24%.[272,278,279,284-286]

Question 2. When and how should glucose (or other treatments to control blood glucose concentration) be used during and after neonatal resuscitation?

There were no human studies directly addressing control of blood glucose during resuscitation, and evidence from animal studies was inconsistent, with some studies suggesting

neuroprotection when glucose was infused during asphyxia or during recovery from hypoxia-ischemia[282,294-314] and others suggesting harm or no benefit.[315-320]

During postresuscitation care, routine commencement of intravenous glucose infusions was a common practice in infants admitted to NICU, typically at infusion rates of 4 mg/kg per minute, but no studies defined an optimal strategy to achieve euglycemia (and avoid iatrogenic hyperglycemia) during the treatment of hypoglycemia after resuscitation at birth.

Question 3. What is the optimal blood glucose concentration range for newborn infants during and after resuscitation?

No studies directly investigated the optimal blood glucose target range for infants immediately after resuscitation at birth. Whether a lower or higher target is better remains unknown.

Task Force Insights

For infants needing advanced resuscitation at birth, it remains unknown if empiric use of glucose during resuscitation improves the success of the resuscitation interventions.

As a whole, the studies addressed only a subgroup of the infants intended in the ScopRev questions (eg, term and late preterm already defined to have—or be at high risk for—hypoxic ischemic encephalopathy), rather than including all infants who had received resuscitation, regardless of gestation. There was also considerable variation in study design and methods. Hence, for infants who have received resuscitation, the task force considered that meta-analysis would not accurately determine the risk of hypo- or hyperglycemia at specific times in the first few hours or the extent to which hypo- or hyperglycemia affects outcomes. No studies compared outcomes from any specific strategy for blood glucose monitoring to any other strategy in a way that allowed determination of an optimal approach. Nevertheless, in the first hours after resuscitation, the evidence that was available suggested that both hypo- and hyperglycemia are

common and that both may be associated with harm. Research is needed to define an optimal target range for blood glucose in the aftermath of resuscitation, optimal strategies for monitoring, and management strategies that improve outcomes and avoid overtreatment or undertreatment.

Prior Treatment Recommendation (2010)

Intravenous glucose infusion should be considered as soon as practical after resuscitation, with the goal of avoiding hypoglycemia.[126]

This recommendation was not supported by a SysRev of the literature using Grading of Recommendations Assessment, Development, and Evaluation methods and should be regarded as superseded. Until sufficient evidence is available to justify a SysRev, the task force generated the following good practice statements.

Treatment Recommendations (2025)

Among newborn infants receiving resuscitation, blood glucose concentration should be measured early in the postresuscitation period and monitored with serial measurements until maintained within a normal range. Infants at greatest risk of hypo- and hyperglycemia during the postresuscitation period include preterm infants, infants receiving chest compressions or epinephrine, and those with hypoxic ischemic encephalopathy (good practice statement).

Treatment with intravenous glucose infusions should be guided by the infant's blood glucose concentration with the goal of avoiding both hypoglycemia and hyperglycemia (good practice statement).

Blood Volume Expansion During Neonatal Resuscitation (NLS 5650: EvUp 2025)

The previous ILCOR assessment of the role of fluids to expand blood volume during neonatal resuscitation focused on the risk of harm if fluid boluses are given to all infants, while recognizing that a few infants have experienced critical blood loss immediately before or during resuscitation and may benefit from volume resuscitation.[126] Surveillance of the literature and an

EvUp in 2020 concluded that the 2010 treatment recommendation was still supported.[5] A further EvUp addressing whether blood volume expansion with any blood products or crystalloids (eg, sodium chloride 0.9%) compared with no blood volume expansion improved survival, neurodevelopmental outcomes, serious morbidity, or short-term outcomes of resuscitation was conducted for 2025. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** January 1, 2021, to July 2, 2024

Summary of Evidence

One narrative review that included a few previously unpublished animal data was identified for inclusion.[321] Because the sparse available evidence from previous reviews has not been evaluated using Grading of Recommendations Assessment, Development, and Evaluation methods, the existing recommendation is now reworded as good practice statements, pending an updated SysRev.

Good Practice Statements (2025)

Early volume replacement with crystalloid or red cells is indicated for newborn infants with blood loss who are not responding to resuscitation (good practice statement).

There is insufficient evidence to support the routine use of volume administration in newborn infants with no blood loss who are 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 (good practice statement).

Intraosseous Versus Intravenous Cannulation for Emergency Access (NLS 5652: EvUp 2025)

A 2020 SysRev for all age groups identified that intraosseous administration of medications and fluids could be accomplished during cardiac arrest, including during neonatal

resuscitation but with some potential for serious complications in newborns.[322] A 2025 EvUp was performed, focusing only on newborn infants. The complete EvUp, including the full PICOST, is provided in Appendix B.

- ***Time frame:*** December 1, 2019, to July 15, 2024

Summary of Evidence

Three new observational studies that reported results of intraosseous access in newborns and infants in the neonatal period were included, but none specifically compared intraosseous with intravenous access.[323-325] Two studies identified cases from databases,[323,325] and 1[324] used self-reported results of questionnaires. The proximal tibial was the most commonly used insertion site.[323,324] Success rates for intraosseous insertion varied from 50% to 86% between studies,[323-325] and complication rates varied from 10.8%[325] to 35%.[323] Complications included extravasation, necrosis, compartment syndrome, subperiosteal infusion, tibial fracture, broken intraosseous needle, osteomyelitis, and soft tissue infection.

The new studies support the current treatment recommendations and appear insufficient to justify a new SysRev at this time.

Treatment Recommendations (2020)

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 intraosseous 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.

POSTRESUSCITATION CARE

Rate of Rewarming Hypothermic Newborns (NLS 5700: SysRev 2024)

The effect of the rate of rewarming on outcomes of newborns who are unintentionally hypothermic after delivery was addressed by a 2024 SysRev, and details of this review, including the complete PICOST, can be found in the 2024 CoSTR summary.[7] The literature search was updated from July 1, 2023, to June 13, 2024, during the process of preparing the SysRev for submission for publication.

Treatment Recommendations (2024)

In newborn infants who are unintentionally hypothermic after birth, rewarming should be started, but there is insufficient evidence to recommend either rapid (≥0.5 °C/h) or slow (<0.5 °C/h) rates of rewarming.

Regardless of the rewarming rate chosen, a protocol for rewarming should be used. Frequent or continuous monitoring of temperature should be undertaken, particularly if using a supraphysiological set temperature point to accelerate the rewarming rate, because of the risk of causing hyperthermia. In any hypothermic infant, monitor blood glucose because there is a risk of hypoglycemia (good practice statement).

Therapeutic Hypothermia in Limited-Resource Settings (NLS 5701: SysRev 2024)

Therapeutic hypothermia for the treatment of moderate or severe hypoxic ischemic encephalopathy in neonates is now the well-established standard of care in high-income countries, but its efficacy in low-resource settings had been unclear.[2] The task force was aware of several new studies in low- and middle-income countries and considered it a sufficiently important aspect of postresuscitation care to prioritize a SysRev. Details of this review, including the complete PICOST, can be found in the 2024 CoSTR summary.[7] The literature search was updated from July 1, 2023, to September 30, 2024, during the process of preparing the SysRev

for submission for publication. During this process, one study was excluded post hoc when the task force recognized some inconsistences that raised concerns about trustworthiness of the findings.[326] Another article[327] was found to have reported additional outcomes for a subset of participants in a previous RCT[328] and so is now only included as a single trial. Amended versions of the online CoSTR and evidence-to-decision table have been posted on the ILCOR website, but the task force concluded that the revised evidence still supports the 2024 treatment recommendations and certainty of evidence.

Treatment Recommendations (2024)

We suggest the use of therapeutic hypothermia in comparison with standard care alone for term (≥37+0 weeks' gestational age) newborn infants with evolving moderate-to-severe hypoxic-ischemic encephalopathy in low- and middle-income countries in settings where a suitable level of supportive neonatal care is available (weak recommendation, low-certainty evidence).

For late preterm infants, 34+0 to 36+6 weeks' gestational age infants, a recommendation cannot be made due to insufficient evidence.

Therapeutic hypothermia 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, antiseizure medication, transfusion services, radiology (including ultrasound), and pathology testing, as required. Treatment should be consistent with the protocols used in RCTs. Most protocols included commencement of cooling within 6 hours after birth, strict temperature control to a specified range (typically 33 °C–34 °C), and most commonly for a duration of 72 hours with rewarming over at least 4 hours. Adoption of

hypothermia techniques without close monitoring, without protocols, or without availability of comprehensive neonatal intensive care may lead to harm (good practice statement).

PROGNOSTICATION DURING CPR

Impact of Duration of Intensive Resuscitation (NLS 5800: EvUp 2025)

Deciding how long to continue resuscitative efforts in a newborn with no heart rate or a very low heart rate with absent respirations after sustained resuscitative efforts is a critical decision. If such a decision is made too early, some newborns with potential to survive without severe neurodevelopmental impairments may die. If left too late, parental engagement during end-of-life care may be impeded. This topic was previously addressed in a 2020 SysRev.[5,329] A 2025 EvUp was conducted, and complete details, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** October 17, 2019, to July 4, 2024

Summary of Evidence

One SysRev[330] (with included studies that extensively overlapped with those in the ILCOR SysRev) was identified. There was 1 additional population-based study[331] and 3 cohort studies nested within RCTs of advanced resuscitation.[332,333,334] Overall, these studies confirm that, for infants who receive resuscitation, survival without severe neurodevelopmental impairment is possible after prolonged asystole or bradycardia. However, this may vary with gestational age, the availability of therapeutic hypothermia, resuscitation practices, and access to other intensive or complex care. The new evidence is not sufficient to justify a new SysRev at this time.

Treatment Recommendation (2020)

Failure to achieve ROSC 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 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).

FAMILY PRESENCE

Family Presence During Neonatal Resuscitation (NLS 5900: SysRev 2021, EvUp 2025)

A SysRev conducted with the Pediatric Life Support Task Force in 2021 addressed the impact of family presence during resuscitation of infants and children on outcomes of resuscitation, on families, or on those providing resuscitation.[9,335,336] A 2025 EvUp assessed whether there were new studies specific to the presence of parents at the resuscitation of newborn infants. The complete EvUp, including the full PICOST, can be found in Appendix B.

- ***Time frame:*** September 1, 2019, to September 5, 2024

Summary of Evidence

Five studies specifically addressing parental presence during resuscitation at birth were included, all from high-income countries and all addressing caregiver perceptions.[337-341] There is a continued absence of studies from culturally diverse settings or where resources are limited, and none of the new studies interviewed parents. The new evidence does not appear sufficient to change the current treatment recommendation or to justify a new SysRev until more studies have accumulated.

Treatment Recommendation (2021)

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

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

Topics Not Included in the 2025 Review

The following PICOSTs are not included in this summary:

- **Anticipation and Preparation**
  - Effect of neonatal resuscitation team composition on outcomes (NLS 5000): not previously reviewed
  - Checklists and cognitive aids for neonatal resuscitation (NLS 5001): addressed by Education, Implementation, and Teams Task Force as EIT 6400
  - Prediction of the need for resuscitation at birth (NLS 5003): not previously reviewed
  - Prediction of outcome after extremely preterm birth (NLS 5004): SysRev underway
  - Prediction of outcome if mother has intrapartum hypothermia or hyperthermia (NLS 5005): not previously reviewed
- **Initial Steps**
  - Prediction of outcomes based on infant temperature during or immediately after resuscitation
- **Ventilation and Oxygenation**

- Upright resuscitator for administering positive-pressure ventilation at birth (NLS 5301): not previously reviewed
- High flow nasal cannula for initial respiratory support (NLS 5302): not previously reviewed
- Mouth techniques for administering positive-pressure ventilation in very low resource settings (NLS 5303): not previously reviewed
- Interfaces for noninvasive positive-pressure ventilation (NLS 5304): not previously reviewed
- Strategies for positive-pressure ventilation (NLS 5325): ScopRev underway
- Respiratory function monitoring during simulation training (NLS 5361): SysRev underway
- Oxygen saturation targeting (NLS 5402): ScopRev underway
- Oxygen use after ROSC (NLS 5403): not previously reviewed
    - **Drug and Fluid Administration**
- Caffeine administration for preterm infants during stabilization (NLS 5311): not previously reviewed
- Surfactant administration during or immediately after neonatal resuscitation (NLS 5370): ScopRev underway
    - **Postresuscitation Care**
- Therapeutic hypothermia, how to identify infants who may benefit (NLS 5702): not previously reviewed
- Therapeutic hypothermia, commencement during resuscitation (NLS 5703): not previously reviewed
- Alternatives to therapeutic hypothermia (NLS 5704): not previously reviewed

- **Other and Special Considerations**
  - Resuscitation for infants with specific congenital anomalies (NLS 5900): ScopRev planned 2025
  - Face-to-face versus remote or distance learning: new question

Readers are encouraged to monitor the ILCOR website[10] to provide feedback on planned SysRevs and to provide comments when additional draft reviews are posted.

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