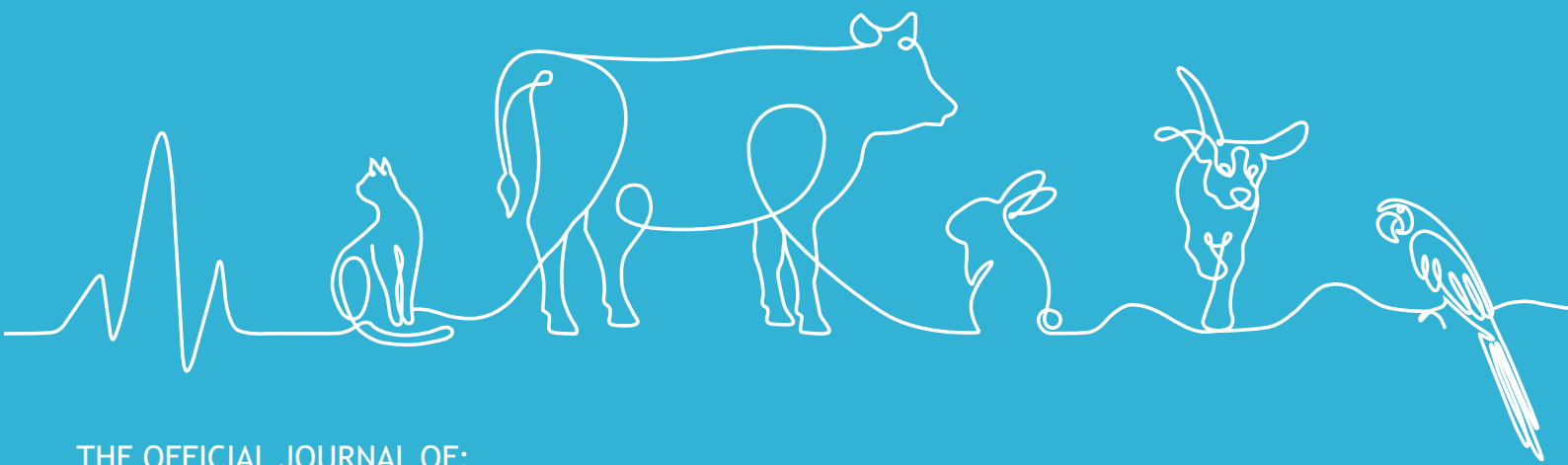
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Contents

Volume 35 | Number S1 | August 2025

2025 RECOVER Special Issue: Newborn Resuscitation

S3 RECOVER Guidelines: Newborn Resuscitation in Dogs and Cats. Evidence and Knowledge Gap Analysis With Treatment Recommendations
Manuel Boller, Jamie M. Burkitt-Creedon, Christopher G. Byers, Daniel J. Fletcher, Kate S. Farrell, Autumn P. Davidson, Suzanne Fricke, Giovanna Bassu, Sophie A. Grundy, Cheryl Lopate & Maria C. Veronesi

S60 RECOVER Guidelines: Newborn Resuscitation in Dogs and Cats. Clinical Guidelines
Manuel Boller, Jamie M. Burkitt-Creedon, Daniel J. Fletcher, Christopher G. Byers, Autumn P. Davidson, Kate S. Farrell, Giovanna Bassu, Erik D. Fausak, Sophie A. Grundy, Cheryl Lopate & Maria C. Veronesi

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SPECIAL ARTICLE OPEN ACCESS

RECOVER Guidelines: Newborn Resuscitation in Dogs and Cats. Evidence and Knowledge Gap Analysis With Treatment Recommendations

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Keywords: birth | cardiopulmonary resuscitation | Cesarean section | consensus guidelines | evidence-based veterinary medicine | neonatal resuscitation

ABSTRACT

Objective: To systematically review the evidence on, to devise clinical recommendations for, and to identify critical knowledge gaps in resuscitation of newborn puppies and kittens.

Design: Standardized, systematic evaluation of literature pertinent to newborn resuscitation following Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology. Prioritized questions were reviewed by Evidence Evaluators, and findings were reconciled by Domain Chairs and Reassessment Campaign on Veterinary Resuscitation (RECOVER) Co-Chairs to arrive at treatment recommendations commensurate with the quality of evidence, risk–benefit relationship, and clinical feasibility. This process was implemented using an evidence profile worksheet for each question that included an introduction, consensus on science, treatment recommendations, justification for these recommendations, and important knowledge gaps. Treatment recommendations underwent a modified Delphi consensus process and were then distributed to veterinary professionals for comment for 2 weeks prior to finalization.

Setting: Transdisciplinary, international collaboration in university, specialty, and emergency veterinary practice.

Abbreviations: CI, confidence interval; CPA, cardiopulmonary arrest; CRI, constant rate infusion; EE, Evidence Evaluator; ET, endotracheal; ETS, endotracheal suctioning; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; HIE, hypoxic–ischemic encephalopathy; HR, heart rate; ILCOR, International Liaison Committee on Resuscitation; IO, intraosseous; ONPS, oronasopharyngeal suctioning; OR, odds ratio; PEEP, positive end-expiratory pressure; PICO, Population–Intervention–Comparator–Outcome; PIP, peak inspiratory pressure; PPV, positive pressure ventilation; ROSC, return of spontaneous circulation; SI, sustained inflation.

Manuel Boller and Jamie M. Burkitt-Creedon contributed equally to this work.

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Results: Twenty-eight questions pertaining to temperature management, respiratory and metabolic support, and CPR were addressed. Of the 59 treatment recommendations formulated, 21 concerned medications, 20 addressed respiratory measures, 20 provided guidance on CPR, and 3 related to temperature management. Taken together, the recommendations emphasize the importance of early administration of bag–mask ventilation in nonvigorous, severely bradycardic newborn puppies and kittens. Most recommendations are either expert opinion ($n = 28$) or based on very low quality of evidence ($n = 26$).

Conclusions: Significant uncertainty remains regarding most resuscitative interventions in newborn puppies and kittens at birth. However, through a comprehensive evaluation of the evidence and a consensus process that included considerations of feasibility, the resulting treatment recommendations lay the foundation for clear, actionable guidance in small animal newborn resuscitation. In addition, a list of prioritized knowledge gaps was identified to guide collaborative clinical research to overcome the significant lack of veterinary scientific data at present.

1 | Introduction

Birth is a tremendous physiologic challenge [1]. The newborn puppy or kitten must expeditiously transition its respiratory and circulatory system to adjust to the outside world. Within minutes, it must aerate its lungs to switch gas exchange from the placenta to the lungs and completely separate pulmonary from systemic circulation [1–3]. Accordingly, the perinatal period is associated with high mortality. In canine Cesarean sections (C-sections) encompassing both elective and emergency surgeries, for example, more than 10% of puppies did not survive the first 2 h of life [4]. Even without C-sections, the mortality in newborn puppies was 5% and 8% in the first 24 h and the first week after birth, respectively [5, 6]. More than 8% of kittens were reported to be stillborn [7]. Providing evidence-based and consensus-agreed recommendations regarding the provision of resuscitative measures to newborn puppies and kittens at birth therefore addresses a real clinical problem and has great impact potential.

In newborn infants, evidence-based treatment recommendations are well established and have been used to create regional clinical newborn resuscitation guidelines and programs for many years [8–10]. In veterinary medicine, evidence- and consensus-based guidelines have been published for CPR in adult dogs and cats, but not for newborns [11, 12]. While multiple peer-reviewed articles have been published to instruct veterinary professionals on how to support newborn puppies and kittens at birth, they are based on the perspectives of individual experts in the field [13–16]. We herein endeavor to generate evidence- and consensus-based treatment recommendations for resuscitation of newborn puppies and kittens to allow for a concise and actionable set of instructions for veterinary professionals. We do so by following the same methodology as applied during the RECOVER 2024 guidelines process for adult animals [17].

2 | Terminology and Scope of Newborn Resuscitation

Terminology of the life stages of immature animals is not uniformly used, especially as it applies to animals at birth. Often, the terms *newborn* and *neonatal* are used interchangeably. For clarity, we use the term *newborn* for a puppy or kitten during the first few hours of life, primarily including the transition period from intra- to extrauterine life. Neonatal puppies and kittens are defined as those from birth until an advanced level of independence from the dam is reached (e.g., independent urination and defecation, walking, initiation of weaning), which corresponds to an age of 3–4 weeks, depending on species and breed. While post-transitional neonates are physiologically still immature [18], their cardiorespiratory systems are more comparable to adult animals, as their lungs are aerated and separate pulmonary and systemic circulatory systems have been established. Thus, if these post-transitional neonates experience cardiopulmonary arrest (CPA), resuscitation techniques follow similar principles as in adult dogs and cats, with the focus on CPR. The primary and immediate endpoint of CPR is to re-establish spontaneous circulation. In contrast, newborn resuscitation encompasses a wide range of interventions that aim to support the newborn through the transition period, with the primary objective being aeration of the lungs, control of body temperature, and metabolic stability [1].

Most newborn puppies and kittens will need no intervention and will be cared for by their dam. However, any newborn puppy or kitten that appears weak or hypotonic rather than irritable and vocal, or is apneic or gasping, is considered nonvigorous and in distress and requires resuscitation. Additionally, all puppies and kittens born by C-section require support at birth. By definition, we consider all supportive measures provided to a newborn puppy or kitten as resuscitative measures. Resuscitative interventions are applied in a measured fashion to meet the perceived needs of the newborn. Thus, resuscitation in the newborn puppy or kitten may consist of as little as removing fetal membranes and applying tactile stimulation (i.e., drying, rubbing), or might also include application of positive pressure ventilation (PPV) or, less commonly, might be escalated to include chest compressions (i.e., CPR) and administration of epinephrine. Based on the premise of sequential, escalating resuscitation measures, we aimed to provide recommendations that fit into a specific clinical context. This context is reflected in the population description for each recommendation and can also be visualized in a newborn resuscitation algorithm provided in an instructional companion article [19]. It is of utmost importance to understand each treatment recommendation in its context for effective clinical applicability. For example, initiation of PPV with pure oxygen (i.e., FiO_2 1.0) carries the risk of increased mortality in newborn infants [20–23], but if 1–2 min of room air PPV fails to produce a response (e.g., an increase in heart rate [HR]), taking this potential risk is justified, and we recommend adding supplemental oxygen at that time (see NB-03).

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3 | Methods

We developed these newborn resuscitation treatment recommendations following a similar process as previously published for the 2024 RECOVER CPR Guidelines (Figure 1) [17]. In short, these treatment recommendations were generated using a modified GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) process for guideline generation in health care and were then further refined by a predetermined consensus process [24]. The project was initiated in 2018 and completed in 2025. A concise summary of the iterative evidence evaluation and consensus process is provided below.

BOX 1: Major controversies

- Heart rate measurement methodologies
- GV 26 (Renzhong) acupoint stimulation
- Efficacy of positive pressure ventilation by face mask
- Feasibility and harm of endotracheal intubation by skilled providers
- Preferred routes of drug administration
- Epidemiology of newborn resuscitation

3.1 | Defining Population–Intervention–Comparator–Outcome (PICO) Questions and Outcomes

The RECOVER Co-Chair overseeing this domain (M.B.) appointed content experts to serve as chairs for the Newborn Resuscitation Domain (C.B., A.D., K.F.). Two of these Domain Chairs, together with the Co-Chair, generated research questions in the PICO format and identified 4 to 6 clinically important outcomes for each PICO question. PICO questions were rated as high priority, moderate priority, or lower priority. Forty PICO questions were developed for evidence evaluation on newborn resuscitation, of which 28 were rated as high priority. Due to the limited number of volunteers available to conduct the evidence evaluations and to generate treatment recommendations, only the high-priority questions were addressed.

For each PICO question, Domain Chairs ranked the outcomes according to their clinical importance, so that treatment recommendations could be weighed based on the evidence pertaining to the highest priority outcomes for which clinically relevant evidence was available. The most commonly included outcomes were favorable neurologic outcome, survival to hospital discharge, hospital length of stay, respiration (i.e., oxygenation, ventilation), and histopathologic damage, usually in this order of priority. Additional outcomes were investigated depending on the PICO question.

3.2 | Literature Search and Screening

Specialist librarians (Information Specialists) worked with RECOVER Co-Chairs to develop the search strategy for the project[a]. Search strings were developed using an iterative process among Information Specialists and Domain Chairs to optimize the number and type of articles returned in the searches. Peer review of search strategies occurred using modified Peer Review of Electronic Search Strategy Guidelines and informal meetings [25]. Databases interrogated included PubMed, CAB Direct, and Scopus, and date coverage included the years 1966–2020. Articles that were non-English, letters to the editors, and other nonanalytical publications were excluded at the level of search strategies.

For each PICO question, 2 Evidence Evaluators (EEs) (e.g., specialist veterinarians, general veterinarians in emergency or specialty practice, or veterinary technician specialists in emergency and critical care) independently reviewed titles and abstracts of initially identified articles to eliminate irrelevant publications and to arrive at potentially relevant primary literature for further review. Reviews, meta-analyses, case reports and case series, and non-peer-reviewed publications (e.g., proceedings) were excluded either during this title and abstract screening process or later at the full-text review stage. Domain Chairs resolved any conflicts between EEs. Full texts of these potentially relevant publications were then reviewed for each PICO by the same EEs; first, they established the relevance of each publication for the PICO question, and if confirmed, they extracted relevant information from these publications for each predefined outcome.

3.3 | Evidence Evaluation and Treatment Recommendations

EEs used a purpose-developed, web-based evaluation platform to proceed through a predetermined, standardized set of questions to evaluate key aspects of evidence quality (e.g., risk of bias, indirectness of population, intervention, and outcomes). Based on EE responses, the evaluation platform generated an Evidence Summary Table for each outcome for every PICO question. EEs also provided succinct overview evidence summaries for their PICO question. From this output, the Domain Chairs or RECOVER Co-Chairs (M.B., J.B., D.F.) drafted Evidence Profile Worksheets for each PICO question. Prior to completing the Worksheets, Co-Chairs executed a bridge search on key publications from the original literature search to identify new or missed relevant research, as the literature searches were 3–5 years old at that time. If additional publications were identified, Co-Chairs conducted an evidence quality evaluation in the Evidence Summary Table for these articles and included these findings in the Evidence Profile Worksheet. These worksheets included a structured summary (introduction, consensus on science, treatment recommendation(s), justifications for the treatment recommendations, and knowledge gaps for future study) and additional notes made during the evaluation of individual studies. The Evidence Profile Worksheets were then collectively reviewed and edited by the Co-Chairs. In accordance with the GRADE system, each treatment recommendation is written either as a *recommendation* where the RECOVER group found stronger evidence (or perceived risk/benefit relationship, where evidence was poor or not available) or as a *suggestion* where the RECOVER group found weaker evidence (or perception of risk/benefit relationship, where evidence was not available) for or against

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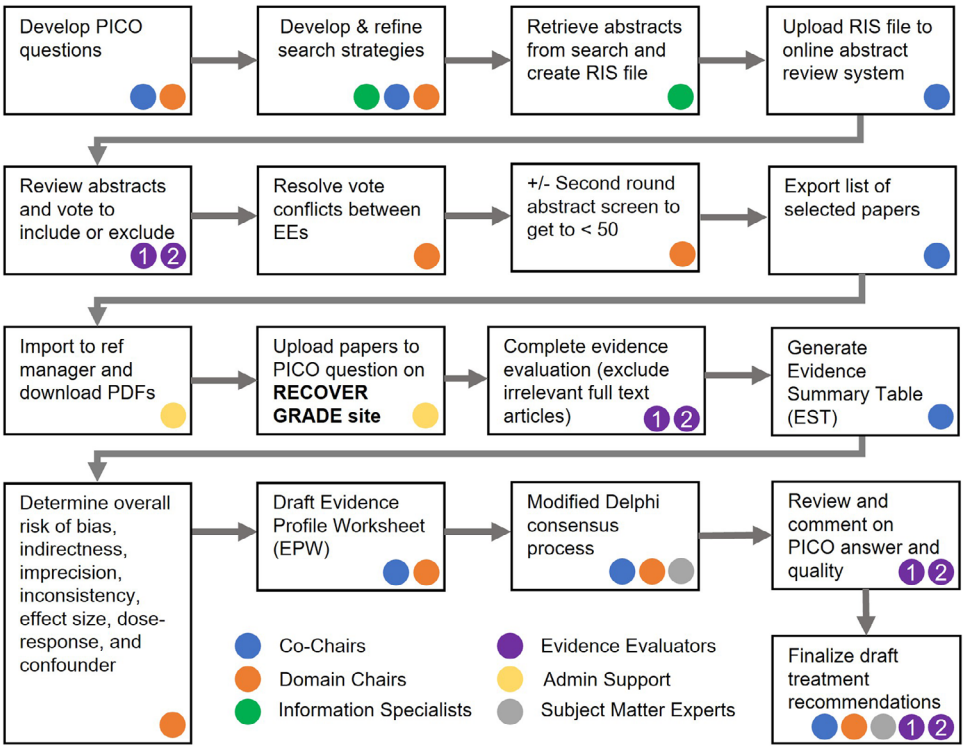


FIGURE 1 | Evidence evaluation process overview for the RECOVER Newborn Resuscitation Guidelines. GRADE, Grading of Recommendations Assessment, Development and Evaluation; PICO, Population–Intervention–Comparator–Outcome; RECOVER, Reassessment Campaign on Veterinary Resuscitation; RIS, Research Information System.

the intervention. From the 28 PICO questions, the Co-Chairs proposed a total of 56 treatment recommendations.

3.4 | Consensus Process

The draft treatment recommendations underwent a modified Delphi process to reach consensus among anonymously voting subject matter experts in the field of small animal theriogenology and reproduction (A.D., C.L., G.B., M.V., S.G.), Domain Chairs (C.B., K.F.), and Co-Chairs (D.F., J.B., M.B.) [26]. For this purpose, an electronic survey for each PICO was sent to all consensus group members to accept or reject a draft treatment recommendation, including a request to raise specific concerns and propose alternative wording. Consensus was a priori defined as at least 80% of respondents agreeing with a recommendation. If that level of agreement was not reached in one round of consensus evaluation, or other substantive concerns were raised, RECOVER Co-Chairs (J.B., M.B.) reworded the recommendation based on feedback, and the process was repeated. If consensus could not be achieved after two rounds of adjusting treatment recommendations, these recommendations were discussed in a third round of consensus finding in a virtual meeting. Of the 56 initial treatment recommendations, consensus was reached for 43 recommendations after the first round, while three more recommendations were added based on reviewer feedback. After the second consensus round, 5 questions (NB-07, NB-08, NB-19, NB-21, and NB-26) remained without consensus and were discussed in a virtual meeting. We were unable to reach consensus for one question (NB-08 on governing vessel [GV] 26 acupoint stimulation) and did not make a recommendation for or against the intervention.

The treatment recommendations and links to the Evidence Profile Worksheets were then uploaded to a commenting platform (NowComment[b]) for stakeholder community feedback over a period of 2 weeks. Links to NowComment were sent directly to EEs and posted on listservs for relevant specialty and other professional organizations, including theriogenology and small animal reproduction medicine organizations globally. Following this period, comments were considered by the Co-Chairs and Domain Chairs, and relevant treatment recommendations were refined to create a finalized set of treatment recommendations for newborn resuscitation in puppies and kittens, which appear in this publication. The structured summary for each newborn resuscitation PICO question appears below, and the additional study evaluation notes appear in the full Evidence Profile Worksheets (Open Science Framework[a]).

4 | Resuscitative Measures in the First Minute After Birth

Most newborn puppies and kittens born naturally are expected to not require any resuscitative measures at birth. If born by normal parturition (e.g., vaginal eutocia) with the dam able to provide immediate postpartum care, and if vigorous, breathing, and vocalizing immediately after birth, then no resuscitation is required, and the newborn should be left with the mother and simply be monitored.

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All puppies and kittens born by C-section and many born by vaginal dystocia will require support at birth. Immediately after birth, the first resuscitation measures include clearing the newborn's airway, drying, and tactile stimulation, which are often accomplished in the same action, and active measures to promote normothermia; these interventions typically occur simultaneously. Once accomplished, assessment of HR and respiratory function should occur as soon as possible so as to initiate respective measures in support of respiratory transition during the first minute after birth, if required. The following are PICO questions, evidence summaries, treatment recommendations and their justifications, as well as knowledge gaps pertaining to steps we recommend be executed as soon as possible after birth. Specifically, actions we considered to be taken in the first minute after birth concern tactile stimulation (NB-15), methods of airway clearance (NB-09 and NB-10), temperature control (NB-11), methods for HR determination (NB-04), initiation of respiratory support including PPV (NB-01 and NB-06), administration of reversal drugs (NB-20), and the use of atropine to treat bradycardia (NB-23).

4.1 | Tactile Stimulation at Birth—NB-15

In newborn dogs and cats that require resuscitation (P), how does the use of no external physical stimulation (I), compared with tactile stimulation (e.g., rubbing) (C), improve outcome (O)?

4.1.1 | Introduction

Human newborn resuscitation guidelines suggest stimulating newborn infants immediately after birth if they are apneic/not crying or are hypotonic [8, 27]. Expert consensus found in the human literature estimates that approximately 10% of newborns will require and respond to drying and stimulation to help initiate breathing and assist in the transition from intrauterine to extrauterine life [8, 28]. However, despite universal recommendations, almost no information is available on the efficacy of these stimulation methods in any species, including newborn puppies and kittens.

4.1.2 | Consensus on Science

For the critical outcomes of survival *to discharge* and *favorable neurologic outcome*, as well as the important outcome of surrogate markers of perfusion, we identified no studies addressing the question.

For the important outcome of *oxygenation*, we identified 1 observational study in people (very low quality of evidence, downgraded for very serious risk of bias and serious indirectness) [29] and 2 experimental studies (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness and imprecision) that addressed the question [30, 31]. In the observational study, preterm newborn infants displayed a significant increase in SpO_2 after tactile stimulation compared to before (from a median of 61.9%–70.7%, $p < 0.001$), but this was not observed in term newborns [29]. This study lacked a control group without tactile stimulation, such that the effect of the intervention itself cannot be assessed. In 1 experimental lamb study, scratching and rubbing the skin of the lower leg of mature fetal lambs in utero induced sustained spontaneous regular breathing [30]. After the sciatic nerve was cut in these lambs, there was no breathing response to electrical stimulation, scratching, rubbing, or vibration of the skin, demonstrating the apparent role of the peripheral somatic nerve in the afferent pathway of this respiratory reflex. This did not, however, affect oxygenation, as PaO_2 and other parameters remained constant. In one experimental study in rats, maternal rats were observed to hold the head of newborns, clean their nares/mouth, and provide additional assistance or stimulation as needed in the form of licking, biting, pushing, or rolling [31]. Rat pups removed from the mother to prevent cleaning/stimulation developed respiratory distress and cyanosis, though oxygenation was not further assessed.

For the important outcomes of *$PaCO_2$ and hospital length of stay*, we identified no studies addressing the question.

4.1.3 | Treatment Recommendations

In newborn puppies and kittens that require resuscitation, we recommend the use of tactile stimulation (e.g., rubbing, drying) immediately after birth without delaying essential interventions such as PPV (strong recommendation, very low quality of evidence).

4.1.4 | Justification of Treatment Recommendation

While the characteristics and effectiveness of newborn tactile stimulation are rarely described in human or animal literature, it remains one of the most common interventions provided to newborns. Evidence examining the question is scarce and of very low quality, and virtually absent for newborn puppies and kittens, but the preponderance suggests benefit. One additional observational study that was not captured in the original search, likely as it concerned preterm infants and did not address one of the predetermined outcomes, included 245 newborn infants and showed that tactile stimulation significantly reduced the risk for intubation (RR 0.41, 95% confidence interval [CI] 0.20–0.85) [32]. This intervention is of high feasibility and low risk as long as it is executed in a gentle, nontraumatic manner and does not delay the institution of other life-saving interventions (e.g., PPV). Thus, we recommend its routine use immediately after birth.

4.1.5 | Knowledge Gaps

There is no information on the optimal methods and timing of physical stimulation in newborn puppies or kittens, nor on the efficacy of providing such stimulation in these animals.

4.2 | Clear Airway Secretions by Suctioning—NB-09

In newborn dogs and cats that require resuscitation at birth (P), how does clearance of the upper airway by suctioning (I), compared with no clearance (C), improve outcome (O)?

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4.2.1 | Introduction

Aeration of airways and lungs is a central event in the transition from intrauterine to extrauterine life. Historically, in people, oronasopharyngeal suctioning (ONPS) was used to help remove oral and nasal secretions of vigorous newborn infants born through clear amniotic fluid. In addition, endotracheal suctioning (ETS) was recommended in nonvigorous newborn infants born through meconium-stained amniotic fluid [33, 34]. Based on an evolving body of evidence, newborn resuscitation guidelines in people now de-emphasize routine ONPS and recommend against routine ETS but have shifted toward early support of ventilation with PPV [8, 35]. Of note, ETS in newborn infants necessitates endotracheal (ET) intubation. Like infants at birth, newborn puppies and kittens may have either clear or meconium-stained secretions of variable quantity in the upper airways, particularly the nasal passages and oropharynx. Veterinarians have employed a variety of techniques, including the use of bulb syringes or suction catheters, to remove upper airway secretions [16]. This question addresses whether there is a need for routine ONPS or ETS in newborn puppies and kittens.

4.2.2 | Consensus on Science

For the most critical outcome of *favorable neurologic outcome*, we identified 1 clinical trial in newborn infants (very low quality of evidence, downgraded for very serious risk of bias and serious indirectness) [36]. In this study, which included 122 nonvigorous, term newborns born through meconium-stained fluid, ETS did not impact neurodevelopmental outcome at 9 months among the 86 infants still alive at that time. No studies examining this outcome after ONPS were identified.

For the next critical outcome of *survival to discharge*, 4r clinical trials (low quality of evidence, downgraded for serious risk of bias and serious indirectness) and 1 observational study (very low quality of evidence, downgraded for very serious risk of bias, serious indirectness, and imprecision), all in a human healthcare setting, were identified [36–40]. Only one study evaluated ONPS without ETS, a multicenter randomized controlled trial (RCT) including 2514 term newborns, born by vaginal birth or C-section and through meconium-stained amniotic fluid [40]. Nine newborns in the ONPS group and 4 in the control group died (RR 0.8; 95% CI 0.1–1.5). All other studies concerned ETS. The clinical trials demonstrated no significant survival benefit of ETS in nonvigorous newborns born through meconium-stained amniotic fluid [36–38]. Chettri and colleagues reported in their study (n = 61 per study arm) a 16% mortality rate at 9 months in the ETS group versus 20% mortality in the control group (p = 0.82) [36]. Nangia et al. randomized 88 newborns to no suctioning and 88 to ETS, with the mortality being 4.6% and 10.3%, respectively (odds ratio [OR], 0.4; 95% CI 0.12–1.4; $p = 0.14$) [37]. Likewise, Kumar et al. found a similar risk of death in newborns treated with ETS versus those not treated (RR, 1.8; 95% CI 0.6–3.4), with mortalities of 13.6% and 7.5%, respectively [38]. In contrast, 1 small (n = 125), single-center, retrospective observational study published in 1975 showed an association between immediate tracheal suction in infants born through meconium-stained amniotic fluid and a reduction in morbidity and mortality [39]. Seven of 28 newborns that did not receive ETS died, while only 1 of 97 newborns receiving ETS died ($p < 0.001$).

For the important outcome of *complications*, we found 4 clinical trials, 1 of which was in newborn puppies (low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision), 1 observational study in people (very low quality of evidence, downgraded for very serious risk of bias, serious indirectness, and imprecision), and 1 experimental study in lambs (very low quality of evidence, downgraded for very serious risk of bias, serious indirectness, and imprecision), addressing the PICO question [36–38, 41–43]. Most studies reporting this outcome concerned the intervention of ETS. Three clinical trials in newborn infants documented no difference in complication rate in infants born through meconium-stained amniotic fluid regardless of whether ETS was applied or not [36–38]. In an experimental lamb study, Lakshminrusimha et al. evaluated the effects of ETS at birth in asphyxiated newborn lambs with meconium aspiration [42]. Lambs that underwent ETS ($n = 15$) did receive PPV significantly later (146 ± 11 s) compared to animals not undergoing ETS ($n = 14$; 47 ± 3 s, $p < 0.001$) and experienced lower HRs during suctioning, with 3 animals proceeding to CPA. We identified 2 studies that reported complications with nasal suctioning or ONPS. Goericke-Pesch et al. evaluated puppies delivered by C-section, randomly allocated to suction of the nostril by either a 1-mL syringe with suction tip (n = 78) or a suction bulb (n = 93) [41]. A small percentage (6.5%) of animals in which the syringe was used, but none in the suction bulb group, showed minor bleeding from the nostrils. A single observational study including term newborn infants born by C-section through clear amniotic fluid did not identify a higher incidence of bradycardia or apnea associated with ONPS (n = 36) when compared to a control group with no such suctioning (n = 36) [43].

For the important outcome of *increase in HR*, we identified 5 clinical trials in newborn infants that all concerned ONPS (low quality of evidence, downgraded for serious risk of bias and serious indirectness) [44–48]. Waltman et al. examined in a small RCT pilot study (n = 10 per treatment arm) the effects of bulb suctioning in healthy term newborn infants. While a statistically significantly higher HR emerged in newborns without ONPS during the first 20 min after birth (difference, 11 ± 5/min, $p = 0.042$), the HR measurements in both groups remained within normal range [44]. In contrast, Gungor et al. found that in healthy, term newborn infants born through clear amniotic fluid (n = 70 per treatment arm), ONPS led to a significantly higher HR from the third minute after birth onward (131.7 ± 4.4/min) compared to those without ONPS (127.3 ± 6.8/min, $p < 0.001$), although this difference is of uncertain clinical significance [46]. In a follow-up study by the same authors but now including healthy newborns born by elective C-section, ONPS led to a similarly small but statistically significant increase in HR early after birth [45]. Bancalari et al. conducted an RCT including 84 vigorous term newborns delivered by C-section ($n = 42$ per treatment arm) and found a small difference in HR after the first minute after birth in newborns receiving ONPS (148 ± 13/min) versus those that did not (137 ± 25/min, p = 0.02) [47]. In a further RCT including 170 term newborns delivered through clear amniotic fluid, ONPS had no effect on HR [48].

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For the important outcome of *hospital length of stay*, we identified 3 clinical trials in newborn infants (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [36–38]. These studies, all evaluating the effects of ETS, documented no statistically significant differences in hospital length of stay in infants born through meconium-stained amniotic fluid who underwent suctioning compared to those that did not. No studies were identified that evaluated this outcome for ONPS.

4.2.3 | Treatment Recommendations

For newborn puppies and kittens that require resuscitation at birth but are vigorous, we suggest using a clean, dry cloth to carefully remove fluid from around the nostrils and mouth (weak recommendation, expert opinion).

For newborn puppies and kittens that are nonvigorous with excessive oropharyngeal fluid (clear or meconium-stained), we suggest gentle nasal or oropharyngeal suctioning immediately followed by PPV (weak recommendation, expert opinion).

For newborn puppies and kittens that are nonvigorous with excessive oropharyngeal fluid (clear or meconium-stained), we suggest against the routine use of ETS (weak recommendation, very low quality of evidence).

4.2.4 | Justification of Treatment Recommendation

We made the above recommendation on airway suctioning in newborn dogs and cats based on very low quality of evidence and expert opinion, keeping feasibility in mind. There is no doubt that the establishment of a patent airway is a key objective early after birth, as it is essential for aeration of the lungs.

Freeing the newborn puppy or kitten from fetal membranes is the first step if the dam is not able to accomplish this; this step is so obviously benefitial that, to our knowledge, no research has been performed in any species to study the efficacy of this action. Next, the question arises for the rescuer team on whether it is advisable to routinely remove airway fluid by ONPS, ETS, or both, and how the quantity of amniotic fluid, its quality (i.e., clear or meconium stained), and the newborn's strength (i.e., vigorous versus nonvigorous) influence decision-making. We considered these factors when making treatment recommendations.

Fluid in the upper airways is typically cleared naturally and rapidly in vigorous, vocalizing newborns [49]. For this reason, no active suction of the nasopharynx or oropharynx is required in most vigorous newborns, regardless of whether the kitten or puppy is born through clear or meconium-stained amniotic fluid. Standard care in this scenario includes drying and stimulation, as well as removing fluid around the nostrils and mouth with a clean, dry cloth.

We could not identify any evidence in dogs and cats, however, that addresses the topic of airway clearance in newborns, and the recommendations are solely based on expert opinion and studies conducted in a human healthcare setting. The preponderance of studies in term, healthy newborn infants, whether born vaginally or by C-section, did not identify any benefit of ONPS concerning the outcomes we examined [44–48, 50, 51]. In addition, we found relevant evidence addressing outcomes other than the ones we initially defined. An RCT examining respiratory mechanics as primary outcome in human, healthy, term newborns with or without ONPS ($n = 20$ per study arm) showed no significant benefit (or harm) of suctioning [51]. However, studies that evaluated the time until SaO_2 exceeded 92% in vigorous term newborn babies born vaginally or by C-section identified that ONPS delayed the increase in oxygenation [45, 46, 50]. In 2 studies by Gungor et al. that included 280 infants, all newborns reached an SaO_2 of 92% by 6 min after birth with standard care (i.e., stimulation, drying), but none of the newborns in the ONPS groups reached the target within that time frame [45, 46]. A large RCT including more than 2000 newborn infants born through meconium-stained amniotic fluid did not show a higher risk of death or meconium aspiration syndrome if no ONPS was performed at birth [40]. Taken together, there is no evidence that routine suctioning in vigorous newborns born through clear or meconium-stained amniotic fluid is beneficial; however, it might interfere with aeration of lungs. Our recommendation is in line with that of the International Liaison Committee on Resuscitation (ILCOR) that recommends against routine ONPS for vigorous newborn infants with clear or meconium-stained amniotic fluid [8]. We suggest the use of a dry, clean cloth to wipe excessive fluid off the surface of the slightly lowered newborn's face, nostrils, and muzzle, as this will minimally interfere with spontaneous breathing and with aeration of the airways and lungs in these vigorous newborn puppies and kittens. Wiping was a common component of the control group interventions in the studies listed above, alongside stimulation, drying, and warming. In addition, the equivalence of wiping to ONPS is supported by 1 study in people, including 488 vigorous or nonvigorous newborns born by vaginal birth or C-section through clear amniotic fluid [52].

In nonvigorous newborns that are apneic, abnormally breathing, or bradycardic, the focus is on early institution of PPV [8]. The use of ONPS alone in these nonvigorous newborns has not been well studied in people or in veterinary species, with clinical research in people and experimental research focused on the utility of removing airway obstruction by a combination of ONPS and ETS. In the absence of any evidence supporting the benefit of routine use of ONPS alone in nonvigorous newborn animals, the primary concern of this intervention is the associated delay in PPV. However, we also acknowledge that PPV through a large amount of oropharyngeal fluid, especially if thick and meconium stained, might compromise its efficacy. We therefore suggest a gentle, single, short ONPS intervention in nonvigorous newborns in which excessive upper airway fluid is present, followed immediately by PPV. The ONPS can be accomplished with a bulb syringe, a DeLee aspirator, or other aspiration device in a way that avoids pharyngeal and laryngeal injury or exposure to excessive negative airway pressure.

The ILCOR treatment recommendations do not recommend routine ETS for nonvigorous newborns delivered through meconium-stained amniotic fluid, although this might be required in those newborns in which PPV is deemed not effective due to airway obstruction [8]. The lack of any benefit from ETS in

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nonvigorous newborn infants is supported by a number of RCTs and by an experimental study in newborn lambs [36–38, 42, 53]. Direct comparison to newborn puppies and kittens is challenged by the indirectness resulting from their small airway caliber at birth and the differences in practice settings and resources available. In particular, ET intubation—the foundation for effective, safe ETS in people—is challenging in newborn puppies and kittens, and suctioning through a very small endotracheal tube (ETT) appears unfeasible at present. To our knowledge, ETS by direct insertion of a suction catheter into the trachea has not been studied and could lead to significant airway injury and swelling, as well as derecruitment of previously aerated lung. In the absence of convincing benefits of ETS in humans and considering the significant practical challenges and potential harm of ETS in newborn puppies and kittens, we advise against its routine use. However, if an airway obstruction is suspected after PPV is initiated, ET intubation and ETS could be considered if feasible.

4.2.5 | Knowledge Gaps

Currently, there is a critical lack of data in veterinary patients, specifically newborn puppies and kittens, regarding the use of airway clearance methodologies in vigorous or nonvigorous animals, as well as those born through clear or meconium-stained amniotic fluid. Studies that show the effect of ONPS in these populations on short- and long-term survival, the duration of PPV until breathing, and the time until HR normalizes would be important.

4.3 | Clear Airway Secretions by Methods Other than Suctioning—NB-10

In newborn dogs and cats that require resuscitation at birth (P), does clearance of the upper airway by any other method (I), compared with airway clearance with suctioning (C), improve outcome (O)?

4.3.1 | Introduction

Newborn kittens and puppies are born with fluid in the upper airways, particularly in the nasal passages and the oropharynx. Part of the fluid originates from the lungs, which contain a large amount of fluid in utero that is then expelled during the natural birthing process and appears in the upper airways [49]. Additional upper airway fluid might constitute aspirated clear or meconium-stained amniotic fluid. The primary methods to remove fluid from the upper airway are ONPS and ETS (see NB-09), although routine removal of fluid by suctioning is generally not recommended, unless fluid is excessive. This question enquires about the utility of airway clearance modalities other than suctioning, such as gravity-based procedures.

4.3.2 | Consensus on Science

We did not locate any evidence to address the outcomes of favorable neurologic outcome, survival to discharge, oxygenation, $PaCO^2$, increase in HR, and hospital length of stay.

4.3.3 | Treatment Recommendations

We suggest against interventions other than suctioning to clear excessive upper airway fluid in newborn puppies and kittens (weak recommendation, expert opinion).

We recommend against the removal of upper airway fluid in newborn puppies and kittens by swinging (strong recommendation, expert opinion).

4.3.4 | Justification of Treatment Recommendation

When asking this question, we tried to identify and judge the benefits and risks of any methods for the clearance of upper airway fluids in newborn dogs and cats other than airway suctioning. Vigorous newborn puppies or kittens will not require any routine clearance of airway fluid by suctioning, and removal of external fluid with a clean, dry cloth (i.e., wiping) is sufficient (see NB-09). The equivalence of wiping to ONPS in term vigorous or nonvigorous newborns born through clear amniotic fluid is supported by an RCT in people including 488 newborn infants [52]. An alternative to ONPS would be most relevant in nonvigorous newborns with excessive upper airway fluid (clear or meconium-stained) and in those in which an airway obstruction is present, as these constitute circumstances for which we suggest upper airway suctioning (see NB-09). For these circumstances, however, we did not identify any studies that investigated alternatives to ONPS. Historically, exposing the newborn to acceleration and deceleration in a head-down position (i.e., swinging) for airway fluid removal has been recommended in human medicine more than 100 years ago and has been practiced in veterinary medicine [14, 54]. Specifically, a resuscitative strategy in newborn infants that incorporated swinging (i.e., the Schultze method) was recommended in the late 19th century in human neonatal resuscitation for airway clearing and as a mode of artificial ventilation but was abandoned in the 1920s [54]. We strongly recommend against the utilization of swinging due to the primary concern of intracranial hemorrhage, the risk for trauma, the possibility of stomach contents to enter the airway, as well as the significant delay in more effective resuscitative measures such as PPV. The only publication pertaining to the topic is a case report by Grundy et al. in which swinging of a puppy at birth was deemed responsible for subarachnoid bleeding that clinically manifested as seizures [55].

An additional recommendation in the veterinary literature is to lower the head below the body to allow for passive draining of upper airway fluid [16]. This recommendation was based on expert opinion by the authors, and we were unable to find any research pertaining to this practice. We suggest against prioritizing this practice for the clearance of airways in newborn puppies and kittens with excessive fluid or airway obstruction due to the lack of evidence of its efficacy and the potential for delaying PPV in this cohort. If used in conjunction with other airway clearance methods (i.e., suctioning), it should not delay initiation of PPV.

4.3.5 | Knowledge Gaps

There is no prioritized need for research into alternatives to airway suctioning.

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4.4 | Temperature Control at Birth—NB-11

In newborn dogs and cats that require resuscitation at birth (P), how does no temperature control (I), compared with maintenance of normothermia (35°C–37.2°C [95°F–99°F]) (C), improve outcome (O)?

4.4.1 | Introduction

Newborn infants, as well as puppies and kittens, are highly susceptible to hypothermia shortly after birth [56, 57]. Compared to adult dogs and cats, newborns have a greater surface area-to-volume ratio and have high evaporative losses from the skin, predisposing them to excessive heat loss [18]. In addition, they have a limited ability compared to adults to regulate their body temperature due to an inability to shiver and have a very limited capacity for metabolic thermogenesis [18, 58]. A strong association between hypothermia and morbidity and mortality was established in newborn infants, and guidelines recommend taking specific measures to maintain normothermia, though these recommendations have been based on low to moderate quality of evidence and were predominantly generated from studies in preterm infants [8, 9, 59, 60]. We herein examine the question of whether active measures to maintain normothermia should be undertaken in newborn puppies and kittens requiring resuscitation.

4.4.2 | Consensus on Science

Many relevant articles were not captured by the literature search strategy conducted for this PICO question. The published literature in people that pertains to this question has undergone an extensive systematic review and has been summarized in the treatment recommendations by ILCOR. For this reason, we adopted the findings of ILCOR's GRADE evaluation of the human data from the most recent systematic review (2015) and adjusted the quality of evidence by downgrading one step for further indirectness due to population differences [59]. The ILCOR treatment recommendations for management of hypothermia at birth remained unchanged in 2020 as the conclusions from additional studies identified in a scoping review were aligned with the 2015 findings [8].

For the critical outcome of *favorable neurologic outcome*, we identified no studies addressing the question.

For the next critical outcome of *survival to discharge*, the ILCOR systematic review identified 4 clinical trials that were relevant to the outcome (adjusted very low quality of evidence, downgraded for very serious indirectness and serious imprecision) [59, 61–64]. One of these trials that evaluated the effect of temperature control measures versus no such measures found improved survival when newborn infants were warmed [61], while 3 trials showed no effect on this outcome [62–64]. The ILCOR treatment recommendations quoted 36 observational studies relating hypothermia to mortality in newborn infants, and we further identified 1 observational study in newborn puppies (adjusted moderate quality of evidence, downgraded for serious indirectness, upgraded for effect size and dose–effect relationship) [59, 65]. In newborn infants, hypothermia was generally defined as a temperature of <36°C. Taken together, the studies in people indicated that hypothermia at admission to neonatal intensive care units (NICUs) is associated with an increased risk of mortality. Two of the observational studies suggest a dose–response effect on mortality [66, 67]. Laptook et al. evaluated 5277 very-low-birth-weight infants and found that 47% had a body temperature <36°C on admission to NICU; temperature was inversely related to mortality, with a 28% increase in mortality per 1°C decrease in body temperature [66]. Mullany et al. evaluated 23,240 infants in Nepal and found that adjusted risk for mortality increased 80% (95% CI, 63%–100%) per 1°C decrease in body temperature and that mortality was strongly associated with temperatures <35°C (95°F) [67]. In an observational study of newborn puppies (n = 340), median rectal temperature in the first 8 h after birth was 33.5°C (IQR, 3.2) and tended to be associated with mortality (p = 0.058) [65].

For the important outcome of *complications* of hypothermia, the ILCOR treatment recommendations specifically addressed respiratory issues, sepsis, and hypoglycemia [59]. For *respiratory problems*, 1 clinical trial including 801 preterm infants found a reduction in pulmonary hemorrhage if temperature was ameliorated by occlusive wrap application immediately after birth (adjusted very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [62]. The ILCOR statement further identified 16 observational studies in newborn infants that examined the impact of accidental hypothermia on respiratory outcomes (adjusted very low quality of evidence, downgraded for serious indirectness) [59]. Most of these studies, which predominantly include preterm infants, suggested a positive association between normalization of body temperature at admission to NICU and respiratory outcomes such as the need for and the duration of oxygen supplementation or mechanical ventilation, or the occurrence of respiratory distress syndrome. Only 2 studies identified no association between temperature and respiratory outcomes [66, 68]. For the complication of *sepsis*, three observational studies were identified that are relevant to this outcome (adjusted very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) [59]. Two of these studies demonstrated an association between hypothermia at NICU admission and sepsis, while one observational study found no association [66, 67, 69].

In animals, we identified no clinical studies that examined the effect of hypothermia on complications such as respiratory, cardiovascular, or infectious disease. However, we identified three experimental animal studies in kittens, piglets, and calves that addressed the PICO question (very low quality of evidence, downgraded for serious risk of bias and serious indirectness) [70–72]. In a study of 12-day-old kittens, oxygen consumption, CO_2 production, O_2 saturation, and systemic arterial pressure during hypoxia did not differ between kittens with and without temperature control; however, cardiac index and HR were greater, and systemic vascular resistance was lower during hypoxia in kittens with temperature control compared to those without [70]. There was overall concern for increased cardiac workload during hypothermia. In a study evaluating calves during the first 24 h after birth, calves provided with radiant warming exhibited increased oxygen saturation and dynamic lung compliance

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compared to controls without any temperature support [71]. In an additional study in newborn piglets (12–72 h old), hypothermia (34.7°C–35.2°C, $n = 11$) after whole-body hypoxia did not ameliorate organ injuries/dysfunction [72]. Moreover, significantly more hypothermic piglets required dopamine to maintain normotension during resuscitation than normothermic piglets.

For the important outcome of *hypoglycemia*, we identified no clinical trial or any animal study that addressed the PICO question. However, ILCOR listed seven observational studies in newborn infants that demonstrated a significant association between hypothermia at birth and hypoglycemia (adjusted very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) [59]. In 2 of these studies, implementation of temperature control was associated with better glycemic control [73, 74].

We identified no studies addressing the PICO question for the important outcome of *hospital length of stay*.

4.4.3 | Treatment Recommendations

In newborn puppies and kittens that require resuscitation, we recommend maintenance of normothermia (35°C–37.2°C [95°F–99°F]) compared to no temperature control (strong recommendation, moderate quality of evidence).

4.4.4 | Justification of Treatment Recommendation

Dozens of human studies conducted over decades have found admission temperature of newborn non-asphyxiated infants to be a strong predictor of mortality and morbidity at all gestational ages, and human guidelines strongly recommend maintenance of normothermia for newborns undergoing resuscitation in the delivery room, based on moderate-quality evidence. While little evidence was found in newborn puppies and kittens, the large negative impact of hypothermia on survival in newborn infants and its strong correlation with poor outcome in that species yield moderate quality of evidence supporting the provision of active temperature control to newborn puppies and kittens. In addition, physiologic similarities across species suggest translatability of this evidence to newborn puppies and kittens requiring resuscitation at birth. Therefore, we strongly recommend temperature control in this population.

While a specific temperature target (i.e., 36.5°C–37.5°C [97.7°F–99.5°F]) is recommended in newborn infants, and a core temperature of <36°C (<96.8°F) is considered hypothermia [59], the exact temperature at which newborn puppies and kittens should be maintained is less well supported by scientific data. In newborn puppies, the rectal temperature at birth was 33.7 ± 1.4°C after C-section and 33.1 ± 3.1°C with eutocia, and 35.1 ± 1.8°C and 33.2 ± 4.7°C, respectively, after 1 h with the dam [75]. It is not clear to what extent those measurements represent core temperature, however. Moreover, this surprisingly low temperature might be protective from hypoxic injury as it will reduce the metabolic need for oxygen during the immediate post-parturient hypoxemic period. In a different study, rectal temperature in newborn puppies within the first 8 h after birth was reported to be 33.5°C (range, 32.0°C–35.2°C), which increased to 36.6°C (35.9°C–37.2°C) after 24 h; temperature was also positively associated with birth weight [65]. Normal body temperature in neonatal puppies and kittens in the first week of life has been reported as 35.0°C–37.2°C (95°F–99°F) [18]. Thus, we consider a rectal temperature in that range to be a reasonable target for maintenance of normothermia. There is no evidence to recommend one temperature control methodology over another, and we recommend using a method of temperature management that does not interfere with other resuscitation measures.

4.4.5 | Knowledge Gaps

The optimal temperature target for newborn puppies and kittens undergoing resuscitation is unknown, and no methodologies to reach and maintain temperature targets have been systematically evaluated in these species.

4.5 | Methods to Measure HR at Birth—NB-04

In newborn dogs and cats without CPA that require resuscitation (P), how does the use of electrocardiography (ECG) (I), compared with any other HR assessment (e.g., pulse oximetry, apex beat palpation, auscultation) (C), improve outcome (O)?

4.5.1 | Introduction

HR is a critically important diagnostic and prognostic metric in newborns, and an abnormal HR dictates the need for vital interventions during newborn resuscitation in infants and small animals [8]. It is essential, therefore, to accurately and rapidly determine a newborn's HR. While auscultation has traditionally been used as the preferred method for HR determination in newborn infants in the delivery room, pulse oximetry has also been utilized as an adjunctive tool [59]. However, given inaccuracies with auscultation, pulse palpation, and pulse oximetry in newborns, ECG monitoring has more recently emerged as the preferred method for assessing HR in human guidelines [8]. As in people, escalation of care during resuscitation of newborn puppies and kittens is guided by HR. This question addresses how to best assess the HR in these species immediately after birth.

4.5.2 | Consensus on Science

For the most critical outcome of *favorable neurologic outcome*, we identified no studies addressing the PICO question.

For the next most critical outcome of *survival to discharge*, we found 1 observational study investigating the use of ECG monitoring in newborn infants (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) [76]. This study included newborns requiring PPV in the delivery room. A retrospective cohort (calendar year 2015) of 263 newborns monitored with standard practice of auscultation and pulse oximetry was compared to a prospective cohort (calendar year 2017) of 369 newborns in which HR was determined with

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standard practice plus ECG. There was no difference in mortality when an ECG was used in addition to standard practice (8.4%), compared to standard practice alone (8.8%; $p = 0.879$).

For the important outcome of *detection of accurate HR*, we identified 1 clinical trial (low quality of evidence, downgraded for serious risk of bias, and serious indirectness) [77], 8observational studies (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) [78–85], and 2 experimental studies (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) [86, 87] that addressed the PICO question. Observational studies in people have demonstrated that HR established by auscultation or palpation of the umbilical cord pulse may be inaccurate or unreliable [78, 82]. In these studies, the physical examination techniques generally underestimated the ECG-reported HR by approximately 5–10/min. Kamlin et al. also showed that healthcare providers could not reliably palpate the umbilical cord pulse in live newborns [82]. For these reasons, pulse oximetry and ECG were considered as additional modalities to evaluate HR. Pulse oximetry was found to underestimate the HR when compared to ECG [77, 80, 85]. Importantly, 2 observational studies in human newborns demonstrated that pulse oximetry failed to detect an HR in bradycardic infants 10% and 69% of the time, respectively [80, 88].

Other methods of HR detection have been investigated as well. An audible Doppler ultrasound probe placed over the sternum in stable, term newborn infants resulted in HR values equivalent to those determined by ECG in 2 observational studies ($r = 0.94$ to 0.98, respectively) [79, 84], but not in a third ($r = 0.54$) in newborn infants delivered by C-section [81]. In a single experimental study using a porcine newborn asphyxia model, Doppler HR was comparable to ECG HR (mean difference: 1.5/min; 95% limits of agreement: −16 to 19/min), but signal quality was influenced by movement, PPV, lower HR, and blood flow [86].

The concern remains that a detectable ECG reading does not always indicate the presence of a heartbeat. An experimental newborn piglet model showed that in cases of pulseless electrical activity, ECG displayed an HR despite the absence of carotid blood flow [87]. In addition, most of these observational studies in people are complicated by the lack of a gold standard for measurement of HR because methods are either compared to each other or ECG is considered the gold standard.

For the important outcome of *time to detection of accurate HR*, we found 1 clinical trial (low quality of evidence, downgraded for serious risk of bias, and serious indirectness) [77] and 10 observational studies (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) [78–81, 83–85, 89–91] that addressed the question. One clinical trial and 5 observational studies in newborn infants demonstrated that ECG can display a reliable HR faster than pulse oximetry [77, 78, 80, 83, 85, 90]. Reported median or mean time intervals from birth to reliable HR measurement using ECG or pulse oximeter ranged from 24 to 82 s and 48 to 122 s, respectively. Compared to pulse oximetry, ECG was more likely to detect a newborn's HR during the first minute of life (56% pulse oximetry vs. 96% ECG) [83]. Despite evidence of rapid, reliable HR detection by ECG, a human clinical trial revealed no difference in the timing of clinical interventions with or without a displayed ECG [77]. Murphy et al. reported that the median (IQR) HR acquisition time was shorter by auscultation (14 s [IQR 8]) than it was using ECG (24 s [19–39]) or pulse oximeter (48 s [36–48], $p < 0.001$) [78]. One observational study in newborn infants showed that portable Doppler ultrasound was significantly faster for acquiring an audible HR (76 s, IQR 40) compared to ECG (97 s, IQR 44), though the time difference was considered clinically negligible [81].

For the important outcome of *length of hospital stay*, we found one observational study in newborn infants (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) [76]. In this study of newborns requiring PPV in the delivery room, there was no difference in hospitalization length between a retrospective cohort monitored with auscultation and pulse oximetry and a prospective cohort that also included ECG.

4.5.3 | Treatment Recommendations

In newborn puppies and kittens requiring resuscitation, we suggest estimating the HR using any of the following techniques: apex beat palpation, cardiac auscultation, ECG, or a Doppler ultrasound probe applied to the thorax (weak recommendation, very low quality of evidence).

In newborn dogs and cats requiring resuscitation, we recommend against the use of pulse oximetry as the only method to evaluate the HR (strong recommendation, very low quality of evidence).

4.5.4 | Justification of Treatment Recommendation

Evidence is lacking in dogs and cats regarding the best method to assess HR in newborns requiring resuscitation, and our recommendations are based on indirect deduction from studies in newborn infants and considerations of feasibility in the veterinary context. Human data generally support the use of ECG in newborns immediately after birth, with evidence suggesting acceptable accuracy and time to detection of an HR. While earlier detection of an accurate HR confers theoretical benefit, the difference in obtained HR across techniques is small, and there is no evidence that HR detection by ECG improves initiation of resuscitation interventions, neurologic outcome, or mortality. Furthermore, we have concerns about the limited scalability of ECG measurement and the effort to apply an ECG to each distressed newborn, given a litter size of five puppies and four kittens on average [92, 93]. However, if an individual newborn puppy or kitten is not responding to initial resuscitation measures and escalation of care is required, continuous HR monitoring by ECG is reasonable. Adhesive ECG electrodes are preferred over ECG clips to mitigate the risk of skin injury.

As auscultation is used frequently in clinical settings in dogs and cats, we believe that this monitoring method is a reasonable alternative to ECG, with no known harm in newborn puppies or kittens and with feasibility across a wide range of practice settings. The above evidence suggests, however, a tendency toward underestimation of HR by auscultation in the human healthcare setting [78, 82].

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Regarding other methods of HR monitoring, portable Doppler ultrasound has shown good correlation with ECG in newborn infants, though data are limited, equipment is less accessible in veterinary medicine, and additional training would likely be required. Due to concerns regarding the accuracy of pulse oximetry in human newborns and the time required to obtain HRs by pulse oximetry, we recommend against the use of a pulse oximeter as a first-line monitor for HR determination in newborn puppies and kittens.

4.5.5 | Knowledge Gaps

Studies regarding the best approach to determine HR in newborn puppies and kittens during resuscitation are lacking. It would be important to conduct studies determining the reliability, feasibility, and time until the first accurate HR measurement when utilizing physical examination modalities (i.e., auscultation and apex beat palpation), Doppler ultrasound, and ECG in these populations. In addition, it would be important to determine whether there is any impact of the use of various HR monitoring modalities on time to initiation of critical interventions (e.g., PPV) and survival.

4.6 | Initiation of Respiratory Support—NB-01

In newborn puppies and kittens that require resuscitation (with or without CPA) (P), how does initiating PPV at any other HR target (I), compared with HR less than 100/min (C), improve outcome (O)?

4.6.1 | Introduction

HR is an important vital sign used to determine both the need for and the response to resuscitation measures in newborn infants at birth [8]. Bradycardia in newborns results from hypoxia through a combination of vagal and nonvagal mechanisms [94]. Transitional newborn puppies and kittens that both remain severely bradycardic and are not adequately breathing despite initial resuscitation steps will require PPV to support clearance of lung fluid, establishment of functional residual capacity, and improvement of oxygenation and ventilation [49]. The current recommendation in human newborn resuscitation is based on expert opinion and is to institute PPV when HR is <100/min or the newborn is gasping or apneic [8]. On the other hand, PPV adds technical complexity to the resuscitation procedure and can be challenging in dogs and cats because they are multiparous species, with the potential for several newborns requiring resuscitation concurrently. An HR cutoff that is too high might unnecessarily divert resuscitation efforts from other newborns in need, while a cutoff that is too low could delay administration of critical PPV and negatively impact the outcome.

4.6.2 | Consensus on Science

We found no relevant evidence addressing this PICO question for any of the outcomes.

4.6.3 | Treatment Recommendations

We recommend initiating PPV in nonvigorous newborn puppies and kittens with cleared upper airways that are bradycardic (strong recommendation, expert opinion).

We suggest using an HR below 120/min as the threshold for initiating PPV in nonvigorous newborn puppies and kittens with cleared upper airways (weak recommendation, expert opinion).

We recommend starting PPV as early as possible in nonvigorous newborn puppies and kittens that are gasping or are apneic, regardless of the HR (strong recommendation, expert opinion).

4.6.4 | Justification of Treatment Recommendation

All newborns are expected to experience hypoxia during transition. In newborn full-term infants, the median initial SpO_2 value at 1 min after birth was found to be 65% and the majority of newborns did not surpass an SpO_2 of >90% until 10 min after birth [95]. Consequently, a low HR is commonly present immediately after birth. In newborn infants, the average HR 2 s after birth was around 120/min and highly variable, but increased to 149 ± 33/min within the first 40 s of birth [96]. In newborn puppies at birth (n = 94), Groppetti et al. reported an average HR of 129 ± 50/min that increases to 210 ± 21/min over the first 24 h [97]. Apgar scores developed for puppies indicate an HR of at least 180/min as normal; however, the first Apgar scores are typically taken within the first 5 min and not immediately after birth [98, 99]. Thus, we believe that a low HR immediately after birth is of little concern if the newborn puppy or kitten is vigorous (i.e., breathing, crying, and with good muscle tone), and the HR is expected to increase markedly over the next 1–2 min. However, in animals that are nonvigorous (i.e., low or absent muscle tone, apneic, or gasping), a low HR indicates the need for PPV as early as possible within the first minute after birth. As we were unable to identify any evidence to support a specific HR cutoff for initiation of PPV, we decided, based on the high normal HR in fully transitioned puppies or kittens, to set the HR threshold at 120/min. Regardless of HR, we acknowledge that the delivery of effective ventilation is a critical support measure for animals with inadequate transition. We therefore recommend PPV be initiated within the first minute after birth in apneic or gasping newborns, independent of the HR, if clearing the airway and tactile stimulation do not immediately lead to a response. With effective PPV, a gradual increase in HR over 15–60 s may be expected [100].

4.6.5 | Knowledge Gaps

The HR below which to institute PPV in newborn puppies and kittens with hypoxia-related bradycardia is not known but is difficult to study as it likely changes with the time that elapsed since birth. Thus, it would be first important to fully describe the time course of HR change in normally transitioning puppies and kittens from the moment of birth and over the first few minutes, ideally capturing these HRs in 10-s intervals. In addition, the temporal course of HR in response to early PPV in newborn

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puppies and kittens and its impact on outcome have not been described.

4.7 | PPV Technique—NB-06

In newborn dogs and cats that require resuscitation with PPV (P), how does the administration of longer inspiratory times, higher inflation pressures, and positive end-expiratory pressure (PEEP) (I), compared with an inspiratory time of 1 s and a peak inspiratory pressure (PIP) of 20 cm H_2O, affect outcome?

4.7.1 | Introduction

The optimal combination of inflation pressures and times to produce adequate expiratory tidal volumes during initial resuscitation in newborn puppies and kittens has not been determined. While resuscitation guidelines for adult dogs and cats recommend targeting an inspiratory time of 1 s at an inspiratory pressure adequate to produce a visible chest rise, it is unknown whether these recommendations are appropriate for newborn puppies and kittens in transition from intra- to extrauterine life [11]. We expect that the appropriate ventilation strategy for newborns with apnea, respiratory distress, or bradycardia (i.e., those requiring PPV) may differ from the strategy in adults, as newborns have fluid-filled lungs and have yet to inhale adequate gas to generate functional residual capacity.

4.7.2 | Consensus on Science

For the most critical outcome of *survival to discharge*, we identified 3 clinical trials (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness), all in preterm infants, that addressed the PICO question [101–103]. In the Sustained Aeration for Infant Lungs ("SAIL") study of 426 extremely preterm infants by Kirpalani et al., newborns making inadequate breathing efforts or with an HR of <100/min were randomized to either standard care or a noninvasive PPV strategy with sustained inflation (SI) of 20 cm H_2O for 15 s (repeated once at 25 cm H_2O if inadequate response) [101]. The SI strategy showed no survival difference compared to standard care; however, this study was discontinued before reaching its predetermined enrollment target due to the suggestion of harm (early death) in the SI group. Jiravisitkul et al. studied 81 preterm infants at birth and compared the effects of SI versus standard resuscitation; as a secondary outcome, there was no difference in survival between the two groups [102]. Finally, Lista et al. prospectively studied the impact of SI on 89 preterm infants with respiratory distress at birth compared to a historical control group of 119 preterm infants treated with standard care. No survival difference was noted between the SI group and the standard care group [103]. Thus, no study identified a survival benefit to SI compared to routine PPV management in preterm human infants requiring resuscitation.

For the critical outcome of *favorable neurologic outcome*, no studies were identified that addressed the PICO question.

For the critical outcome of *oxygenation*, we identified 1 CT (very low quality of evidence, downgraded for very serious indirectness and imprecision) that addressed the PICO question [102]. Jiravisitkul et al. compared the effects of SI versus standard resuscitation on physiologic responses in 81 preterm human infants during resuscitation and found no difference in SpO_2 between those treated with SI and those treated with standard resuscitation measures [102]. We identified 1 observational study (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) that addressed the PICO question [104]. Van Vonderen et al. evaluated the clinical effect of an initial SI of 10 s at an airway pressure of 25 cm H_2O in 70 preterm infants at birth and found SpO_2 to be no different when infants were treated with SI compared to standard care [104]. We identified 4 experimental studies (very low quality of evidence, downgraded for very serious indirectness, imprecision, and inconsistency), all in lambs, that addressed the PICO question [105–108]. Tingay et al. studied 109 steroid-exposed, preterm lambs and found no difference in oxygenation using lung recruitment strategies (SI at 35 cm H_2O to effect or a 3-min dynamic stepwise PEEP strategy) compared to no recruitment maneuver (PPV with 7 mL/kg tidal volume at PEEP 8 cm H_2O) at birth [105]. Klingenberg et al. studied 18 near-term lambs delivered by C-section and found improved PaO_2 with a 30-s SI compared to lambs not treated with SI (conventional ventilation or 5 inflations of 3 s duration with 1-min expiratory times; all peak inflation pressures 35 cm H_2O, all PEEP 5 cm H_2O, all FiO_2 0.21) [106]. Tingay et al. studied 24 preterm lambs and found that a 20 s SI at 40 cm H_2O improved oxygenation compared to a gradual increase in tidal volume over 5 min; however, the tested SI strategy conferred no benefit when compared to consistent PPV with 7 mL/kg tidal volumes. PEEP was identical (5 cm H_2O) across the 3 groups [107]. Finally, Probyn et al. investigated the effects of variable degrees of PEEP during transitional resuscitation of 19 extremely preterm lambs and found improved oxygenation when 4, 8, or 12 cm H_2O of PEEP were applied compared to no PEEP; however, all 4 lambs exposed to a PEEP of 12 cm H_2O experienced pneumothorax and died during the experiment, while no lambs assigned to 0, 4, or 8 cm H_2O PEEP died or experienced pneumothorax [108].

For the important outcome of *$PaCO_2$*, we identified 3 experimental studies (very low quality of evidence, downgraded for very serious indirectness and imprecision), all in transitional lambs, that addressed the PICO question [106–108]. All these studies, with their interventions already detailed above in the oxygenation outcome section, found no effect of SI or PEEP on $PaCO_2$.

For the important outcome of *hospital length of stay*, we identified 1 clinical trial (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) that addressed the PICO question [103]. Lista et al. prospectively studied 89 preterm infants with respiratory distress at birth treated with SI and compared their outcome to a historical control group of 119 preterm infants treated with standard resuscitation care (see further details above, under survival to discharge outcome). No difference was found between the SI group and the historical control group in length of hospital stay.

For the important outcome of *increase in HR*, we identified 2 clinical trials (very low quality of evidence, downgraded for very serious indirectness and inconsistency), both in preterm infants,

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that addressed the PICO question [101, 102]. Details of both studies are listed above, in the survival to discharge outcome. The SAIL study of 426 extremely preterm infants reports that HR was lower (worse) in infants treated with SI, with an adjusted relative risk increase of 24.7% (95% CI 12%–37.5%; $p < 0.001$) for an HR of <60/min when treated with SI [101]. Jiravisitkul et al. found no difference in HR for infants treated with SI versus without [102]. We identified 1 experimental study (low quality of evidence, downgraded for serious indirectness and imprecision, upgraded for large effect) in near-term, near-asphyxiated lambs delivered by C-section that addressed the PICO question [106]. Details of the ventilatory strategies across treatment groups are provided above in the oxygenation outcome section. Klingenberg et al. found that lambs treated at birth with 30 s of SI experienced a faster increase in HR to >120/minute (median 8 s [IQR 6]) compared to lambs exposed to five inflations of 3 s each (median 38 s [IQR 114]) or those treated with standard care of 0.5s inflations at a rate of 60/min (median 64 s [IQR 75]; $p < 0.05$) [106].

4.7.3 | Treatment Recommendations

In newborn puppies and kittens that require resuscitation with PPV, we suggest administering PPV with an inspiratory time of 1 s and a PIP of 20–25 cm H_2O (weak recommendation, very low quality of evidence).

In newborn puppies and kittens that require resuscitation with PPV, we suggest applying at least 4 and no more than 8 cm H_2O of PEEP (weak recommendation, very low quality of evidence).

In newborn puppies and kittens with bradycardia, cyanosis, or inadequate breathing efforts that persist despite 30–60 s of standard PPV using 1 s inspiratory time at a PIP of 20–25 cm H_2O, we suggest giving a single 30 s SI at 30–35 cm H_2O, followed by continued standard PPV if indicated (weak recommendation, low quality of evidence).

4.7.4 | Justification of Treatment Recommendation

No evidence in either target species was available to inform our recommendations regarding ventilatory strategy in newborn puppies and kittens requiring PPV at birth. The evidence available did not suggest a survival or neurologic functional benefit with SI in newborns; however, all clinical trials and many experimental studies were conducted in extremely preterm newborn infants or lambs whose pulmonary tissues are underdeveloped compared to the target population of full-term newborn puppies and kittens. While no studies evaluating neurologic outcome were identified, two studies in preterm infants reported no difference in the incidence of intraventricular hemorrhage when SI was applied in the delivery room versus standard resuscitation [109, 110]. The relevance of intraventricular hemorrhage as a complication of ventilatory strategy in full-term newborn puppies and kittens, however, is unknown. One study showed marked benefit of 30 s of SI at 35 cm H_2O on oxygenation and HR in the most direct population studied: near-asphyxiated, near-term lambs delivered by C-section in an experimental setting [106]. No study found clear harm associated with SI or with PEEP at 4–8 cm H_2O in newborns with inadequate breathing efforts. Finally, guidelines for resuscitation of newborn infants recommend that standard PPV be used routinely [8, 9]. Neither of these guidelines makes specific recommendations for SI or PEEP in full-term infants requiring resuscitation due to a lack of evidence in that patient cohort [8, 9]. Unfortunately, the dedicated respiratory support equipment available in the human delivery room and in an experimental setting, such as airway manometers and newborn face masks with integrated PEEP valves, is not widely available in the delivery areas of most veterinary clinics. Lack of this specialized equipment to ensure adequate patient care and to limit harm due to very high airway pressures limits the applicability of these techniques to newborn puppies and kittens. The indirectness (and some inconsistency) of the identified evidence, in combination with the technical challenges of accomplishing precise airway pressure measurements in newborn puppies and kittens, limits our ability to create a strong recommendation for a specific airway inflation pressure and PEEP value.

4.7.5 | Knowledge Gaps

Whether full- or near-term newborn puppies and kittens that require resuscitation with PPV would benefit from augmented ventilatory strategies (e.g., application of PEEP, SI) is unknown. Considering the potential benefits to oxygenation and HR in this setting, answering this question with clinical trial(s) in target species is considered a high-priority knowledge gap. Development of equipment to measure airway pressures and provide PEEP in newborn puppies and kittens undergoing noninvasive PPV, such as purpose-designed face masks, should be considered.

4.8 | Reversals—NB-20

In newborn dogs and cats that require resuscitation after Cesarean birth (with or without CPA) (P), how does no administration of antagonists (e.g., naloxone) to sedatives given to the dam (I), compared with parenteral administration of antagonists (C), improve outcome (O)?

4.8.1 | Introduction

Perioperative analgesia is important for animals undergoing C-sections to reduce the requirement of induction and maintenance doses of cardiovascular-depressing general anesthetics, to allow postoperative interaction with the offspring, and on animal welfare grounds. However, the vast majority of anesthetics are expected to cross the placental barrier, are taken up into the fetal circulation, and exert a pharmacological effect on the fetus [111]. This PICO question aims to determine whether reversal drugs should be administered to newborn puppies and kittens requiring resuscitation at birth after intrauterine exposure to opioids, α2-adrenoceptor agonists, or benzodiazepines.

4.8.2 | Consensus on Science

For the critical outcomes of *favorable neurologic outcome* and *survival to discharge*, and the important outcomes of *hospital length of stay* and *histopathologic or other surrogate injury*, we

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identified no studies addressing the question of exposure to any opioid, α_2-adrenoceptor agonist, or benzodiazepine.

For the important outcome of *respiration ($PaCO_2$ and oxygenation, combined)*, we identified 7 clinical trials (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) [112–118] and 1 observational study in newborn infants (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) that addressed the PICO question [119]. All studies evaluated the reversal of opioids using naloxone, and none explored the use of benzodiazepine or α_2-adrenoceptor antagonists. All seven clinical trials, all in newborn infants, were conducted shortly after naloxone was released on the market in the early 1970s; they were generally small, with 289 subjects enrolled across all studies, and while patient allocation was randomized, the authors provided no indication of concealment of group allocation or blinding. In addition, the studies excluded newborns with the very population characteristics that this question is asking for (i.e., newborns born by C-section requiring resuscitation) and only included term infants that were born vaginally and were vigorous at birth. The majority of the studies showed that naloxone administered in the first minute after birth reduced $EtCO_2$ or $PaCO_2$, increased minute ventilation, or affected other measures of alveolar ventilation, suggesting increased ventilatory function [112, 114–118], with only one study showing no such effect [113]. However, metrics of ventilation in these studies were within normal limits reported for newborns, even without naloxone. Only one study evaluated oxygenation and found no effect of naloxone [114]. Naloxone doses ranged from 0.01 to 0.04 mg/kg, and all were injected into the umbilical vein, except in 1 study where a much higher dose (0.2 mg/kg) was administered IM [117]. Infants receiving IM naloxone displayed greater CO_2 elimination and alveolar ventilation for 48 h compared to controls that did not receive naloxone.

The observational study involved 670 newborn infants born by vaginal birth, where the mother received an opioid during labor. It compared the frequency and effect of naloxone administration prior to an internal guideline change that recommended against the routine administration of naloxone (i.e., retrospective cohort) with those after the release of that guideline (prospective cohort) [119]. Of 236 retrospective deliveries, 26 (11%) received naloxone, but only 1 (0.2%) of 434 deliveries in the prospective group received naloxone. In the latter group, no increase in the incidence of respiratory symptoms was noted ($p = 0.85$), and none of the infants required resuscitation.

None of the identified studies contained information regarding the administration of reversal agents for benzodiazepines or α_2-adrenoceptor antagonists.

4.8.3 | Treatment Recommendations

In newborn puppies and kittens that require resuscitation after a C-section for which the dam was administered an opioid, α_2-adrenoceptor agonist, or benzodiazepine, we recommend administration of the appropriate reversal drug (strong recommendation, very low quality of evidence).

In newborn puppies and kittens that are vigorous at birth and in which the dam was administered an opioid, α_2-adrenoceptor agonist, or benzodiazepine, there is insufficient evidence to suggest for or against the routine administration of reversal drugs (weak recommendation, very low quality of evidence).

4.8.4 | Justification of Treatment Recommendation

Medications that cross the blood–brain barrier, including most centrally acting sedatives and analgesics, are expected to cross the placental barrier. The extent and speed by which placental transfer occurs are influenced by compound properties such as molecular weight, lipid solubility, and degrees of ionization and protein binding, with highly lipid-soluble, less protein-bound drugs transferring more readily [111]. Analgesics and sedatives (e.g., opioids, α_2-adrenoceptor agonists, benzodiazepines) that are used during C-sections widely vary regarding these properties [120, 121]. Thus, specific opioids or other analgesics and sedatives administered to the dam may variably impact newborn kittens and puppies.

We did not identify any studies that directly address the PICO question, with population indirectness being the most severe concern. The studies cited in the consensus on science statement all examined naloxone administration in the first hour after birth and included only newborn infants who were vigorous, with ventilatory parameters within normal range and all surviving without receiving any resuscitative measures. Thus, there is no evidence to suggest a difference in the effectiveness of standard resuscitative measures, including HR-directed provision of ventilatory support with PPV, when naloxone is or is not administered. In fact, the observational study suggested that a more restrictive approach to naloxone administration to infants whose mothers received an opioid during labor may not worsen newborn outcomes [119]. In addition, naloxone alone did not alleviate asphyxiation-induced respiratory depression unrelated to exogenous opioids, contrary to what was speculated earlier [122, 123]. Furthermore, there is experimental evidence in animals, albeit limited, to suggest potential harm of naloxone administration to newborns, including endogenous epinephrine release and sustained hyperalgesia [124, 125]. Considering this information, human guidelines recommend since 2010 against the initial use of naloxone in newborns with respiratory depression and instead prioritize early effective ventilation and airway support [126]. We decided to recommend the use of naloxone in nonvigorous newborn puppies and kittens after C-section if the dam received opioids during the perioperative period. This is in part based on the small but consistently positive effect of naloxone on quantitative measurements of ventilation in opioid-exposed newborn infants. Additionally, the target population (newborn puppies and kittens that require resuscitation after C-section) is very different in species, degree of illness, and delivery method compared to the populations studied in the identified evidence. Despite the lack of direct evidence, we consider it reasonable to believe that the potential for more pronounced benefit of naloxone is realistic in newborn puppies and kittens that are nonvigorous and require PPV, and that harm is minimal. In the resource-restricted environment of veterinary medicine, we therefore recommend administration of naloxone in newborns requiring resuscitation after C-section

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but emphasize that such administration should not compromise other immediately effective resuscitation measures such as PPV, oxygen supplementation, and chest compressions as applicable.

There is very limited evidence to determine the risk–benefit ratio of routine reversal of α_2-adrenoceptor agonists or benzodiazepines, and none of the studies identified in the initial search regarding these drugs qualified to be included in the GRADE process because they are all studies without control groups (i.e., case reports or case series). For the use of benzodiazepine antagonists, we found three case reports in newborn infants that pertain to the topic [127–129]. The lack of research inquiring into these drugs might be related to the fact that periparturient diazepam is generally not recommended in people, as floppy baby syndrome, lethargy, and apnea after delivery have been described [130]. The case reports, in which diazepam was administered in a variety of special circumstances, demonstrated the risk for severe and protracted sedation and apnea in newborn infants, with clinical signs readily reversed with flumazenil administration [127–129]. In addition, Mandelli et al. described extensive placental transfer of diazepam and a long elimination half-life of 31 ± 2 h in newborn infants, indicative of the newborn infant's limited capacity to eliminate the drug [131]. We were unable to locate any reports on newborn puppies and kittens. Despite this uncertainty, we recommend administering flumazenil to nonvigorous newborn puppies and kittens born after C-section if the dam received a benzodiazepine.

For the use of α_2-adrenoceptor antagonists, we identified two observational studies that pertain to the topic but that did not meet inclusion criteria for the formal evidence evaluation as the study designs did not involve control groups [132, 133]. De Cramer et al. retrospectively evaluated a specific perioperative management protocol for C-sections in dogs that included medetomidine (7 μg/kg IV) for premedication [132]. The study involved 2232 puppies from 292 C-sections. Atipamezole was administered to all puppies (50 μg/kg SQ) immediately after delivery, regardless of the need for resuscitation, and to the bitches (20 μg/kg IV) immediately after surgery. Since all of the puppies received atipamezole, it was not possible to evaluate whether there was an outcome difference between neonates receiving or not receiving an α_2-adrenoceptor antagonist. However, this routine administration of atipamezole led to survival rates similar to other anesthetic protocols, not including medetomidine [134]. Survival varied depending on breed from 94% to 98% at birth and from 87% to 92% at 7 days. In a second observational study of dogs, also without a control group, Groppetti and colleagues described the use of preoperative administration of dexmedetomidine (2 μg/kg IV) in nine bitches undergoing C-section [133]. Puppies would only receive atipamezole if resuscitation efforts of >5 min were required. Of the 54 puppies born, 78% were vigorous at birth and none required atipamezole administration. Thus, there is no convincing evidence to suggest the need for routine administration of atipamezole to newborns when the dam received a small dose of medetomidine or dexmedetomidine for premedication, but there is also no evidence of harm. For the same pragmatic reason as noted for naloxone, and to form a single uniform guideline across all reversal drugs, we decided to recommend the administration of atipamezole to nonvigorous newborns after C-section if the dam received an α_2-adrenoceptor agonist for premedication.

Suggested dosing and routes for administration of reversal medications reflect those used in the above studies or are based on expert opinion and pharmacokinetic considerations. For naloxone, 10–40 μg/kg should be given preferentially IV, with IM and SQ also described, or a higher dose (e.g., 100 μg/newborn puppy or kitten) for sublingual transmucosal administration [112–118, 135]. For atipamezole, dosing of 50 μg/kg IV, IM, or SQ has been suggested, and a two to three times higher dose for sublingual transmucosal administration is reasonable, given a mucosal bioavailability of 33% compared to IV administration [132, 135, 136]. Flumazenil has been used in newborn infants at 10–20 μg/kg IV or IM, and due to the prolonged effect of benzodiazepines in this population, it is reasonable to continue it as a constant rate infusion (CRI) (10 μg/kg/h IV) or by repeating the initial reversal dose every hour or as clinically indicated [127–129]. As the transmucosal absorption of flumazenil is close to 100%, the same dose given IV/IM can be administered by the sublingual transmucosal route and is expected to lead to an effective flumazenil serum concentration in 2–4 min [137].

4.8.5 | Knowledge Gaps

Controlled trials studying the effect of naloxone and atipamezole in nonvigorous newborn puppies and kittens are required to improve the certainty of the clinical recommendations on reversal drugs, including studies to explore more clinically feasible routes of drug administration compared to injections into the umbilical vein.

4.9 | Atropine for Bradycardia—NB-23

In newborn dogs and cats that require resuscitation and are bradycardic (P), how does routine parenteral administration of atropine (I), compared with no atropine administration (C), improve outcome (O)?

4.9.1 | Introduction

Severe bradycardia is a potentially life-threatening problem in newborns at birth. Hypoxemia is the cause of bradycardia in fetal mammals and in newborns that struggle to transition to extrauterine oxygenation (i.e., fail to adequately aerate the lungs) [8, 94, 138, 139]. It has been shown that bradycardia can result from parasympathetic (i.e., "vagal") influence in late-term fetuses and newborns [140, 141], and that the bradycardia of hypoxemia is at least partially vagally mediated [94, 139]. However, the main treatment for bradycardia in transitional newborn infants is respiratory support in the form of PPV to reverse hypoxemia, rather than treatment with a vagolytic drug such as atropine [8]. It is unknown whether newborn, transitional puppies and kittens that are severely bradycardic at birth would achieve improved survival, neurologic function, or other important benefits from the administration of atropine.

4.9.2 | Consensus on Science

For the most critical outcomes of *survival to discharge* and *favorable neurologic outcome*, and *the important outcome of hospital*

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length of stay, no studies were identified that addressed the PICO question.

For the important outcome of *surrogate markers of perfusion*, we identified one clinical trial (very low quality of evidence, downgraded for very serious risk of bias, serious indirectness, and imprecision) and 2 experimental studies (very low quality of evidence, downgraded for very serious indirectness and imprecision) that addressed the PICO question [94, 139, 142]. Balikci et al. studied the effects of atropine compared to caffeine or doxapram on vital parameters, acid–base status, and blood gas variables in 3 groups ($n = 8$ in each group) of live, newborn, asphyxiated calves and found that atropine had a less favorable effect on HR, arterial pH, $PaCO_2$, and PaO_2 than did doxapram. In this study, atropine exerted no different effect on rectal temperature, arterial HCO_3, or arterial base excess than caffeine or doxapram. The study did not include a control group with a placebo [142]. Giussani et al. studied 26 preterm, fetal lambs and showed that atropine prevented hypoxemia-induced bradycardia and supported femoral blood flow in this condition compared to saline control [94]. Finally, Walker et al. found that hypoxemia caused bradycardia in late-term fetal lambs and that this bradycardia was obliterated with atropine administration [139]. No studies in newborn animals of any species were identified that compared atropine to a placebo or to a lack of intervention.

For the important outcome of *histopathologic damage*, no studies were identified.

4.9.3 | Treatment Recommendations

In newborn puppies and kittens that require resuscitation and that are bradycardic, we suggest against routine atropine administration (weak recommendation, expert opinion).

4.9.4 | Justification of Treatment Recommendation

No direct evidence, and very little, seriously indirect evidence addressing less important outcomes, was found to address the question of whether bradycardic newborn puppies and kittens should receive atropine during resuscitation. However, bradycardia in transitional newborns is nearly always caused by hypoxemia. Thus, the mainstays of treatment for bradycardia in transitional newborns include progressively advanced methods to support lung aeration (i.e., from tactile stimulation to PPV with a tight-fitting face mask to ET intubation for PPV, when feasible) to improve oxygenation until the HR improves. No evidence was identified to suggest that time and resources should be directed away from these vital respiratory support measures to administer a vagolytic drug to the bradycardic newborn. The 2 experimental lamb studies both suggest that the bradycardia associated with hypoxemia is likely vagally mediated and thus could probably be reversed with atropine [94, 139], although experimental data suggest that responsiveness to atropine might generally be blunted in newborn puppies compared to mature dogs [143]. However, methods to increase the HR in the absence of lung aeration serve only to circulate blood of progressively poorer oxygen saturation. Increasing HR in the presence of progressive hypoxemia is not only physiologically counterproductive, but it could predispose to more severe myocardial hypoxia and thus myocyte injury with resultant cardiac arrhythmias and dysfunction. In addition, administration of atropine might disconnect HR from hypoxemia and pose a challenge to rescuers using HR for making informed resuscitation decisions. Moreover, the 3 most recent resuscitation guidelines for newborn infants, spanning the last 15 years, recommend PPV to support transitional infants with bradycardia and do not recommend the use of atropine or other medication in this setting [8, 59, 126]. We thus suggest against the routine use of atropine to treat bradycardia in newborn puppies and kittens, so that time and resources can be dedicated to treating hypoxemia by aerating the lungs as the top priority.

4.9.5 | Knowledge Gaps

Whether specific bradyarrhythmias (i.e., diagnosed by ECG) in the transitional newborn may benefit from vagolytic therapy is unknown.

In transitional puppies and kittens in which a vagolytic may be indicated, the preferred drug, dose and route of administration are unknown.

5 | Resuscitative Measures After the First Minute of Birth

The initial goal after the first minute of supportive measures is to assess the effectiveness of these actions and to either escalate or deescalate the intensity of resuscitative measures accordingly. Next to determining the animal's vigor (muscle tone, movement) and its respiratory effort (apnea, bradypnea, strong with vocalization), the newborn's HR is an important metric to determine the progression or resolution of hypoxemia. In the absence of a positive response of the newborn puppy or kitten to PPV alone, for example, if the newborn is experiencing continued severe bradycardia, ET intubation (NB-05) and oxygen supplementation (NB-03) alongside PPV are options moving forward.

5.1 | PPV via ETT—NB-05

In newborn dogs and cats without CPA that require resuscitation and with the need for intermittent PPV (P), how does ventilation via ET intubation (I), compared with using a tight-fitting face mask (C), improve outcome (O)?

5.1.1 | Introduction

There are no evidence-based recommendations regarding techniques of respiratory support during resuscitation of newborn puppies and kittens without CPA that require PPV. ET intubation in newborn puppies and kittens can be technically challenging, and ETTs sized to fit most of these animals are cuffless, compromising attempts at PPV. Thus, we endeavored to evaluate the impact of a tight-fitting face mask for the delivery of PPV compared to ETT on outcomes for live newborn puppies and kittens making inadequate breathing efforts.

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5.1.2 | Consensus on Science

For the most critical outcome of *survival to discharge*, we identified one observational study (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) that addressed the PICO question [144]. This study retrospectively evaluated the association between respiratory support method (standard care, noninvasive PPV, or ET intubation) in the delivery room and a variety of outcomes in 439 preterm newborn infants requiring resuscitation. Of 188 newborns receiving noninvasive PPV, 182 (97%) survived, while 185 of 229 (81%) receiving ET intubation survived ($p < 0.0001$); this finding is difficult to interpret since sicker infants are more likely to be intubated. Indeed, when adjusting for a variety of baseline characteristics, the OR of noninvasive PPV methods (such as bag–mask or T-piece–mask ventilation with or without continuous positive airway pressure [CPAP]) for "death" was 0.45 (95% CI, 0.16–1.25, $p > 0.05$) when compared to the use of ETT. Ultimately, therefore, no treatment advantage was noted for one method compared to the other; however, the risk of confounding by indication and other bias is inherently high in any retrospective comparison of treatments, despite investigators' attempts to adjust for differences in illness severity. Time and circumstances of death (in delivery room vs. neonatal ICU vs. prior to discharge; all-cause vs. specific-cause mortality) were not specified.

For the critical outcome of *favorable neurologic outcome*, we identified no studies addressing the PICO question.

For the important outcomes of *oxygenation/PaO_2* and *ventilation/$PaCO_2$*, we identified 1 clinical trial (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) [145] and a single experimental study (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [146] that addressed the PICO question. Zhu et al. studied 369 infants (gestational age ≥34 weeks, expected birth weight ≥2.0 kg) requiring PPV at birth. They assigned infants requiring respiratory support who were born on odd dates to be treated with bag–mask ventilation (BMV, $n = 164$) and those born on even dates to laryngeal mask airway (LMA, $n = 205$). Investigators found no difference in oxygenation or $PaCO_2$ for newborns treated with BMV versus LMA in this study [145]. Armstrong et al. anesthetized seven healthy, 2- to 11-day-old calves with alfaxalone, inducing hypercapnia. Calves were then ventilated using either an LMA (generally applied first) or using BMV (generally administered second, after washout period); both methods improved oxygenation and $PaCO_2$, though the 2 methods were not compared to 1 another since LMA usually preceded BMV, which increased the risk of bias [146]. ET intubation was not investigated in either study, which introduces one element of indirectness for this PICO; however, since LMA delivers gas directly to the airway, avoiding the esophagus (similar to an ETT), it was considered a reasonable surrogate for ETT.

For the outcome of *hospital length of stay*, we identified 1 observational study (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) that addressed the PICO question [144]. Study details appear above (see outcome survival to discharge). In this study, the median (IQR) length of stay for 188 infants undergoing noninvasive PPV method(s) was 48 days (IQR 30), and for 229 infants receiving ET intubation, it was 62 days (IQR 52). The length of stay difference was not compared directly for the two treatment groups, but there was a difference in length of stay found among those undergoing routine care (no ventilatory support), those receiving noninvasive PPV measures, and those intubated with an ETT ($p < 0.0001$) [144]. Additionally, "length of stay" was not defined in this study (e.g., stay in the neonatal ICU vs hospital vs including external care facilities), leading to uncertainty on the directness of the outcome.

For the outcome of *histopathologic damage*, we identified no studies addressing the PICO question.

5.1.3 | Treatment Recommendations

In newborn puppies and kittens without CPA that require PPV, we suggest the use of a tight-fitting face mask attached to a self-inflating resuscitator (i.e., "bag") to deliver positive pressure breaths within 60 s of birth (weak recommendation, very low quality of evidence).

In newborn puppies and kittens without CPA undergoing PPV by face mask that fail to respond within 60 s (e.g., HR remains <120/min despite intervention), we suggest ET intubation where feasible for continued PPV (weak recommendation, expert opinion).

5.1.4 | Justification of Treatment Recommendation

Very little evidence was available to inform the treatment recommendation, and no studies involved newborn puppies or kittens. None of the three studies identified showed a clear advantage to more invasive airway management (e.g., ETT, LMA) in newborns requiring resuscitation for any outcome studied when compared to less invasive, simpler methods (e.g., bag–mask or T-piece–mask ventilation). Particularly considering most ETTs that fit newborn puppies and kittens are uncuffed and thus compromised for delivery of PPV, BMV using a tight-fitting face mask seems a reasonable first choice in newborn puppies and kittens not in CPA that require ventilatory support in transition. Additionally, ET intubation in newborn puppies and kittens is challenging due to their very small size compared to standard equipment size and rescuers' fingers, and the fact that their fleshy tongues compromise laryngeal visualization. ET intubation in these circumstances may carry an increased risk of patient injury associated with difficult intubation. However, if PPV by face mask is not leading to a significant improvement of the newborn's condition (e.g., no change or a worsening in HR), then ventilation by ETT is reasonable, if skilled personnel and adequate equipment are available. When intubation is required, options may include Cole-style ETTs or cone-shaped devices intended for intubating rodents.

These treatment recommendations are in alignment with the recommendations in newborn infants, in whom less invasive, tight-fitting face masks are generally recommended first, followed by LMA or ET intubation if BMV or T-piece–mask ventilation fails [9].

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5.1.5 | Knowledge Gaps

To date, there are no randomized controlled clinical trials investigating the outcomes of different methods of respiratory support in transitional newborns in any species and no information in newborn puppies and kittens without CPA that need intermittent PPV. Important investigations could include sizes and shapes of masks that allow for appropriate fit across multiple muzzle sizes and shapes, and equipment designed for expedient, safe ET intubation of newborn puppies and kittens.

5.2 | Oxygen Supplementation With PPV—NB-03

In newborn dogs and cats that require resuscitation with PPV (P), how does any other concentration of inspired oxygen (I), compared with 100% oxygen (C), improve outcome (O)?

5.2.1 | Introduction

Newborn puppies and kittens have been historically resuscitated with 100% oxygen, as asphyxiation is the predominant concern [16]; this approach was in line with the recommendations for resuscitation of newborn infants in the early 2000s [34]. However, the scientific evidence supporting the administration of 100% oxygen has not been established in newborn puppies and kittens. In addition, there is concern that delivery of high inspiratory oxygen concentrations and the associated hyperoxemia may lead to oxidative injury and could lead to harm [147]. Conversely, inadequate oxygen supplementation and subsequent hypoxia can be harmful as well. Thus, there is a need to determine whether newborn puppies and kittens requiring resuscitation should be resuscitated with an inspiratory oxygen concentration other than 100%. This question concerns the initial administration of oxygen in newborn puppies and kittens requiring PPV immediately after birth. These animals are typically nonvigorous (i.e., low muscle tone, apneic/bradypneic, or severely bradycardic [e.g., HR < 120/min]). The question regarding oxygen supplementation in newborns requiring chest compressions is addressed elsewhere (see NB-18).

5.2.2 | Consensus on Science

For the critical outcome of *survival to discharge*, we located 4 clinical trials that addressed the PICO question (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) [20–23]. No relevant observational or experimental studies were identified. Saugstad et al. evaluated, in the Resair-2 trial, the survival of asphyxiated term newborn infants that were ventilated with either room air (n = 267) or 100% O_2 (n = 294) immediately after birth [20]. If cyanosis or bradycardia persisted after 90 s of ventilation with room air, the inspired gas was changed to 100% oxygen. The mode of ventilation was bag–mask in most cases, while 25% of newborns in either group were intubated. Room air administration did not lead to a significant difference in mortality (RR = 0.76, 95% CI = 0.53–1.10). The remaining RCTs showed similar results. All data taken together (n = 1280) demonstrated a 23% relative risk reduction in mortality with initial room air administration compared to 100% oxygen in term newborn infants requiring PPV (RR = 0.77, 95% CI = 0.59–0.99).

For the critical outcome of *favorable neurologic outcome*, we located the same 4 clinical trials (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) as reported above [20–23]. These articles report neurological outcomes as the presence or absence of hypoxic–ischemic encephalopathy (HIE) based on a commonly used scoring system (Sarnat Stage II or III) [148]. While a single study including 418 asphyxiated newborns showed some benefit of room air over 100% oxygen (RR = 0.66, 95% CI = 0.44–0.98) [22], the pooled data from all studies showed no significant impact on HIE (RR = 0.82, 95% CI = 0.63–1.10). Importantly, there was no evidence that initial PPV with room air worsened neurological outcome. Two experimental studies (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) involving swine and rat models of newborn asphyxiation showed neither benefit nor harm of PPV with room air on neurological recovery when compared to 100% oxygen [149, 150].

For the important outcome of *oxygenation (PaO_2)*, 3 clinical trials directly evaluated PaO_2, SpO_2, or SaO_2 in intrapartum asphyxiated newborn infants resuscitated with either room air or 100% oxygen (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) [20, 151, 152]. Saugstad et al. found no difference in PaO_2 in newborn infants resuscitated with room air or 100% oxygen during the first 10 min of life [20]. These findings contrasted with Vento et al., who documented mild hyperoxemia (PaO_2, 126.3 ± 21.8 mm Hg) in infants resuscitated with 100% oxygen compared to room air (PaO_2, 72.2 ± 6.8 mm Hg, $p < 0.01$) in the first 10 min after birth [152]. Note that in this study, the PaO_2 at birth in non-asphyxiated newborns was also very low (PaO_2, 30.3 ± 4.5 mm Hg) and not different from asphyxiated newborns (PaO_2, 27.8 ± 5.2 mm Hg in the room air group; 30.0 ± 6.8 mm Hg in the 100% oxygen group). A third study, including 134 term newborns requiring PPV, demonstrated mild hyperoxemia in infants resuscitated with 100% O_2 at 5 min of PPV (157 ± 27 mm Hg) compared to those ventilated with room air (88 ± 9 mm Hg, $p < 0.001$) [151]. Numerous experimental studies in newborn piglets and lambs compared the effects of FiO_2 on PaO_2 and $PaCO_2$. The majority were excluded as these studies did not evaluate oxygenation and ventilation in newborns during transition but in neonatal animals that were several days old [153–162]. Only one experimental study (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) was identified that utilized a transitional newborn lamb model, in which the animals were asphyxiated by cord clamping while in utero, followed by delivery and PPV with room air or 100% oxygen [163]. Ventilation with 100% oxygen led to marked hyperoxemia (PaO_2, 454 ± 33 mm Hg) compared to resuscitation with room air (PaO_2, 68 ± 15 mm Hg) after 5 min of PPV.

For the important outcome of *ventilation ($PaCO_2$)*, the same human clinical trials mentioned above provided data (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) pertaining to this PICO question [20, 151, 152]. They all showed no significant impact of the inspiratory oxygen concentration on ventilation. The

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same was true for an experimental study in newborn lambs [163].

There were no studies identified that evaluated the impact of inspiratory oxygen concentration on *hospital length of stay*.

For the important outcome of *histopathologic damage*, we identified 1 clinical trial (low quality of evidence, downgraded for serious indirectness, and imprecision) [147] and 27 experimental studies (very low quality of evidence, downgraded for serious risk of bias and serious indirectness) relevant to the PICO question [149, 150, 153, 155, 158, 162–183]. While we included studies reporting markers of tissue injury, such as indicators of oxidative injury or matrix metalloproteinase (MMP) activity as outcomes, we excluded animal models that studied reoxygenation after CPR.

Vento and colleagues reported circulating markers of oxidative injury (reduced glutathione [GSH], oxidized glutathione [GSSG], superoxide dismutase [SOD]) and myocardial (cardiac troponin T [cTNT]) and kidney injury (*N*-acetyl-glycosaminidase [NAG]) in severely asphyxiated newborn infants randomized to resuscitation with room air ($n = 17$) or 100% oxygen ($n = 22$) [147]. Oxidative injury and increases in NAG and cTNT concentrations were present in both groups compared to non-asphyxiated controls but were more severe in newborns resuscitated with 100% O_2.

Among the 27 experimental studies, only 2 of them involved newborn animals in transition [163, 166], and all other studies included neonatal animals that were at least 12-h old and had fully (and normally) transitioned. Species represented were swine (22 studies) [149, 153, 155, 158, 162, 164, 167–174, 176–183], sheep (2 studies) [163, 166], rabbits (1 study) [165], and rats (2 studies) [150, 175], but not dogs or cats. Most commonly, asphyxiation was induced by exposing animals to a low inspiratory oxygen concentration for a defined duration or until either a hemodynamic (e.g., MAP < 20 mm Hg) or metabolic (e.g., BE < −20 mmol/L) goal was achieved. Animals were then allocated to resuscitation with room air or 100% oxygen, followed by variable lengths of observation time. Reported outcomes included oxidative, histopathologic, or circulatory markers of tissue injury in the brain [150, 153, 162, 165, 167–170, 175, 177, 180, 183], heart [149, 164, 171, 172, 181, 182], lung [163, 166, 179, 182], kidney [149, 182], liver [158, 182], adrenals [176], and small intestines [155], as well as systemic markers of oxidative injury [166–169, 173, 174, 178, 183]. Taken together, the studies either showed no difference in outcome between resuscitation with 21% oxygen compared to 100% oxygen or demonstrated a benefit of resuscitation with room air. No study reported worse outcomes with room air resuscitation.

5.2.3 | Treatment Recommendations

We suggest the use of room air (21% oxygen) over 100% oxygen during early assisted ventilation of newborn puppies and kittens (weak recommendation, very low quality of evidence).

We suggest the use of 100% oxygen in newborn puppies or kittens in which the HR fails to increase despite 1–2 min of PPV (weak recommendation, expert opinion).

5.2.4 | Justification of Treatment Recommendation

While there are no clinical data on the optimal selection of the inspiratory oxygen concentration in newborn puppies and kittens requiring PPV, the above-cited evidence suggests that room air is as effective as 100% oxygen and that oxygen might do harm. This has been a consistent finding in clinical and experimental studies and across multiple species and populations. Many studies suggest harm associated with PPV with high inspiratory oxygen concentrations, including evidence of increased mortality in newborn infants, increased oxidative injury in newborn infants and newborn animal models, and tissue injury in various organs. Until differing evidence emerges, we suggest using room air to initiate PPV in newborn puppies and kittens.

A transition to a higher inspiratory concentration of oxygen might be beneficial in some newborn puppies and kittens, if clinical signs of severe hypoxemia (e.g., severe bradycardia) persist despite adequate PPV. No studies have systematically evaluated when to best switch from room air to 100% oxygen, but we propose a transition guided by HR. HR is invariably decreased with perinatal asphyxiation, and an increase in HR in response to PPV is considered an indicator of the resolution of hypoxemia [184, 185]. Studies in newborn children and experimental animals suggest that the time course with which HR increases after initiation of effective PPV is variable and can be instantaneous or gradual, and accordingly may take as little as 10–20 s or as long as several minutes [100, 185, 186]. Balancing benefit against risk, we therefore suggest switching from room air to 100% oxygen if no marked increase in HR is observed after 1 - 2 min of PPV.

5.2.5 | Knowledge Gaps

There is a lack of clinical studies in animals to address the issue of supplemental oxygen administration in transitional newborn puppies and kittens in general and in those requiring PPV specifically.

6 | Cardiopulmonary Resuscitation

We expect that CPR—the combined administration of PPV and chest compressions—will only be required in a small subset of newborn puppies and kittens that need support at birth. However, there is currently no epidemiological information available to substantiate that anecdotal impression. Equivalent data in people, however, indicate that 85% of term newborn infants take their first breath within seconds of birth, a further 10% do so after drying/tactile stimulation, 5%–10% receive PPV, and only 0.1%–0.3% require chest compressions [8, 187–189]. If no heartbeat is identified at birth or at any time during resuscitation, CPR should be started immediately. However, as in newborn resuscitation guidelines in people, initiation of chest compressions could also be considered with bradycardia severe enough to lead to critical compromise of cardiac output and thereby exacerbation of tissue hypoxia [8]. The PICO questions below inquire whether there is a particular HR below which to initiate chest compressions (NB-02). We further attempt to address how to best deliver chest compressions in newborn puppies and kittens, including compression rate (NB-12) and depth (NB-17), animal position

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and compression point (NB-16), whether to synchronize breaths with chest compressions (NB-14) by alternating compressions and breaths at a certain compression:ventilation ratio (NB-13), whether oxygen supplementation is of benefit (NB-18), and whether there is support for the use of epinephrine (NB-21, NB-22) and atropine (NB-24). We finally pose the important question of whether there is a particular duration of CPR after which the resuscitation effort should be terminated due to futility (NB-25).

6.1 | HR and When to Start CC—NB-02

In newborn dogs and cats that require resuscitation in which PPV has been initiated (P), how does starting chest compressions below any other HR (I), compared with less than 60/min (C), improve outcome (O)?

6.1.1 | Introduction

Intrapartum fetal asphyxiation leads to a reduction in HR at birth, and this bradycardia can further exacerbate vital organ hypoxia [190]. PPV and oxygen administration are expected to increase HR in many cases, but where these interventions fail to increase the HR above a critical threshold, chest compressions might increase tissue blood flow and tissue oxygen delivery. However, once effective PPV and oxygen supplementation have been started in newborn puppies or kittens, the ideal HR below which to initiate chest compressions is unknown. The current recommendation in newborn infants is to initiate chest compressions if the HR drops below 60/min [8].

6.1.2 | Consensus on Science

We found no evidence relevant to this PICO question for the outcomes of favorable neurologic outcome, survival to discharge, surrogate markers of perfusion, hospital length of stay, and histopathologic damage.

6.1.3 | Treatment Recommendations

In very severely bradycardic newborn puppies and kittens that have received effective PPV and oxygen supplementation for at least 30 s, we recommend initiating chest compressions (strong recommendation, expert opinion).

We suggest using an HR below 50/min as the threshold for initiating chest compressions in newborn puppies and kittens that have received effective PPV and oxygen supplementation for at least 30 s (weak recommendation, expert opinion).

6.1.4 | Justification of Treatment Recommendation

As in human medicine, we identified no studies that investigate the HR threshold at which to initiate chest compressions in asphyxiated newborn puppies and kittens; thus, there is considerable uncertainty regarding below which HR to initiate chest compression [191, 192]. During asphyxiation in newborns, the HR decreases and cardiac output declines [193]. While this is initially compensated for by counterregulatory mechanisms to maintain blood flow to the heart and brain, severe global tissue hypoxia and end-organ injury, including HIE, eventually ensue [190]. Although we did not identify any direct evidence to inform at which HR chest compressions should be initiated in any species, a reduction to a median HR of 46/min in an experimental asphyxia model in newborn lambs demonstrated a reduction in cerebral blood flow to 25% of baseline, with a linear correlation between reduction of cerebral blood flow and HR [194]. Another study in asphyxiated newborn lambs found no improvement of cerebral and coronary blood flow when chest compressions were administered during bradycardia with an HR of 63 ± 8/min [195]. There are some physiological concerns that chest compressions in newborns with bradycardia could be harmful [196]. In addition, the concurrent administration of chest compressions and PPV is challenging and may distract the rescuer from effectively providing PPV, which is likely the most beneficial intervention in asphyxiated newborns. Given that compressions started at an HR of approximately 60/min did not improve cerebral and coronary blood flow and that an HR of approximately 46/min led to a severe reduction in cerebral blood flow, we suggest starting chest compression only when the HR falls below 50/min. Below that HR, vital organ blood flow is likely less than what is generated by chest compressions. With effective PPV, experimental evidence from asphyxiated piglets suggests that the HR will start to increase with PPV alone after 15–30 s in those animals that are able to respond [100]. We therefore considered PPV for 30 s to be a reasonable first step before escalating resuscitation to include chest compressions if the HR fails to increase during that time. We suggest that chest compressions be administered when the HR remains below 50/min after 30 s of effective PPV and oxygen administration. If there is no heartbeat identified (i.e., as with asystole or pulseless electrical activity), CPR should be started immediately with concurrent initiation of chest compressions and PPV.

6.1.5 | Knowledge Gaps

There is no clinical or experimental evidence to assess harm or benefit for chest compressions in newborn puppies and kittens when initiated at any HR cutoff. An initial study could explore whether in newborn puppies and kittens with severe bradycardia (HR ≤ 50/min), chest compression and PPV versus PPV alone are associated with improved outcome. It would also be important to determine how fast an increase in HR can be expected with PPV alone.

6.2 | Chest Compression Rate—NB-12

In newborn dogs and cats with CPA (P), how does any other specific rate for external chest compressions (I), compared with a compression rate of 120/minute (C), improve outcome (O)?

6.2.1 | Introduction

Chest compressions are of key importance in pediatric and adult CPR and an essential part of basic life support (BLS) [11]. In

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contrast, respiratory support is of primary concern in transitional newborns requiring resuscitation. Enhancing circulation by means of chest compression is a late intervention for select newborns that fail to respond to respiratory support measures alone and in which myocardial hypoxia has resulted in CPA. In human newborn resuscitation in the delivery room, a chest compression rate of 120/min is currently recommended [8]. Due to the much smaller size of newborn kittens (approximately 100 g) and puppies (80–800 g depending on breed) when compared to newborn infants, mathematical modeling suggests that a compression rate higher than 120/min might be of benefit in these species [197].

6.2.2 | Consensus on Science

We did not identify evidence for the most critical outcome of *favorable neurologic outcome* and the important outcome of *duration of hospitalization*.

For the critical outcome of *survival to discharge*, we identified 3 experimental studies in neonatal, post-transitional piglets (very low quality of evidence, downgraded for serious bias, very serious indirectness and imprecision) that address the PICO question [198–200]. In these studies that together included 68 piglets of 1–14 days of age and weighing at least 2 kg, a reduction of chest compression rate to below 120/min (i.e., 90–100/min) did not impact mortality (RR = 1.5; 95% CI, 0.8–2.6) compared to 120/min or higher. However, these experimental studies reported survival as return of spontaneous circulation (ROSC) of more than 20 min or survival to 4 h after ROSC, rather than the more clinically relevant outcome of survival to discharge.

For the important outcome of *surrogate marker(s) of perfusion*, we identified 4 experimental studies in piglets (very low quality of evidence, downgraded for serious bias, very serious indirectness, and imprecision) that addressed the question [198–201]. An experimental study of 16 piglets (2 kg body weight) found no significant advantage of a chest compression rate of 120/min over 90/min on hemodynamic metrics such as cerebral oxygenation or coronary blood flow [198]. A further experimental study including 28 piglets (3–4 kg body weight) in which the compression rate was adjusted to optimize $EtCO_2$ revealed that diastolic and mean blood pressures, systemic perfusion pressure, and cerebral perfusion pressure were higher for the $EtCO_2$-guided group (compression rate: 143 ± 10/min) when compared to the standard group (compression rate: 102 ± 2/min) [199]. A third experimental study including 24 piglets (2 kg body weight) identified no effect of investigated compression rates (120/min compared to 90/min or 100/min) on intra-arrest hemodynamics but improved postarrest circulatory function in animals receiving chest compressions at the highest rate studied (i.e., 120/min) [200]. A final study in newborn piglets (2 kg body weight) with asphyxial CPA, which received chest compressions at a rate of either 60/min, 90/min, 120/min, 150/min, or 180/min, found that the highest cardiac output and arterial blood pressure were achieved at 150/min and 180/min [201].

For the important outcome of *histopathological damage*, we identified 2 experimental studies in piglets (very low quality of evidence, downgraded for serious bias, very serious indirectness, and imprecision) that addressed the question [199, 200]. Animal injury such as epicardial hemorrhage and hemothorax only occurred in the aforementioned $EtCO_2$-guided chest compression group with high compression rates and not in the control group with standard of care, although the authors indicate technical reasons (pacing leads) to be responsible [199]. Patel et al. reported reduced concentrations of proinflammatory cytokines in the frontal cortices of piglets resuscitated at compression rates of 120/min compared to 90/min or 100/min [200].

Of note, the piglets in the above-cited studies had already passed the transition phase, were 1–14 days old, and weighed 2–4 kg, which is dissimilar to newborn puppies and kittens requiring chest compressions immediately after delivery.

6.2.3 | Treatment Recommendations

We suggest delivering chest compressions in newborn puppies and kittens at 120–150 compressions per minute (weak recommendation, very low quality of evidence).

6.2.4 | Justification of Treatment Recommendation

There is no direct evidence on the optimal chest compression rates in small mammals of 100–800 g, and none in transitional newborns of any size where the lungs are not yet aerated and remain fluid filled. Thus, the certainty with which any recommendation can be given is very low, and the optimal chest compression rates in newborn puppies and kittens remain unknown. Very low-quality evidence from the piglet models cited above suggests some benefit of a compression rate of at least 120/min. Mathematical modeling furthermore suggests that the combination of small flow distances and volumes involved in very small animals results in the optimal chest compression rate to be higher than in larger animals and in excess of 120/min [197]. It is standard to resuscitate rats of similar body weight of approximately 350 g in experimental CPA models with chest compressions delivered at rates of 200–300/min, although no studies have been performed to establish the optimal chest compression rate in this setting either [202, 203]. We also believe that delivering chest compressions at 120–150/min is feasible in newborn puppies and kittens without excessive rescuer fatigue, given the associated small compression depth of 1–2 cm and the low compression force required; however, this assumption awaits testing in newborn puppies and kittens. Taken together, we suggest administering chest compressions at a higher rate in newborn puppies and kittens (120–150/min) than in adult dogs and cats (100–120/min) [11, 204].

6.2.5 | Knowledge Gaps

There is significant uncertainty regarding the optimal chest compression rate in newborn puppies and kittens. Furthermore, rescuer performance over time, including rescuer fatigue, at these higher compression rates has not been studied.

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6.3 | Chest Compression Point—NB-16

In newborn dogs and cats receiving chest compressions (P), how does the administration of ventrodorsal chest compressions (i.e., over the sternum) (I), compared with laterolateral chest compressions (C), improve outcome (O)?

6.3.1 | Introduction

Effective chest compressions are essential for circulatory support during CPR. Patient position and compression point are factors that may significantly affect the efficacy of chest compressions. In newborn infants, current guidelines recommend performing chest compressions over the sternum using a two-thumb technique with fingers encircling the chest [8]. In experimental CPR models of swine and rodents, chest compressions are also uniformly recommended to be performed over the sternum with the subjects positioned in dorsal recumbency [202, 205]. In adult dogs and cats, chest compressions are most commonly performed in lateral recumbency, but almost no studies have evaluated the question of optimal positioning [11]. No information regarding this topic is available for newborn puppies and kittens.

6.3.2 | Consensus on Science

For the critical outcomes of *survival to discharge* and *favorable neurologic outcome*, as well as the important outcomes of *surrogate markers of perfusion*, *hospital length of stay*, and *histopathologic damage*, we identified no studies addressing the question in newborn puppies and kittens.

6.3.3 | Treatment Recommendations

In newborn puppies and kittens requiring chest compressions, we suggest application of chest compressions in the laterolateral direction (weak recommendation, expert opinion).

In newborn puppies and kittens requiring chest compressions, we suggest ventrodorsal (sternal) chest compressions when additional resuscitation measures (e.g., umbilical cord cannulation, monitoring modalities) are facilitated by dorsal recumbency (weak recommendation, expert opinion).

In newborn puppies and kittens requiring chest compressions in lateral recumbency, we recommend that one or two fingers are located over the heart to compress the chest toward the tabletop or, alternatively, that one or two fingers (index and middle finger) and opposing thumb are used to compress the chest directly over the heart (strong recommendation, expert opinion).

In newborn puppies and kittens requiring chest compressions in which dorsal recumbency is preferred (e.g., for cannulation of the umbilical vein or pronounced wide-chested thorax conformation), we recommend that one or two fingers (index and middle finger) compress the sternum toward the tabletop to achieve the targeted chest compression depth (strong recommendation, expert opinion).

6.3.4 | Justification of Treatment Recommendation

For newborn puppies and kittens, there is insufficient evidence to provide a treatment recommendation regarding the administration of ventrodorsal versus laterolateral chest compressions. We believe, however, that factors other than chest compressions themselves impact the preferred body position during CPR. Effective bag–mask ventilation, a critical component of newborn resuscitation, is presumed to be compromised in supine newborn puppies and kittens as the large, fleshy tongue might increase upper airway resistance when muscle tone is absent [206]. In addition, dorsal positioning precludes the placement and maintenance of an intraosseous (IO) cannula. And finally, veterinary professionals are generally more familiar with a laterolateral approach to chest compressions, as this is the recommended technique for most adult dogs and cats [11].

Unlike newborn infants that typically weigh 2–4 kg at birth, even newborn puppies of giant breeds weigh less than 800 g [207, 208] such that chest compression techniques used in human newborns may not translate into newborn puppies and kittens.

6.3.5 | Knowledge Gaps

There is no evidence in newborn puppies and kittens evaluating outcomes of chest compressions in lateral or dorsal recumbency. It is not known what the most common practices are in animal and finger positioning during CPR in newborn cats and dogs.

6.4 | Chest Compression Depth—NB-17

In newborn dogs and cats receiving chest compressions (P), how does another chest compression depth (I), compared with 1/3 of chest width (C), improve outcome (O)?

6.4.1 | Introduction

Chest compression depth is a factor that may alter cardiac output and perfusion to vital organs during CPR, with veterinary guidelines identifying adequate compression depth as critical for optimizing blood flow in dogs and cats during closed-chest CPR [11, 204]. Ideal compression depth may vary depending on patient conformation and position, intracardiac volume, and other parameters. Compressions that are too shallow may result in inadequate cardiac output, while excessive force and depth may result in mechanical injury to underlying thoracic or abdominal structures. In newborn infants, the American Heart Association and the Neonatal Resuscitation Program recommend a sternal compression depth of one-third of the anterior–posterior (AP) diameter of the chest, though these guidelines are based on very limited data [8]. Identifying a compression depth target for newborn puppies and kittens undergoing CPR is investigated here.

6.4.2 | Consensus on Science

For the critical outcomes of *favorable neurologic outcome* and *survival to discharge*, we identified no studies addressing the PICO question.

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For the important outcome of *surrogate markers of perfusion*, we identified 2 observational human studies that address the question (very low quality of evidence, downgraded for very serious risk of bias, very serious indirectness, and inconsistency) [209, 210]. In a retrospective cohort study of 6 infants requiring cardiac surgery and subsequent CPR, the depth of chest compressions was initiated at approximately one-third of the AP chest diameter and then increased to one-half of the AP chest diameter if systolic blood pressure remained <60 mm Hg [209]. The mean systolic blood pressure was 52 mm Hg for the one-third diameter approach and 83 mm Hg for the one-half diameter approach ($p < 0.001$), representing a 62% increase in systolic blood pressure. Other outcomes were not measured, however, and only one of the six patients survived to hospital discharge with a favorable neurologic outcome. In another retrospective observational study, images from 54 neonatal chest CT scans were analyzed to compare theoretical compression depths of one-fourth, one-third, and one-half the AP chest diameter [210]. Ejection fraction (normal value of 69%) was estimated with mathematical modeling and increased incrementally with increasing chest compression depth (51% with one-fourth AP chest compression depth, 69% with one-third depth, and 106% with one-half depth, $p < 0.001$). Undercompression (defined as compression inadequate to obtain an ejection fraction of at least 50%) was predicted to occur in 54% of infants receiving chest compression with a depth of one-fourth of the AP diameter but in none resuscitated with other compression depths ($p < 0.001$). Overcompression (defined as lack of adequate residual chest depth) was predicted in 91% of infants in which the chest was compressed to one-half its AP diameter but not in other groups ($p < 0.001$). The authors concluded, based on mathematical modeling, that one-third AP chest compression depth should be more effective than one-fourth depth and safer than one-half depth.

For the important outcomes of *hospital length of stay* and *histopathologic damage*, we identified no studies addressing the question in newborns.

6.4.3 | Treatment Recommendations

In newborn puppies and kittens receiving chest compressions, we suggest a compression depth of one-third to one-half the width of the chest for laterolateral compressions (weak recommendation, very low quality of evidence).

In newborn puppies and kittens receiving chest compressions, we suggest a compression depth of one-third the AP diameter of the chest for ventrodorsal (i.e., sternal) compressions (weak recommendation, very low quality of evidence).

6.4.4 | Justification of Treatment Recommendation

There is very limited and no direct evidence to answer this question in newborn puppies and kittens. While one very small observational study in human infants demonstrated improved blood pressure with compression by one-half compared to one-third of the AP chest diameter, another study using mathematical modeling on neonatal CTs estimated adequate ejection fraction in the group with compression of one-third of the AP chest diameter and overcompression with one-half of the AP chest diameter. Human newborn guidelines typically recommend a sternal compression depth of one-third of the AP diameter of the chest; however, newborn puppies and kittens have different chest conformations, and the use of laterolateral chest compressions is likely more common. It is reasonable to target a compression depth of one-third to one-half the width of the chest with laterolateral chest compressions, as in adult dogs and cats, though caution must be exercised to avoid overcompression of the highly compliant newborn chests. With sternal compression, a proportion of the AP chest diameter is occupied by the vertebral column, diminishing the compressible portion of the chest cavity. We therefore suggest a compression depth of one-third the AP diameter of the chest when delivering sternal compressions.

6.4.5 | Knowledge Gaps

The optimal compression depth in newborn puppies and kittens in any position has not been established, and further research is needed in this area. Specifically, it is unclear whether rescuers can note the difference between one-half and one-third of chest width during compressions, given that this might constitute as little as a 2–3 mm difference in compression distance. Furthermore, CT studies might provide some initial direction regarding the intrathoracic location of the heart in laterally recumbent or supine newborn kittens and puppies and the appropriate compression depth and compression point.

6.5 | C:V Ratio in Nonintubated Animals During CPR—NB-13

In newborn dogs and cats receiving chest compressions (P), how do other compression-to-ventilation ratios (e.g., 30:2; 15:2, 9:3, 5:1) (I), compared with a compression:ventilation ratio of 3:1 (C), improve outcome (O)?

6.5.1 | Introduction

Ventilation is of higher importance during resuscitation of transitional newborns than post-transitional newborn, pediatric, or adult animals undergoing CPR, as the respiratory transition from fluid-filled to aerated lungs is a key process at birth and its failure is the main cause of CPA at the time of delivery [2]. Current guidelines in newborn infants, based on expert opinion, suggest synchronized administration of compressions and ventilation at a ratio (i.e., C:V ratio) of 3:1 given at a rate to allow 90 compressions and 30 breaths to be delivered per minute [8]. The interruption of chest compressions to deliver a breath is expected to optimize lung aeration when compared to concurrently administered ventilations and compressions, but this has not been conclusively evaluated (see NB-14). Moreover, in newborn puppies and kittens that are most often nonintubated during CPR, concurrent ventilations and compressions are not recommended due to the presumed lack of efficacy of breaths delivered during chest compressions in this setting and the risk for severe gastric insufflation, regurgitation, and aspiration [211].

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A lower C:V ratio (e.g., 3:1) is generally expected to deliver more breaths per minute and favor ventilation, while a higher C:V ratio (e.g., 15:2) will lead to more compressions per minute and favor circulation.

We herein ask whether in newborn puppies and kittens undergoing CPR with compressions alternating with ventilations at a particular ratio (C:V ratio), resuscitators should target a C:V ratio of 3:1 as recommended for newborn infants, or whether another C:V ratio is preferable.

6.5.2 | Consensus on Science

For the critical outcome of *favorable neurologic outcome*, we identified no studies addressing the question.

For the next most critical outcome of *survival to discharge*, we identified 3 experimental neonatal piglet studies that addressed the question (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [212–214]. All the studies involved post-transitional piglets of 12–96 h of age in which asphyxial arrest was induced by a combination of a hypercarbic/hypoxic inspiratory gas mixture and ETT clamping. Resuscitation included a 30-s ventilation-only period, followed by ventilation and chest compressions synchronized such that chest compressions were alternating with breaths at a certain ratio. Specifically, C:V ratios of 2:1, 4:1, 9:3, and 15:2 were compared to a C:V ratio of 3:1. No differences in survival to 4 h after ROSC emerged between any of the C:V ratios examined. Pooled analysis showed no difference between those piglets resuscitated with a C:V ratio of 3:1 ($n = 40$), compared to other C:V ratios ($n = 48$) (RR = 0.97, 95% CI 0.85–1.10, $p = 0.63$).

For the important outcome of *hospital length of stay*, we identified no studies addressing the question.

For the important outcome of *respiratory function (oxygenation and ventilation)*, we identified 8 experimental studies that addressed the question (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision), 4 of which included neonatal piglets [212–215], and 4 were manikin studies [216–219]. All piglet studies were again utilizing post-transitional piglets of 1–4 days of age that underwent asphyxial arrest, and all studies compared resuscitation with a C:V ratio of 3:1 with other compression-to-ventilation ratios, including 2:1, 4:1, 9:3, and 15:2. No significant differences were identified between 3:1 groups and any of the other groups in $EtCO_2$ during resuscitation or $PaCO_2$ or SpO_2 values immediately after ROSC [212–214]. Pasquin et al. found that median tidal volumes were higher in the 2:1 group (27 mL, IQR 12) than in the 4:1 group (14 mL, IQR 7; $p = 0.02$), with intermediary values resulting from the 3:1 approach (22 mL, IQR 6) [214]. Dannevig et al. compared the effect of 3:1 and 9:3 compression-to-ventilation ratios on markers of lung injury (e.g., TNF, ICAM-1, and MMP2/9) and found no differences between the studied C:V ratios [215]. The 4 studies conducted in newborn infant manikins indicated that the lower C:V ratio of 3:1, compared to 5:1, 9:3, 10:2, or 15:2, leads to higher minute ventilation [216, 218, 219] and tidal volume [217–219] and leads to more effective breaths based on chest rise [219].

For the important outcome of *surrogate markers of perfusion*, we identified 3 experimental studies in neonatal piglets that addressed the question (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [212–214]. These studies were those already discussed above. They found hemodynamic outcomes (i.e., MAP, lactate) immediately after ROSC were comparable among different C:V groups in all studies.

6.5.3 | Treatment Recommendations

In newborn puppies and kittens receiving chest compressions and synchronized PPV, we suggest a C:V ratio of 4:1 (weak recommendation, expert opinion).

6.5.4 | Justification of Treatment Recommendation

In making this recommendation, we acknowledge there is insufficient published information to arrive at an evidence-based recommendation for the preferred ventilation and compression strategy in newborn puppies and kittens requiring chest compressions. We consider ET intubation of the very small newborn puppies and kittens not routinely feasible due to technical difficulties and the fact that often several newborns require attention concurrently. Without ET intubation, the delivery of PPV without concurrent compressions is highly important for breath efficacy, and effective ventilations are a higher priority in transitional newborns. The studies above suggested lower C:V ratio will support higher TV and higher efficacy of breaths [214, 217–219]. However, lower C:V ratios will also lead to reduced chest compressions delivered per minute, which could compromise blood flow and thus oxygen delivery to vital organs. To balance the need for a low C:V ratio to optimize ventilation with the need for an adequate number of compressions per minute, we suggest a C:V ratio of 4:1, while the chest compressions should be delivered at 150 compressions per minute. Mathematical modeling suggests that a higher compression rate than in adult dogs and cats is preferable in newborns (100–800 g bodyweight) (see NB-12) [197]. In addition, newborn puppies and kittens are markedly smaller than the piglets (>2 kg body weight) included in the study by Pasquin and colleagues [214]. The time required to deliver an adequate tidal volume is therefore shorter. We suggest delivering 150 actions per minute: 4 chest compressions followed by 1 breath (C:V = 4:1), repeated 30 times per minute (i.e., rounds of 4 chest compressions + 1 breath every 2 s). Over the course of 1 min, this will cumulatively amount to 120 compressions delivered at a tempo of 150/min and to 30 breaths.

6.5.5 | Knowledge Gaps

There is a need to determine (1) whether one C:V ratio is better than another in newborn puppies and kittens; (2) whether rescuers can administer compressions at a rate of 150/min; and

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(3) how many rounds of 4:1 CPR and in extension ventilations per minute are actually delivered with this strategy.

6.6 | Synchronization of Ventilation With Intubated PPV—NB-14

In newborn dogs and cats receiving chest compressions and PPV via ETT (P), how does pausing chest compressions to administer breaths (I), compared with simultaneous ventilations and chest compressions (C), improve outcome (O)?

6.6.1 | Introduction

Asphyxia is the main reason transitional newborns require PPV and CPR [220]. Transitioning from liquid- to air-filled lungs is the key objective early after birth, and therefore, effective ventilation plays a much larger role in the resuscitation of newborns at birth compared to adult animals [221]. For this reason, ventilation is prioritized in newborn CPR to facilitate aeration of the lungs and pulmonary gas exchange. Current resuscitation guidelines in people suggest a compression:ventilation (C:V) ratio of 3:1, synchronized such that compressions and ventilation are separated to ensure adequate tidal volume delivery; however, this constitutes a weak recommendation supported by very low quality of evidence [8, 191]. This PICO question asked on whether a similar approach in which chest compressions are interrupted to deliver breaths (i.e., synchronous ventilation) is beneficial in intubated newborn puppies and kittens, or whether breaths should be administered without interrupting chest compressions (i.e., chest compressions with simultaneous, asynchronous ventilation [CCaV]), in much the same way as is recommended for adult dogs and cats [11].

6.6.2 | Consensus on Science

For the most critical outcome of *favorable neurologic outcome*, we identified no studies addressing the question.

For the next most critical outcome of *survival to discharge*, we identified 3 experimental neonatal piglet studies that addressed the question (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [222–224]. All studies included post-transitional piglets that were 1–4 days old and thus animals that had aerated lungs and a closed ductus arteriosus. Asphyxiation was induced by clamping of the ETT. Piglets were randomized to receive resuscitation with either standard CPR (i.e., C:V ratio of 3:1, 90 compressions/min, 30 ventilations/min, $n = 28$ across the three studies) or CCaV with 90–120 compressions/min and 30 ventilations/min. Breaths were administered via a cuffed ETT. Survival rates to the end of the study period were reported, which varied between 2 and 4 h following ROSC, with a lower mortality noticed in the piglets resuscitated with CCaV (RR = 0.38, 95% CI 0.16–0.94). Survival to discharge as a clinical outcome was not directly assessed in any of these experimental animal studies, and none of the studies included transitional newborns.

For the important outcome of *surrogate markers of perfusion*, 5 experimental studies in piglets and 1 experimental study in newborn lambs were identified that addressed the question (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, imprecision, and inconsistency) [222–227]. All 5asphyxial arrests were induced by clamping the ETT or administering potassium chloride. They compared the effect of CPR delivered at a C:V ratio of 3:1 (90 compressions/min and 30 ventilations/min) or CCaV on a variety of circulatory metrics, including arterial blood pressure, carotid blood flow, carotid oxygen delivery, or lactate concentration. In the CCaV group, all studies used a compression rate of 120/min except 1 in which the compression rate was the same as in the synchronized ventilation group (90/min). Schmölzer et al. identified similar cardiac output, mean systemic and pulmonary arterial pressures, and regional blood flows between groups [222]. Mendler et al. found no difference between groups in lactate concentrations or mean arterial blood pressures during resuscitation or immediately after ROSC [223, 226]. In a fourth experimental piglet study, hemodynamic metrics immediately after ROSC (i.e., HR, arterial blood pressure, carotid blood flow) were also similar between groups [227]. In contrast to these studies, Aggelina et al. found improved hemodynamics with CCaV compared to 3:1 CV, including diastolic blood pressure (51 ± 18 mm Hg vs. 26 ± 6 mm Hg, $p < 0.001$) and coronary perfusion pressure (46 ± 17 mm Hg vs. 22 ± 6 mm Hg) during resuscitation [224]. Unlike the studies in swine, Vali et al. included near-term lambs ($n = 22$) that were asphyxiated during transition at birth by concurrently clamping the ETT and ligating the umbilical cord [225]. Animals in the CCaV group received 120 compressions/min, while those in the 3:1 C:V group received 90 compressions/min. No significant differences were found during CPR in diastolic blood pressure or lactate concentration, but CCaV was associated with significantly higher carotid blood flow (7.5 ± 3.1 mL/kg/min vs. 4.2 ± 2.6 mL/kg/min, $p < 0.01$) and cerebral oxygen delivery (0.40 ± 0.15 mL O_2/kg/min vs. 0.13 ± 0.07 mL O_2/kg/min, $p < 0.01$) compared to synchronized ventilations/compressions.

For the important outcome of *oxygenation*, we identified 3 experimental studies in neonatal piglets and 1 experimental study in newborn lambs (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [223, 225–227]. Synchronized administration of breaths (i.e., C:V ratio of 3:1) did not alter measures of arterial oxygenation (i.e., PaO_2, SaO_2) when compared to CCaV in any of the piglet studies either during resuscitation [226, 227] or immediately after ROSC [223, 227], nor was there any significant impact on cerebral oxygenation [227]. As previously mentioned, the studies in piglets were conducted in anesthetized, intubated, post-transitional animals at least 1 day old. The study by Vali et al. in newborn, transitional lambs showed significant improvement in SaO_2 and PaO_2 during resuscitation of animals ($n = 11$) with CCaV (SaO_2 = 33 ± 11%; PaO_2 = 22 ± 5.3 mm Hg) versus the synchronized group ($n = 11$; SaO_2 = 19 ± 7.5%; PaO_2 = 15 ± 3.5 mm Hg; $p < 0.01$) [225].

For the important outcome of *ventilation*, we identified 6 experimental studies (4 in neonatal piglets, 1 in newborn lambs, and 1 manikin study) that addressed the question (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [218, 222, 223, 225–227].

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The piglets involved were post-transitional, anesthetized, and intubated animals of at least 1 day of age [222, 223, 226, 227], while a single study in newborn lambs examined the question in transitional animals taking their first breaths [225]. In these studies, tidal volume or minute ventilation was not different between synchronized ventilation (C:V ratio of 3:1) and CCaV. In contrast, the median tidal volumes measured in a simulation-based study involving newborn infant manikins were higher when CPR was administered with synchronized ventilation (C:V ratio of 3:1) compared to CCaV (22.3 mL [IQR 1.9] vs. 19.7 mL [IQR 2.4], $p = 0.002$) [218].

Multiple animal studies reported $PaCO_2$ as an outcome [222, 223, 225, 226]. Schmölzer et al. found in a post-transitional piglet model of newborn CPR that the $PaCO_2$ values immediately after ROSC were lower with synchronous ventilation ($n = 6$, $PaCO_2 = 55 \pm 10$ mm Hg), compared to CCaV ($n = 5$, $PaCO_2 = 81 \pm 25$ mm Hg, $p < 0.05$) [222]. In another post-transitional piglet study involving 10 animals per group, median $PaCO_2$ values trended in the opposite direction: with synchronous (C:V = 3:1) ventilation, the $PaCO_2$ values were 100.8 mm Hg (IQR 25) compared to CCaV (74.1 mm Hg; IQR 14.6), though the difference did not reach significance ($p = 0.077$) [226]. In the study including transitional lambs, which is most direct to the population of newborn puppies and kittens relevant to this question, the $PaCO_2$ values were similar in animals receiving synchronous ventilation ($n = 11$, 119 ± 14 mm Hg) and those undergoing CCaV ($n = 11$, 112 ± 20 mm Hg, $p = 0.38$) [225]. Furthermore, no difference in $PaCO_2$ immediately after ROSC was found in post-transitional piglets undergoing synchronous or asynchronous ventilation during CPR [223, 227].

For the important outcome of *hospital length of stay*, we identified no studies addressing the question.

6.6.3 | Treatment Recommendations

In newborn puppies and kittens receiving chest compressions and PPV with a cuffed ETT in place, we suggest delivering breaths concurrently to chest compressions (asynchronized ventilation) (weak recommendation, very low quality of evidence).

In newborn puppies and kittens receiving chest compressions and PPV that are not intubated with a cuffed ETT, we recommend synchronized ventilation by pausing chest compressions to deliver breaths (strong recommendation, expert opinion).

6.6.4 | Justification of Treatment Recommendation

In adult dogs and cats undergoing chest compressions that are intubated, current guidelines recommend continuous chest compressions with asynchronous (simultaneous) ventilation [11]. However, there are no data in human literature and very limited information from experimental animal models addressing the question of ideal timing and delivery of breaths in newborns. In addition, none of the piglets used in the animal research were transitional newborns but 1–10 days old with aerated lungs and breathing spontaneously prior to induction of cardiac arrest [222–224, 226, 227]. As such, very serious indirectness limits the confidence with which the findings of these studies can be applied to our PICO question. While we found CCaV improved short-term survival (to 2–4 h after ROSC) in the pooled data from the 3 piglet studies ($n = 28$ per group), it is uncertain how this applies to survival in a clinical environment for newborn, transitional puppies and kittens [222–224]. A single study in newborn, transitional lambs did not show any difference in ROSC rates or time to ROSC between synchronized compressions/ventilation and CCaV (91% in each group), but a post-ROSC observation period was not reported in this study [225]. Likewise, ROSC rates and time to ROSC reported in 4 of the aforementioned piglet studies were similar with a synchronized approach (C:V = 3:1) or with CCaV [222–224, 227]. However, both surrogate markers of perfusion and oxygenation were improved by CCaV in transitional lambs compared to a synchronized approach to compressions and ventilation [225]. Taken together, we decided to suggest CCaV over synchronized compressions and ventilation during CPR of newborn puppies and kittens with a cuffed ETT in place.

Recent experimental studies in animals and 2 small clinical trials in newborn infants have also explored alternative methods of ventilation during CPR, specifically the so-called SI [228–233]. With SI, the lungs are inflated to a peak pressure of 20–30 cm H_2O, and this inflation is maintained for 20–30 s, followed by deflations of 1-s duration, another SI, and so forth. Chest compressions are delivered concurrently. The preponderance of the study results thus far showed a faster return to ROSC with SI, compared to the synchronized C:V = 3:1 approach, but no significant impact on ROSC rates or survival. However, many of these studies were very small and thus underpowered so that data are preliminary and further investigations are required. Moreover, a cuffed ETT is required for SI to avoid excessive leakage from the airway, which is unfeasible in most newborn puppies and kittens.

While we suggest CCaV for newborns that are intubated with a cuffed ETT, we provide a strong recommendation for the use of synchronized ventilation and compressions in newborns undergoing CPR that are not intubated with a cuffed ETT (i.e., uncuffed or no ETT). While we could not locate any evidence to support this treatment recommendation, it is based on the premise that breaths delivered by bag and mask during ongoing chest compressions may not lead to adequate lung expansion and thus could fail to achieve critically important lung aeration in newborn puppies and kittens with asphyxial cardiac arrest.

6.6.5 | Knowledge Gaps

The optimal ventilation strategy in intubated newborn puppies and kittens undergoing CPR is uncertain, with very few experimental animal studies and no clinical studies in people examining this question in transitional newborns.

6.7 | Epinephrine During CPR—NB-21

In newborn dogs and cats with very low HR (e.g., HR < 50/min) despite adequate PPV and chest compressions (P), how does routine parenteral administration of no epinephrine (I), compared with epinephrine administration (C), improve outcome (O)?

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6.7.1 | Introduction

Epinephrine is recommended for adult dogs and cats undergoing chest compressions with asphyxial (nonshockable rhythm) CPA [11], and asphyxia is the main reason transitional newborns require PPV and in some cases CPR [220]. It is unknown whether transitional puppies and kittens receiving chest compressions for persistent, severe bradycardia (i.e., HR < 50/min) or cardiac arrest benefit from routine parenteral administration of epinephrine.

6.7.2 | Consensus on Science

No studies reporting were identified in the initial literature search that addressed any of the critical and important outcomes of this PICO question.

A Medline search performed on November 24, 2024, using the following search term strategy: "(((epineph*[Title/Abstract] OR adren*[Title/Abstract])) AND (pupp*[Title/Abstract] OR kitten[Title/Abstract])) AND ((CPR[Title/Abstract] OR chest compress*[Title/Abstract]))," returned 2 articles, neither relevant to the PICO question [234, 235]. Searches for other Newborn PICO questions yielded many relevant experimental studies in transitional lambs. Thus, on November 29, 2024, a Medline search was performed using the following search term strategy: "(((epineph*[Title/Abstract] OR adren*[Title/Abstract])) AND (lamb*[Title/Abstract])) AND ((CPR[Title/Abstract] OR chest compres*[Title/Abstract]))," which returned 22 articles, all experimental studies in lambs.

Eight identified experimental transitional lamb studies (moderate quality of evidence, downgraded for serious indirectness and imprecision, upgraded for large effect and dose-response relationship) were relevant to the PICO question [236–243].

Two of these studies investigated parenteral epinephrine compared to saline placebo during chest compressions and PPV in asphyxiated, transitional, term lambs [239, 242]. Polglase et al. showed that 9 out of 9 lambs treated with IV epinephrine at 0.02 mg/kg achieved ROSC versus only 1 out of 6 lambs treated with saline placebo ($p < 0.01$); allocation of animals to the saline placebo group was stopped short of the target of nine subjects because investigators felt it unethical to continue to allocate animals to placebo [239]. Songstad et al. found IV epinephrine (50 μg, ~0.012 mg/kg; six lambs) led to faster ROSC (mean 2.4 ± SEM 0.4 min) than did IV saline placebo (11.2 ± 1.2 min, five lambs; $p < 0.05$) [242]. Thus, both of these studies support the use of epinephrine in transitional newborns undergoing CPR.

One of the studies compared epinephrine to vasopressin. A study by Rawat et al. found no difference in ROSC incidence or time to ROSC when lambs were treated with 0.03 mg/kg epinephrine IV (7/10 achieved ROSC in 8 ± 2 min) versus 0.4 U/kg vasopressin IV (3/9 achieved ROSC in 13 ± 6 min) [240].

Seven studies in asphyxiated, transitional, term lambs compared various parenteral routes of epinephrine during PPV and chest compressions and their impact on ROSC [236–239, 241–243]. Roberts et al. studied the effect of IO epinephrine compared to IV epinephrine on the incidence of and time to ROSC in asphyxiated, transitional, near-term lambs. This study found no difference in ROSC incidence when lambs were treated with epinephrine IV (10/12) versus IO (7/9); similarly, there was no difference in the number of epinephrine doses required or time to ROSC between the 2 groups. $[\text{Epinephrine}]_{pl}$ was similar at all studied time points between the 2 groups [241]. Thus, this study supports the use of IO epinephrine if IV access is difficult or not possible. Four studies using similar asphyxiated, transitional, term lamb resuscitation models evaluated IV epinephrine (doses 0.01–0.03 mg/kg) versus ET epinephrine at 0.1 mg/kg [237, 239, 242, 243]. All 4 studies showed more rapid achievement or higher incidence of ROSC with standard (0.01–0.03 mg/kg) IV epinephrine doses compared to 0.1 mg/kg epinephrine given endotracheally. Some of these studies also evaluated $[\text{epinephrine}]_{pl}$ and found significantly lower and/or delayed increases in $[\text{epinephrine}]_{pl}$ in lambs treated with ET epinephrine compared to those treated IV [237, 243]. These 4 studies uniformly found ET epinephrine at 0.1 mg/kg inferior to standard dose IV epinephrine for achieving ROSC in asphyxiated transitional lambs. The Polglase study allocated 1 group (9 lambs) to receive high-dose (1 mg/kg) ET epinephrine and found no difference in ROSC incidence between the high-dose ET epinephrine group (7/9) compared to the group of lambs that received epinephrine 0.02 mg/kg IV (9/9); however, epinephrine 1 mg/kg ET led to delayed ROSC compared to 0.02 mg/kg IV epinephrine ($p < 0.001$). Also, high-dose ET epinephrine was associated with more cerebral microbleeds than the standard IV epinephrine group in this study [239]. Finally, Nair et al. showed peak $[\text{epinephrine}]_{pl}$ was lower in transitional lambs compared to post-natal lambs when epinephrine was given by the ET route [238]. Two studies evaluated intranasal (IN) epinephrine compared to standard IV administration [237, 242]. Songstad et al. allocated IN epinephrine (0.125 mg/kg) and IV epinephrine (0.0125 mg/kg) to 6 asphyxiated, transitional, term lambs and found that lambs randomized to IV epinephrine achieved ROSC faster (mean 2.4 ± SEM 0.4 min) than lambs that received IN epinephrine (9.2 ± 2.2 min; $p < 0.05$). Lambs allocated to IN epinephrine also received a significantly larger total dose of epinephrine to achieve ROSC than those that received epinephrine IV [242]. Similarly, de Jager et al. found time to ROSC was significantly shorter in eight lambs treated with 0.02 mg/kg epinephrine IV (173 ± SD 32 s) compared to seven lambs given 0.1 mg/kg epinephrine IN (401 ± 175 s; $p < 0.05$). This study also found lower, delayed $[\text{epinephrine}]_{pl}$ in lambs treated with IN compared to IV epinephrine [237]. The effect of IM administration of epinephrine was examined by Berkelhamer and colleagues, who administered epinephrine 0.1 mg/kg IM (deltoid muscle) to four asphyxiated, transitional, term lambs during PPV and chest compressions and found no increase in $[\text{epinephrine}]_{pl}$ with IM epinephrine administration until after ROSC [236].

6.7.3 | Treatment Recommendations

In newborn puppies and kittens with very low HR (i.e., HR < 50/min) despite 60 s of adequate PPV and chest compressions, we recommend the administration of epinephrine (strong recommendation, moderate quality of evidence).

In newborn puppies and kittens with very low HR (i.e., HR < 50/min) despite 60 s of adequate PPV and chest compressions, we recommend IV or IO administration of epinephrine over intratracheal or IN administration (strong recommendation, moderate quality of evidence).

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In newborn puppies and kittens with very low HR (i.e., HR < 50 bpm) despite adequate PPV and chest compressions, we suggest against IM administration of epinephrine (including intralingual IM administration) (weak recommendation, very low quality of evidence).

6.7.4 | Justification of Treatment Recommendation

While no clinical trials were identified that compared epinephrine using various doses (including placebo) or routes during resuscitation of transitional newborns in any species, the experimental data are reasonably convincing that parenteral epinephrine improves ROSC rates in asphyxiated, transitional lambs. Additionally, given that the studied population of asphyxiated, term, transitional lambs varies from transitional puppies and kittens only in species, and the high conservation of adrenoreceptors across species, it is likely that the findings of these studies apply to newborn puppies and kittens. The dose–response relationship of $[epinephrine]_{pl}$ with ROSC rate across the studies further supports the usefulness of epinephrine in this setting. Thus, we recommend parenteral epinephrine in newborn puppies and kittens undergoing CPR. The transitional lamb models on which this recommendation is based all included a period of PPV alone, followed by the institution of chest compressions for 30–120 s before drug administration; some lambs were resuscitated with only PPV and/or chest compressions prior to randomization (i.e., without medication). Therefore, we recommend epinephrine administration in transitional puppies and kittens only if HR remains <50/min despite 1 min of PPV and chest compressions. Regarding the route of epinephrine, the transitional lamb studies evaluated here consistently showed better outcome (faster ROSC) with IV epinephrine compared to other routes (ET, IN) [237, 239, 242, 243], though in 1 study, higher dose (1 mg/kg) of ET epinephrine was found efficacious at the cost of more cerebral microbleeds [239]. Similarly, IN epinephrine was associated with delayed ROSC in two studies [237, 242] and a higher total epinephrine dose [242] than IV epinephrine. Meanwhile, IO epinephrine was found noninferior to IV epinephrine [241]. Intramuscular epinephrine administration failed to increase $[epinephrine]_{pl}$ in 4 asphyxiated transitional lambs, and thus, there are inadequate data to support the use of epinephrine via the IM route in this setting [236]. There is no evidence to suggest sublingual IM injection of epinephrine has a different effect. Therefore, we recommend IV or IO epinephrine, with ET or IN administration reserved for cases in which IV or IO access is not possible or significantly delayed. However, we emphasize the fact that ET administration is challenging given the small patient size, and the risk of harm due to upper airway injury must be carefully balanced against the benefit.

These recommendations align with guidelines for resuscitation of newborn infants, which recommend epinephrine IV or IO if CPR alone does not increase the HR above the threshold for instituting chest compressions [8]. If IV or IO access is not available, human guidelines recommend ET epinephrine administration at a higher dose (approximately 10 times) in newborn infants [8]. These human guidelines base their recommendations largely on 2 observational studies in a total of 97 infants whose findings align with those of the lamb studies evaluated here [244, 245]. Specific epinephrine dosage and administration interval are addressed in NB-22.

Comparison of epinephrine with other vasoconstrictor(s) in transitional newborns requiring chest compressions and PPV for severe bradycardia was outside the scope of this PICO question; thus, investigations regarding other vasopressors would not have been reliably identified by the searches performed. Therefore, no recommendation can be made regarding other vasoconstrictors in this population.

6.7.5 | Knowledge Gaps

No studies regarding the use of epinephrine in transitional puppies and kittens requiring chest compressions and PPV are available. However, based on the strong experimental evidence of epinephrine's utility in lambs in similar conditions, we do not believe a comparison of epinephrine to placebo in newborn puppies and kittens is justified. Rather, comparison of epinephrine to other vasopressor(s), evaluation of varying vasopressor doses, and comparison of various administration routes in transitional puppies and kittens requiring chest compressions and PPV are warranted.

6.8 | Epinephrine Dose During CPR—NB-22

In newborn dogs and cats with a very low HR (i.e., HR < 50/min) despite adequate PPV and chest compressions (P), does a different dose of IV/IO epinephrine (I), compared with 0.01 mg/kg IV/IO (C), improve outcome (O)?

6.8.1 | Introduction

In human newborn resuscitation, the administration of chest compressions and epinephrine in the delivery room is uncommon and affects only 2% of newborn infants receiving PPV [246, 247]. This is because newborn resuscitative measures are administered in most cases at a time when a heartbeat is still detectable, and the primary goal of care is to improve pulmonary gas exchange to reverse asphyxiation. It is anticipated that the circulation will improve once oxygenation has normalized. However, when the HR is very low (e.g., <50/min in puppies and kittens) and chest compressions are administered, epinephrine might increase coronary and cerebral blood flow in this situation as it does in the adult animals (see NB-02 and NB-21). In adult dogs and cats, high-dose epinephrine (i.e., 0.1 mg/kg IV/IO) is not recommended as it could compromise outcome [248]. In newborn puppies and kittens with an HR of <50/min despite adequate PPV and chest compressions, it is unknown whether a standard 0.01 mg/kg epinephrine IV/IO dose is optimal, or whether a different dose may lead to better outcomes.

6.8.2 | Consensus on Science

For the critical outcome of *favorable neurologic outcome*, we identified 1 experimental study in 3-month-old pigs with asphyxial

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CPA (very low quality of evidence, downgraded for very serious indirectness and imprecision) that addressed the PICO question [249]. This study demonstrated no benefit or harm of epinephrine at 0.1 mg/kg IV compared to epinephrine at 0.01 mg/kg IV on functional outcome. All animals had severe neurological deficits at the end of the study, 24 h after ROSC. Of note, the preplanned search did not identify any studies that directly evaluated epinephrine dosing in transitional newborns of any species. Consequently, the quality of evidence as in the study above is compromised by very serious indirectness.

For the critical outcome of *survival to discharge*, we found 2 clinical trials in human pediatric patients [250, 251] (very low quality of evidence, downgraded for very serious indirectness and imprecision) and 1 study in adolescent swine [249] (very low quality of evidence, downgraded for very serious indirectness and imprecision) that addressed the PICO question. Two of these studies showed no survival benefit of high-dose epinephrine (0.1 mg/kg or higher) when compared to standard dosing [249, 251]. Perhaps most concerning, in 1 study, none of the children in the subgroup with asphyxial cardiac arrest survived after high-dose (0.1 mg/kg) epinephrine, while a survival rate of 21% was noted in children receiving low-dose epinephrine only ($p = 0.02$) [250]. In addition, the aforementioned swine study by Berg and colleagues suggested a potentially harmful effect of high-dose epinephrine on post-resuscitation morbidity, with 4 of 15 animals not surviving 2 h after ROSC, while all animals in the low-dose group survived [249]. However, at 24 h after ROSC, there was no difference, with 3 of 15 animals surviving in each group.

For the important outcome of *hospital length of stay*, we identified no studies addressing the PICO question.

We identified 2 experimental studies reporting *hemodynamic surrogate measures* (very low quality of evidence, downgraded for very serious indirectness and imprecision) that addressed the PICO question [249, 252]. In newborn lambs with asphyxiation-induced severe bradycardia and circulatory compromise but not CPA, an epinephrine dose of 0.1 mg/kg IV led to increased afterload and reduced cardiac output compared to any lower dose [252]. In adolescent swine with asphyxial cardiac arrest undergoing CPR, intra-arrest high-dose but not low-dose epinephrine was associated with post-cardiac arrest tachyarrhythmias [249].

For the important outcome of *histopathologic damage*, we identified no studies addressing the PICO question.

Searches for other newborn PICO questions yielded many experimental studies in transitional lambs that reported outcomes not considered above, including ROSC. Thus, on November 29, 2024, a Medline search was performed using the following search term strategy: "(((epineph*[Title/Abstract] OR adren*[Title/Abstract])) AND (lamb*[Title/Abstract])) AND ((CPR[Title/Abstract] OR chest compres*[Title/Abstract]))," which returned 22 articles, all experimental studies in lambs. Of the 22 studies identified, two experimental, term, transitional lamb studies (very low quality of evidence, downgraded for very serious indirectness and imprecision) were relevant to the PICO question [239, 253]. Sankaran et al. compared ROSC in 28 term, asphyxiated, transitional lambs randomized to four different IV epinephrine treatment groups: either 0.01 or 0.03 mg/kg IV epinephrine, followed by either 1 mL total volume or 3 mL/kg IV saline flush. Nine of 9 lambs in the group receiving 0.03 mg/kg epinephrine followed by 3 mL/kg saline flush achieved ROSC, whereas 5 of 7 that received 0.03 mg/kg epinephrine IV followed by 1 mL total volume saline flush achieved ROSC, and only 2 of 6 and 3 of 6 receiving 0.01 mg/kg epinephrine followed by 1 or 3 mL/kg saline flush, respectively, achieved ROSC [253]. In this study, asphyxiated transitional lambs receiving 0.03 mg/kg epinephrine IV had improved ROSC compared to those that received 0.01 mg/kg epinephrine IV ($p = 0.04$), regardless of flush volume. Both 0.03 mg/kg epinephrine dose ($p = 0.005$) and higher flush volume ($p = 0.02$) were associated with faster ROSC [253]. Polglase et al. studied 33 term transitional lambs using an asphyxiation model of arrest. Nine of 9 lambs in the reference group receiving 0.02 mg/kg epinephrine IV achieved ROSC. Of the lambs that received 0.1 mg/kg epinephrine via ET route, none achieved ROSC (0/9; $p < 0.0001$ vs. IV epinephrine 0.02 mg/kg). However, when lambs were treated with a higher dose of 1 mg/kg epinephrine ET, ROSC rates were comparable to the group that received IV epinephrine 0.02 mg/kg (7/9 lambs; $p > 0.05$ compared to IV epinephrine group) and were higher than ROSC rates in lambs that received only 0.1 mg/kg epinephrine ET ($p < 0.001$ vs. standard-dose ET epi). Lambs receiving 1 mg/kg epinephrine ET experienced more cerebral microbleeds than those receiving epinephrine using other doses and routes [239].

6.8.3 | Treatment Recommendations

In newborn puppies and kittens that remain very severely bradycardic (i.e., HR < 50/min) despite 60 s of PPV and chest compressions, we recommend 0.01–0.03 mg/kg epinephrine IV/IO (strong recommendation, very low quality of evidence).

In newborn puppies and kittens that remain vseverely bradycardic (i.e., HR < 50/min) despite 60 s of PPV and chest compressions, we recommend against high-dose epinephrine (0.1 mg/kg IV/IO) (strong recommendation, very low quality of evidence).

In newborn puppies and kittens that remain very severely bradycardic (i.e., HR < 50/min) despite 60 s of PPV and chest compressions, in which epinephrine is given endotracheally because IV/IO access is not possible or significantly delayed, we suggest 0.05–0.1 mg/kg epinephrine ET (weak recommendation, very low quality of evidence).

6.8.4 | Justification of Treatment Recommendation

No studies regarding the use of epinephrine in transitional puppies and kittens requiring chest compressions and PPV are available. However, 1 experimental study in asphyxiated, term, transitional lambs showed improved ROSC when 0.03 mg/kg IV epinephrine was administered compared to 0.01 mg/kg IV [253]. As this was a single study in a nontarget species, the direct applicability of this finding is uncertain, and thus,

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evidence is considered of very low quality for this PICO. Given the reports of harm with epinephrine doses of more than 0.05 mg/kg epinephrine IV/IO [249, 250], we suggest avoiding these higher IV/IO epinephrine doses until more direct evidence becomes available. We have some concern that different dose recommendations in newborns (i.e., 0.03 mg/kg IV in newborns vs 0.01 mg/kg IV in adults) may confuse rescuers. Thus, we elected to recommend an acceptable range of 0.01–0.03 mg/kg epinephrine IV/IO in newborn puppies and kittens with a very low HR (i.e., HR < 50/min) despite 60 s of PPV and chest compressions. The IO route appears in the treatment recommendation as an equivalent choice because a study evaluating for NB-21 found that IO epinephrine was noninferior to IV epinephrine in asphyxiated, term, transitional lambs [241]. Our IV/IO dosing recommendation for epinephrine mirrors the recommendation in human newborns undergoing CPR [8].

When IV/IO access is not possible or significantly delayed, ET epinephrine administration may be a viable option (see NB-21). One experimental study in asphyxiated, term, transitional lambs found 0.1 mg/kg epinephrine ET was inferior to 0.02 mg/kg epinephrine IV for achieving ROSC [239]. This study also found that when lambs were treated with a higher dose of 1 mg/kg epinephrine ET, ROSC rates were comparable to the group that received IV epinephrine 0.02 mg/kg at the expense of more cerebral microbleeds. Considering the paucity of clear evidence even in this indirect population, we elected to mirror the human newborn recommendation of 0.05–0.1 mg/kg ET epinephrine in newborn puppies and kittens undergoing CPR when IV/IO access is not possible or severely delayed [8].

6.8.5 | Knowledge Gaps

There is currently no evidence that explores the question of epinephrine dosing in transitional newborn puppies and kittens, and such information is critically important to inform a recommendation with higher certainty.

6.9 | Atropine During CPR—NB-24

In newborn dogs and cats that require resuscitation that are in CPA (P), how does routine parenteral administration of atropine (I), compared with no atropine administration (C), improve outcome (O)?

6.9.1 | Introduction

Atropine, a parasympatholytic, is recommended to prevent CPA in adult animals with bradycardia secondary to high vagal tone. However, atropine has been removed from human CPR guidelines due to lack of evidence for its benefit. The 2024 RECOVER CPR Guidelines suggest that atropine may be administered once and early during CPR in adult dogs and cats with nonshockable arrest rhythms, especially if CPA was preceded by vagally mediated bradycardia [11, 248]. This question investigates whether newborn puppies and kittens requiring resuscitation with chest compressions would benefit from the routine administration of atropine.

6.9.2 | Consensus on Science

For the most critical and important outcomes of survival to discharge, favorable neurologic outcome, hospital length of stay, surrogate markers of perfusion, and histopathologic damage, no studies were identified.

6.9.3 | Treatment Recommendations

In newborn puppies and kittens that require resuscitation that are in CPA, we suggest against the routine administration of atropine during CPR (weak recommendation, expert opinion).

6.9.4 | Justification of Treatment Recommendation

We did not identify any evidence in any direct population for species (dog or cat), life stage (transitional newborn), and circumstance (CPA) to inform the treatment recommendation. In puppies or kittens born free of overt fatal defects (e.g., anasarca, gastroschisis), the most likely reversible cause of CPA is hypoxemia associated with acute peri-parturient events. Hypoxemia causes severe bradycardia in fetuses and newborns, which can be so severe and prolonged that it leads to CPA.

CPA in the newborn puppy or kitten may be due to asystole progressing from severe bradycardia; hypoxemia-induced bradycardia has been shown to be vagally mediated in near-term lamb models [94, 139]. Additionally, late fetal or newborn canine, ovine, and human cardiac myocytes experiencing vagally mediated bradycardia have the capacity to respond to atropine [94, 140, 141]. That said, the priority during resuscitation of the newborn in distress is support of the transition from intrauterine to extrauterine physiology with aeration of the lungs; in other words, the priority lies in support of the respiratory system. While newborn puppies and kittens in CPA or with severe bradycardia (i.e., HR < 50/min) should receive chest compressions to facilitate circulation, the primary focus lies on lung aeration with PPV rather than on the administration of medications.

While there is no evidence that a single parenteral dose of atropine would itself harm a newborn puppy or kitten in CPA, we believe time and resources are best directed to respiratory support with PPV and chest compressions to aid in the delivery of oxygen to hypoxic tissues, including the myocardium.

6.9.5 | Knowledge Gaps

Whether routine parenteral atropine administration in newborn puppies or kittens would improve outcomes is unknown. This knowledge gap is currently considered of low priority, considering the lack of evidence that atropine administration is associated with improved survival for dogs and cats in CPA at any life stage. Additionally, the overwhelming majority of newborns with reversible-cause CPA have experienced CPA due to severe hypoxemia, a problem not improved using parasympatholytic drugs.

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6.10 | Oxygen Supplementation During CPR—NB-18

In newborn dogs and cats receiving chest compressions (P), how does ventilation with any other oxygen concentration (I), compared with 100% oxygen (C), improve outcome (O)?

6.10.1 | Introduction

Oxygen supplementation has been an integral part of resuscitation in newborn puppies and kittens, and was recommended in people until the turn of this century [34]. However, PPV with 100% oxygen and the associated hyperoxemia were found in experimental animal studies and clinical research in newborn infants to lead to a number of injurious effects including inflammatory changes to the heart, lung, and brain; kidney and myocardial injury; oxidative stress; lower Apgar scores; and other harmful effects without concurrent benefit [254]. On the flip side, sustained hypoxia can be harmful as well, in particular leading to worsening of HIE. Based on current evidence, we suggest using room air for the first 1–2 min of PPV in newborn puppies and kittens that do not require chest compressions. Administration of 100% oxygen is only suggested if the HR continues to be low despite 1–2 min of PPV (see NB-03). The current question specifically interrogates what oxygen treatment strategy to use in those newborn puppies and kittens that require chest compressions. These are newborns that either have no detectable HR at birth or have maintained or developed severe bradycardia (i.e., HR < 50/min) or cardiac arrest despite initial PPV. As such, only literature pertaining directly to oxygen administration during newborn CPR was examined, and research studying oxygen treatment strategies during PPV only without chest compressions was reviewed elsewhere (see NB-03).

6.10.2 | Consensus on Science

For the most critical outcome of *survival to discharge*, we located 5 experimental studies that addressed the PICO question (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [160, 161, 215, 255, 256]. These studies were all conducted in post-transitional piglets of 14–72 h of age, with one study including animals up to 23 days of age. As these populations differ from transitional newborn puppies and kittens, we considered the information obtained from these studies compromised by very serious indirectness. Regardless, all studies revealed no difference in short-term survival rates (i.e., to the end of the study at 4 h after ROSC) when PPV was administered with room air versus 100% oxygen during chest compressions, both when analyzed individually and when pooling the data (RR = 0.96, 95% CI 0.78–1.19, $p = 0.70$) [160, 161, 215, 255, 256].

For the critical outcome of *favorable neurologic outcome*, we identified no studies addressing the question.

For the important outcome of *oxygenation*, we located 4 experimental studies that addressed the PICO question (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and serious imprecision) [160, 161, 257, 258]. Solevag et al. reported in 2 different studies involving an asphyxial cardiac arrest model of post-transitional piglets (age 14–72 h) the impact of FiO_2 (i.e., 0.21 vs. 1.0) on metrics of oxygenation [160, 161]. These oxygenation metrics, including SpO_2 and cerebral and renal oxygenation measured by near-infrared spectroscopy (NIRS), were obtained not during chest compressions but immediately after ROSC. At that time, no significant effect of FiO_2 on brain or kidney NIRS was identified [161], although SpO_2 was found to be higher in the 100% O_2 group (SpO_2 = 95 ± 10%) compared to the room air group (SpO_2 = 88 ± 6%, $p = 0.029$) [160]. Continued ventilation with 100% oxygen after ROSC led to higher than baseline SpO_2 and supranormal cerebral oxygen saturation when compared to room air [160]. A single study by Sankaran et al. evaluated the effect of inspiratory oxygen concentration on oxygenation metrics in a near-term transitional lamb resuscitation model [258]. In this study, lambs were exteriorized via C-section, followed by asphyxiation to asystole by umbilical cord occlusion and ETT clamping. Animals were then delivered, the umbilical cord was ligated, and resuscitation was started after 5 min of asystole. Animals were randomized to receive CPR with PPV at an FiO_2 of 0.21 ($n = 6$) or 1.0 ($n = 13$). After ROSC, FiO_2 in the pure oxygen group was either abruptly ($n = 6$) or gradually ($n = 7$) reduced to meet preductal SpO_2 targets during the 1-h post-cardiac arrest observation period. During chest compressions, the PaO_2 values were similar in animals resuscitated with room air (10.7 ± 4.3 mm Hg) and 100% oxygen (18.5 ± 5.5 mm Hg gradual group; 13.7 ± 11.0 mm Hg abrupt group) but were remarkably low. Fetal PaO_2 pre-asphyxiation varied between 20 ± 8 mm Hg and 25 ± 3 mm Hg. Likewise, the cerebral oxygen delivery during chest compressions was similar across groups (room air: 0.06 ± 0.02 mL/kg/min; 100% O_2 groups: 0.07 ± 0.07 mL/kg/min to 0.08 ± 0.07 mL/kg/min) and was a fraction of fetal values prior to asphyxiation (room air: 3.0 ± 1.3 mL/kg/min; 100% O_2 groups: 2.9 ± 0.7 to 2.7 ± 11 mL/kg/min). Rawat et al. used a similar transitional lamb model and reported similar PaO_2 values during chest compression and ventilation (C:V = 3:1) with either 100% oxygen (n = 16, 23.9 ± 6.8 mm Hg) or room air (n = 6, 21.6 ± 1.6 mm Hg, $p = 0.16$) [257]. This study also documented very low average cerebral oxygen deliveries during CPR regardless of oxygen supplementation (100% oxygen group: 0.11 ± 0.09 mL/kg/min; air group: 0.05 ± 0.06 mL/kg/min; pre-asphyxia: 2.1 ± 0.3 mL/kg/min); however, maximum oxygen delivery at high peak flow during the chest compression phase of 3:1 CPR was markedly higher in the 100% group (1.4 mL/kg/min, IQR 0.35) compared to the room air group (0.08 mL/kg/min, IQR 0.2 , $p < 0.0001$). Immediately after ROSC, PaO_2 increased to hyperoxemic concentrations at almost 200 mm Hg if 100% oxygen was administered, and cerebral oxygen delivery was significantly higher with 100% oxygen (5 ± 2 mL/kg/min) compared to room air (3 ± 3 mL/kg/min).

For the important outcome of *hospital length of stay*, we identified no studies addressing the question.

For the important outcome of *histopathologic damage* including markers of tissue injury, we located seven experimental studies that addressed the PICO question (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [160, 161, 215, 255, 256, 258–260]. Six of these studies were conducted using the aforementioned post-transitional piglet models. In a series of experimental studies, Solevag and

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colleagues reported higher concentrations of myocardial GSSG:GSH ratio, a marker of oxidative stress, in 1 study when animals received 100% oxygen during chest compressions [255]; however, no effects on markers of oxidative injury (i.e., GSSG:GSH ratio in brain or heart) or tissue inflammation (IL-1β, IL-6, IL-8, and TNF-α in brain; IL-1β, IL-1β, MMP-2, and MMP-9 in heart) were found in most of the studies [160, 161, 255]. Dannevig and colleagues conducted two post-transitional piglet studies comparing the effect of ventilation with 100% and 21% oxygen during CPR on various metrics of brain (S100, MMP-2, MMP-9, IL-6, TNF-α, ICAM-1, and Caspase 3) and lung (IL-8, TNFα, ICAM-1, MMP-2, and MMP-9) injury and found no significant effects on these markers [215, 260]. Nyame et al. in their asphyxial arrest model using more mature piglets (20–23 days old) also did not find any effect of PPV with 100% during CPR on the GSSG:GSH ratio in the brain ($p = 0.39$), heart ($p = 0.32$), or lung ($p = 0.07$) 30 min after ROSC [256]. Finally, Sankaran et al. in a transitional asphyxiation model in lambs did not find any difference in markers of oxidative injury (hypoxanthine/xanthine ratio, methionine sulfoxide/methionine ratio) in the plasma or brain, although the study may have been underpowered for these outcomes [258].

6.10.3 | Treatment Recommendations

In newborn puppies and kittens receiving chest compressions, we suggest PPV with 100% oxygen (weak recommendation, very low quality of evidence).

6.10.4 | Justification of Treatment Recommendation

When making this recommendation, we considered the fact that at the time when chest compressions are initiated, the newborn puppy or kitten will already have received a period of PPV with room air and then 100% oxygen, yet still does not respond to these interventions. We therefore considered it reasonable to continue PPV with pure oxygen whilst chest compressions are initiated. This recommendation is made despite the majority of experimental studies in piglets indicating equipoise between PPV with room air and 100% oxygen during CPR [160, 161, 215, 255, 256, 260]. However, all these studies were conducted in post-transitional, healthy piglets with fully aerated lungs in which pulmonary gas exchange deficits are of minor concern. In contrast, the 2 studies in transitional animals, specifically lambs, suggest severe hypoxemia with PPV with room air, and in 1 study, resuscitation with 100% led to improved, although not normalized, cerebral oxygen delivery [257, 258]. If hyperoxemia occurred, then this was a post-cardiac arrest phenomenon, and evidence suggests it is reasonable to reduce the FiO_2 once ROSC is established, which might be the most effective strategy to prevent oxidative injury [257, 258]. The importance of post-resuscitation regulation of FiO_2 has also been demonstrated in a near-term lamb model by a different group of investigators [261].

Clinical studies are needed to provide more clarity on the benefits or harms of a high FiO_2 during CPR. The fact that we did not find any clinical studies conducted in the field is a testament to the legal and procedural difficulties of conducting clinical trials in newborn infants [233]. In addition, while around 5% of newborn infants require resuscitation with PPV in the delivery room, only around 2% of these progress to require chest compressions, and obtaining an adequate sample size is therefore challenging [246, 247]. Until clinical studies are available to provide more certainty in what oxygen strategy is optimal, we consider it prudent to provide PPV with 100% oxygen during CPR to minimize the risk of hypoxemia; following ROSC, it is reasonable to reduce FiO_2 if feasible to attenuate oxidative injury while avoiding hypoxemia.

6.10.5 | Knowledge Gaps

There are no clinical studies that directly examine the effect of ventilation with 100% versus 21% oxygen during CPR in transitional newborn puppies or kittens, or infants.

6.11 | Discontinuation of CPR—NB-25

In newborn dogs and cats receiving chest compressions (P), how does continuation of well-executed chest compressions beyond 10 min (I), compared with discontinuation of chest compressions after 10 min (C), improve outcome (O)?

6.11.1 | Introduction

Many newborns born without a heartbeat have experienced an indeterminate period of ischemia prior to birth and initiation of CPR. This potential for extended periods of a hypoxic–ischemic state prior to initiation of resuscitative efforts introduces variability and uncertainty regarding the usefulness of CPR efforts in newborns as a group. Certainly, there is a group of newborns for which the intrauterine period of hypoxia is brief enough that resuscitation at birth can lead to good outcomes, and so initiating CPR on individuals born without a heartbeat is reasonable in many cases. In addition, the rescuer does typically not know which newborns have potential for a good outcome at birth. Additionally, longer periods of the low-flow state experienced during CPR are associated with worse outcomes due to lack of adequate oxygen delivery to vital tissues such as the brain and heart.

Historically, ILCOR recommendations have stated it is reasonable to consider stopping resuscitative measures if a newborn's heartbeat remains undetectable for ≥10 min after birth [126]. However, more recent information shows that some individuals survive with good neurologic function if high-quality resuscitative measures continue despite remaining pulseless at ≥10 min, and updated human guidelines suggest individualizing the decision of when to terminate resuscitation if the newborn remains pulseless at ≥10 min [8, 59]. The prognosis for survival with a favorable neurologic outcome in newborn puppies and kittens undergoing CPR for more than 10 min at birth is unknown.

6.11.2 | Consensus on Science

For the most critical outcome of *survival to discharge*, we identified 5 observational studies (very low quality of evidence,

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downgraded for very serious risk of bias, serious indirectness, and imprecision) that addressed the PICO question [262–266]. Steiner et al. reported a single-center case series of 22 newborn infants with perinatal arrest, 14 of which occurred in the delivery room setting; 3 of these 14 infants underwent CPR for ≥10 min, and 2 survived beyond 1 and 2.5 years of age, respectively [262]. Sproat and others reported a series of 87 newborn infants with no audible heartbeat for the first 10 min of life (median time to heartbeat 16 min, range 10–35 min). Of the 87 infants, eight (9%) were alive at 2 years of age [265].

The 3 other studies suffer from a very serious risk of bias for this outcome based on selection criteria because only newborns who achieved ROSC were included; the survival results follow here. Patel et al. presented a case series of 29 full-term newborn infants with Apgar 0 (no detectable heartbeat) from birth to ≥10 min of life; median time to heartbeat was 15 min (range 11–40 min), and all cases included were successfully resuscitated at their birth hospital and were then presented at 1 of the study group's tertiary referral facilities. Therefore, overall survival cannot be determined from this study, but of the 29 infants included, 9 (31%) survived to hospital discharge [263]. Kasdorf et al. compiled cases from 4 prior clinical trials ($n = 81$) and added 9 author institution cases of newborns with an Apgar score of 0 at 10 min that either were ($n = 56$) or were not ($n = 34$) managed with therapeutic hypothermia (TH). With hypothermia being the study intervention, all included newborn infants had achieved ROSC to be enrolled in the TH trials. Overall mortality for babies with an Apgar score of 0 at 10 min who also lived to participate in the cooling trials was 50% (45/90) at 18 months of age [264]. Finally, a study by Shibasaki et al. in term newborn infants ($n = 28$) that had experienced an Apgar of 0 at 10 min after birth and were enrolled in a cooling study reported a survival rate of 68% (19/28) at ≥18 months of age [266]. These three studies would all overestimate the likelihood of survival in newborns with Apgar 0 at 10 min of age because only babies who achieved ROSC were included.

For the critical outcome of *favorable neurologic outcome*, we identified 5 observational studies (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) that addressed the PICO question [262–266]. These were the same studies already cited for the outcome of survival to hospital discharge. In the study by Steiner et al., the newborn infants who did survive did so with good neurologic outcomes beyond 1 and 2.5 years of age [262]. In the study by Sproat and colleagues that included 87 newborn infants who had no detectable heartbeat for at least 10 min after birth, 5 of the 9 surviving infants were neurodevelopmentally normal at ~2 years of age [265]. In the study by Patel et al., eight of the 9 surviving infants (89%) experienced severe disability, and 1 (11%) had moderate disability [263]. Kasdorf et al. found that of 90 newborn infants enrolled in the study, 27% (15/56) of those treated with hypothermia and 21% (7/34) in the normothermia group were neurologically normal at 18–24 months. Thus, overall, 22 out of 90 (24%) newborns that achieved ROSC following ≥10 min of CPR achieved a good long-term neurologic outcome [264]. The study by Shibasaki et al. found that of the 19 infants that survived to ≥18 months of age, 16 (84%) had severe disability based on psychological, motor, and intelligence scales, while 3 (16%) had normal neurologic outcome [266].

For the important outcomes of *length of hospital stay* and *histopathologic damage*, no studies were identified.

6.11.3 | Treatment Recommendations

In newborn puppies and kittens receiving chest compressions, we suggest continuation of CPR for at least 15 min before abandoning resuscitation efforts, as long as such efforts do not detract from necessary care of littermates with a better prognosis (weak recommendation, very low quality of evidence).

6.11.4 | Justification of Treatment Recommendation

Case series in newborn infants have shown that survival with a good neurologic outcome is possible even in babies with no heartbeat for 10 or more minutes after birth. Particularly considering the relatively lesser executive function expected from dogs and cats compared to people, survival with the opportunity to achieve adequate neurologic function was considered the most critical outcome. Reported numbers in the less biased populations are small: 2 out of 3 newborns survived in 1 small case series published in 1975 [262], while 8 out of 87 (9%) survived in another [265]. Such survival likelihood is similar to that for CPR in adult small animals, so it seems reasonable to pursue.

No evidence was found in newborn puppies and kittens, and many studies were biased because cases were selected from post-resuscitation study populations, which likely biases the results of those studies toward survival. Indeed, for infants who lived long enough to be enrolled in a cooling trial, survival to discharge was found to be 31% in 1 trial, and the 2 studies that followed babies to ≥18 months found survival of 50% and 68%. These high survival frequencies are unlikely in the general population of newborn puppies and kittens requiring resuscitation because every newborn infant enrolled in these studies had already achieved ROSC.

Moreover, we chose to suggest continuing CPR efforts in newborn puppies and kittens without spontaneous circulation for at least 15 min after birth, as long as such efforts do not detract from necessary care of littermates with a better prognosis. Other factors may influence the decision to perform CPR and its duration, including the presence of an obvious, severe congenital abnormality or clear signs of death (e.g., anasarca, depilation). As in newborn infants [8], the decision to discontinue resuscitative efforts after 15 min should be undertaken with both the clinical team's and the pet owner's goals in mind.

6.11.5 | Knowledge Gaps

It is important to better delineate what the survival rate, functional outcome, and level of post-resuscitation care requirements are in newborn puppies and kittens that undergo incremental durations of CPR.

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7 | Additional Interventions During Newborn Resuscitation

The final 6 PICO questions concern interventions considered adjunctive measures that have been recommended in the veterinary literature to support respiration (doxapram [NB-07] and GV 26 stimulation [NB-08]) or for metabolic support during and after resuscitation (glucose [NB-21 and NB-26]), or that have been shown to have a modulatory effect on HIE in newborn infants (TH [NB27] and rewarming rate [NB-28]) [16, 267].

7.1 | Doxapram—NB-07

In newborn dogs and cats that do not demonstrate adequate spontaneous ventilation efforts at birth (P), does administration of doxapram (I), compared with no administration of doxapram (C), improve outcome (O)?

7.1.1 | Introduction

Doxapram is an analeptic drug that can act as a respiratory stimulant through effects on peripheral (i.e., carotid and aortic chemoreceptors) and central (i.e., brainstem respiratory control center) sites [268]. The drug has historically been recommended and used to stimulate breathing in newborn puppies and kittens with apnea after delivery, with the first report in veterinary medicine published more than 50 years ago [269–271]. However, data supporting this intervention in transitional newborns are lacking and adverse effects might be a concern, though the clinical relevance of side effects is uncertain [268, 272]. This PICO question was asked to determine whether doxapram improves critical outcomes in newborn puppies and kittens that do not demonstrate adequate spontaneous ventilation efforts at birth.

7.1.2 | Consensus on Science

For the most critical outcome of *survival to discharge*, we identified 1 clinical trial (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) and one observational study (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) that addressed the PICO question [273, 274]. The clinical trial in preterm infants with apnea of prematurity found that doxapram decreased infants' apnea episodes when using the infants' pretreatment period as their own controls [274]. This study also found that survival was better in infants treated with both methylxanthines and doxapram compared to survival in control infants in whom doxapram was not used either because they did not have apnea or because their apnea responded to methylxanthines alone. After the literature search and evidence evaluation process were complete for this PICO question, another relevant clinical trial was published (moderate quality of evidence downgraded for serious indirectness) [275]. This study evaluated 7-day survival in 171 puppies delivered by elective C-section, randomized to receive either doxapram (~10.7 mg/kg) or placebo by intralingual injection at birth; all puppies for which investigators had time to assess Apgar scores were randomized, regardless of Apgar score. No difference was found in 7-day survival between puppies receiving doxapram (79/86, 92%) and those receiving placebo (80/85, 94%; $p = 0.634$) [275]. An observational study found a decreased risk of death or neurodevelopmental delay (combined outcome) in preterm infants treated with doxapram for persistent apnea of prematurity compared to those not treated with doxapram, even though those not receiving doxapram were less severely ill [273]. Overall, these 3 studies suggest doxapram may have a positive impact on survival in preterm infants with apnea of prematurity, and there is no evidence of survival benefit when doxapram is given indiscriminately to every puppy at birth.

For the critical outcome of *favorable neurologic outcome*, we identified 3 observational studies (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and inconsistency) that addressed the PICO question [273, 276, 277]. Czaba-Hnizdo et al. evaluated electroencephalography in preterm infants and found doxapram treatment was associated with a greater percentage of time in continuous activity, more electrographic evidence of seizure activity, and less sleep–wake cycling, suggesting possible harm in preterm infants [276]. Sreenan et al. investigated factors associated with isolated mental delay in infants weighing <1250 g at birth and showed that isolated mental delay was associated with total dosage and duration of doxapram therapy for severe apnea of prematurity [277]. However, authors acknowledge that confounding by indication makes it impossible to determine causality. Conversely, Ten Hove et al. showed that doxapram-treated preterm infants with apnea of prematurity had a lower risk of death or neurodevelopmental delay (combined outcome) after adjusting for confounding factors [273]. Thus, these 3 observational studies yielded conflicting information regarding the association of doxapram and neurologic outcomes, and all studies included preterm infants treated for apnea of prematurity in NICUs rather than newborn puppies or kittens treated at birth.

For the important outcome of *oxygenation*, we identified 3 clinical trials (very low quality of evidence, downgraded for very serious indirectness and imprecision) and three experimental studies (very low quality of evidence, downgraded for very serious indirectness and imprecision) that addressed the PICO question [142, 278–282]. A randomized controlled clinical trial of 24 newborn calves with neonatal asphyxia by Balikci et al. found that doxapram treatment led to higher PaO_2 compared to atropine or caffeine treatment (no placebo group) [142]. In a very small clinical trial of seven premature infants, Flint et al. found SpO_2 and HR increased, and that the number of desaturation events and time spent below SpO_2 80% decreased after initiating doxapram treatment for a duration of at least 36 h [282]. Poets et al. evaluated the effects of doxapram on hypoxemia in 15 preterm infants with apnea of prematurity and documented that doxapram decreased the frequency of hypoxemic events within 1 day of treatment, an effect that was sustained for 6 days [280]. In an experimental study in 5-day-old rats with bilateral carotid artery occlusion, Uehara et al. showed PaO_2 increased significantly (no p-value provided) to 53.9 ± 8.9 mm Hg at 15 min, 52.4 ± 9.9 mm Hg at 60 min, and 56.0 ± 5.4 mm Hg at 90 min following doxapram injection [281]. Bleul et al. documented that

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doxapram administration to calves at birth led to increased PaO_2 compared to baseline [278, 279].

For the important outcome of *ventilation ($PaCO_2$)*, we identified 4 clinical trials (very low quality of evidence, downgraded for very serious indirectness and imprecision), 2 observational studies (very low quality of evidence, downgraded for very serious indirectness and imprecision), and 5 experimental studies (very low quality of evidence, downgraded for very serious indirectness, imprecision, and inconsistency) that address the PICO question [142, 278, 279, 281, 283–289]. Barrington et al. documented a correlation between increasing doxapram dose and an increase in minute ventilation and a decrease in $PaCO_2$ in preterm infants with apnea of prematurity refractory to therapeutic levels of aminophylline; mean postnatal age in this study was 25 days [284]. Two very small clinical trials (combined total of 21 infants with a mean age of 4 and 9 days, respectively) with apnea of prematurity found that doxapram caused a decrease in $PaCO_2$ compared to baseline [283, 285]. A randomized controlled clinical trial including 24 newborn calves with neonatal asphyxia found that doxapram treatment (40 mg IV) at birth led to a small but statistically significant reduction in $PaCO_2$ compared to atropine or caffeine treatment (no placebo group) [142].

An observational study by Sagi et al. showed a reduction in $PaCO_2$ from baseline in five preterm infants with apnea of prematurity when receiving a doxapram infusion [289]. Similarly, Giguère et al. evaluated eight foals with HIE treated with doxapram and found a significant decrease in $PaCO_2$ compared to baseline [288].

In an experimental study of 5-day-old rats, Uehara et al. documented a significant reduction in $PaCO_2$ from the baseline (51.83 ± 2.84 mm Hg) at 15 min (41.17 ± 7.61 mm Hg), 30 min (40.97 ± 3.32 mm Hg), and 90 min (45.00 ± 5.96 mm Hg) after doxapram injection [281]. Similarly, Giguère et al. showed doxapram administration led to a significant, dose-dependent decrease in $PaCO_2$ in healthy, anesthetized, 1- to 3-day-old foals with iatrogenic respiratory acidosis [287]. Bleul et al. documented that doxapram administration caused a decrease in $PaCO_2$ compared to baseline in healthy newborn calves [278, 279]. In contrast to these studies, Coté et al. found no change in $PaCO_2$ following doxapram administration in sleeping 7-day-old swine [286].

For the next important outcome of *duration of hospital stay*, we identified 1 observational study (very low quality of evidence, downgraded for very serious indirectness) that addressed the PICO question [290]. In this study, Prins et al. found the response to doxapram was associated with a significantly shorter neonatal ICU stay in 122 infants with apnea of prematurity [290]. Length of hospitalization in general was not evaluated.

For the next important outcome of *increase in HR*, we identified 3 clinical trials (very low quality of evidence, downgraded for very serious indirectness and imprecision), 1 observational study (very low quality of evidence, downgraded for very serious indirectness), and 2 experimental studies (very low quality of evidence, downgraded for very serious indirectness and imprecision) that addressed the PICO question [142, 280, 282, 286, 291, 292]. Balikci et al. found in the study of 24 newborn calves with neonatal asphyxia mentioned above that doxapram treatment ($n = 8$) increased HR compared to baseline and yielded a significantly higher HR than atropine ($n = 8$) [142]. Poets et al. found that doxapram administration significantly reduced the frequency of bradycardia in preterm infants with caffeine-resistant apnea of prematurity [280]. Flint et al. studied the effects of doxapram in seven preterm infants and found HR increased after the institution of doxapram treatment [282].

In a population of 47 infants with apnea of prematurity, Finer et al. found that doxapram treatment was associated with a smaller proportion of apnea episodes being accompanied by bradycardia. Doxapram was also associated with a less severe decrease in HR during periods of apnea compared to theophylline or no treatment [291].

An early toxicologic study of doxapram that included dogs and cats showed doxapram treatment was associated with "simple tachycardia" on ECG in dogs; details are not provided, and it is unclear what effect was noted on the HR in cats [292]. Interestingly, Coté et al. showed HR decreased slightly but significantly following doxapram therapy in seven sleeping 7-day-old piglets [286]. The authors postulate that the increases in HR and respiratory parameters seen with doxapram in other studies are due only to its stimulant effects, which are abolished when the drug is given during sleep.

7.1.3 | Treatment Recommendations

We recommend against the routine administration of doxapram in newborn puppies and kittens undergoing resuscitation (strong recommendation, moderate quality of evidence).

In apneic or gasping newborn puppies and kittens that are not responding to PPV, we suggest doxapram administration (weak recommendation, very low quality of evidence).

In newborn puppies and kittens that are bradypneic and that fail to respond to timely administration of other supportive measures, we suggest the use of doxapram (weak recommendation, very low quality of evidence).

7.1.4 | Justification of Treatment Recommendation

Clinical trials in preterm infants with apnea of prematurity and in newborn calves with asphyxia at birth suggest that doxapram improves critical outcomes such as survival, oxygenation, and ventilation in neonates and newborns without clear evidence of harm. Also, a systematic review of doxapram for the treatment of apnea in premature infants found evidence to suggest the use of doxapram in this population [293]. However, apnea of prematurity in neonatal infants is a distinct syndrome that occurs hours to days after birth in the neonatal ICU, and doxapram in such cases is administered over an extended period of time. Apnea of prematurity is not a problem that arises in the delivery room, which is the target setting for this PICO question. Indeed, nearly all clinical evidence identified regarding doxapram was highly indirect in species and life stage. Only Balikci's study in calves mirrored the conditions relevant to the PICO question, but species and comparator were still indirect [142].

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While no evidence was identified regarding doxapram in the target population (i.e., newborn puppies and kittens that do not demonstrate adequate spontaneous ventilation efforts at birth), studies involving newborn kittens have shown increased carotid chemoreceptor response to doxapram, which is promising for efficacy when apnea occurs in this target species [294, 295]. Until more scientific data in the target population becomes available, we therefore suggest the use of doxapram in transitional puppies and kittens with respiratory compromise that do not respond to standard measures of support, foremost PPV. The intention of this recommendation is to first direct rescuer focus to other interventions for which there is less uncertainty of a positive effect before considering doxapram. This is particularly true for apneic or gasping newborns in which PPV is the most important intervention. In apneic newborns, we considered by consensus a reasonable nonresponse time to be 10 min. This delay could be shorter in those newborns who are breathing but not well (i.e., bradypnea). A respiratory rate of <15/min at birth was considered bradypnea, although much higher respiratory rates were reported with normal birth (e.g., >40/min in puppies and >70/min in kittens) [99, 296, 297].

We do not recommend doxapram be used indiscriminately for every puppy and kitten receiving assistance at birth, which is a statement based on the results of an adequately powered, randomized, placebo-controlled clinical trial including transitional puppies born by scheduled C-section [275].

7.1.5 | Knowledge Gaps

The benefit of doxapram administration in newborn kittens or puppies that do not demonstrate adequate spontaneous ventilation efforts at birth is unknown.

7.2 | GV 26 Stimulation—NB-08

In newborn dogs and cats that do not demonstrate adequate spontaneous ventilation efforts at birth (P), how does no needle stimulation (I), compared with insertion of a needle in the nasal philtrum (GV 26) (C), improve outcome (O)?

7.2.1 | Introduction

GV 26, also known as Renzhong or JenChung, is an acupuncture point found on the philtrum (the vertical line on the upper lip) at the lower edge of the nares [298]. Needle stimulation of this point has been suggested as an option to stimulate breathing of newborn puppies and kittens based on clinical experience [13, 16]. This question examines the evidence on the effect of GV 26 acupuncture on important outcomes in newborn puppies and kittens with inadequate respiratory efforts at birth.

7.2.2 | Consensus on Science

No relevant evidence was identified for any of the 6 outcomes during the initial literature search.

An additional literature search conducted in Medline (October 9, 2024) using the term [GV 26 veterinary] revealed 2 experimental studies, 1 in ponies and 1 in dogs (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [299, 300].

Dill et al. studied 7 healthy adult ponies that underwent 2 episodes of halothane anesthesia. Ponies were treated with either electroacupuncture or moxibustion at GV 26, or with electrical or heat stimulation of non-acupuncture points on the lateral muzzle area as a control. This study found no differences in cardiac output, arterial blood pressure, or HR when GV 26 stimulation was compared to control points for either electroacupuncture or moxibustion [299]. Graboschii et al. studied 20 healthy adult female dogs undergoing ovariohysterectomy under ketamine–midazolam anesthesia; half of the animals received GV 26 acupuncture and half served as a control group that did not undergo needle stimulation at any location. HR and "amplitude of chest cage" were both greater in dogs that received acupuncture at GV 26 compared to controls. Respiratory rate, capillary refill time, and body temperature were the same in dogs that received acupuncture and those that did not [300]. Considering there was no stimulation applied to the non-acupuncture dogs, it is unclear whether the changes in HR and chest wall movement were due to GV 26 stimulation specifically, or if these changes may have reflected general stimulation due to needle insertion.

A search using the term [GV 26 acupuncture] revealed six potentially relevant experimental studies in the English language, all of which were subsequently found to involve acupuncture after reperfusion from an ischemic event and were therefore deemed irrelevant to the PICO question. A search using [GV 26 acupressure] did not yield any studies.

7.2.3 | Treatment Recommendations

Consensus was not reached on whether to suggest for or against GV 26 stimulation in newborn puppies and kittens with inadequate spontaneous ventilation at birth.

7.2.4 | Justification of Treatment Recommendation

There are currently no data available to support the use of GV 26 acupuncture in newborn kittens and puppies with inadequate breathing at birth. While a single case series has been published that included 3 apneic newborn kittens, 2 of which survived after receiving GV 26 stimulation in addition to other supportive measures, the study design does not allow for drawing any conclusion regarding cause and effect [301]. The remaining data in adult ponies and dogs suggest no benefit but also no overt negative impact in the studied populations. However, GV 26 stimulation could delay or prevent rescuers from instituting recommended respiratory support measures such as PPV, which in most cases is initiated with a tight-fitting face mask. Thus, Domain Chairs and Co-Chairs initially suggested against the use of GV 26 stimulation. However, a subset of subject matter experts very strongly advocated for the use of GV 26 stimulation in puppies and kittens that are nonvigorous and not adequately

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breathing at birth and cited extensive personal experience and the absence of direct harm when performed expeditiously. However, they also acknowledged the lack of scientific evidence and the urgent need to execute high-quality clinical trials to address this question. Until then, we agreed to not provide a recommendation for or against the use of GV 26 in the target population. We, however, uniformly emphasized that if rescuers elect to use GV 26 stimulation in the absence of a clear directive, the intervention should be brief (i.e., 2–3 s) and not compromise timely initiation or quality of PPV.

7.2.5 | Knowledge Gaps

Currently, there are no studies evaluating the efficacy of acupuncture at GV 26 in newborns with inadequate spontaneous breathing efforts at birth. While other methods of newborn resuscitation show clear promise for respiratory support in newborn puppies and kittens, foremost PPV, GV 26 stimulation is widely employed in clinical veterinary practice, and there is an urgent need to conduct trial(s) on the effectiveness of GV 26 needle stimulation in the clinical setting in newborn puppies and kittens.

7.3 | Glucose Management During Resuscitation—NB-19

In newborn dogs and cats that require resuscitation (with or without CPA) (P), how does routine parenteral administration of dextrose (I), compared with targeted administration of dextrose (C), change outcome (O)?

7.3.1 | Introduction

When newborn puppies and kittens require resuscitation (with or without CPR), it is unknown how routine or standard-dose parenteral dextrose administration compares to dextrose administration targeted to a specific blood glucose (BG) concentration. It is established that hypoglycemia is associated with brain injury in human infants during the transition from intrauterine to extrauterine life [302].

Hypoglycemic puppies become lethargic with decreased mobility and progressively lose righting, sucking, and withdrawal reflexes; severe hypoglycemia in puppies causes seizures and death [303]. Hypoglycemia may occur in distressed newborn puppies and kittens due to a lack of glycogen stores and delayed nursing, and hypoglycemia independently predicts nonsurvival in neonatal puppies [65]. Additionally, it has been established that hyperglycemia exacerbates brain injury in newborn piglets after a period of hypoxia–ischemia; therefore, dextrose administration cannot be considered safe at every dose [304]. Recent human guidelines state it is reasonable to administer 0.25 g/kg dextrose to transitional infants during prolonged resuscitation [9]. This PICO question was designed to determine whether standard-dose dextrose (e.g., 0.25–0.5 g/kg) should be supplemented routinely to all transitional newborn puppies and kittens during resuscitation or whether dextrose should be given to target a specific BG concentration.

7.3.2 | Consensus on Science

For the most critical outcome of *favorable neurologic outcome*, we identified four experimental studies (very low quality of evidence, downgraded for very serious indirectness and imprecision) that addressed the PICO question [305–308]. All 4 experimental studies were conducted in 4-day-old rats undergoing a standardized hypoxemic event and assignment to receive treatment with glucose, oxygen, and/or epinephrine. All animals underwent a 30 min period of hypoxemia, with some rats randomized to receive 0.5 g/kg intraperitoneal (IP) dextrose at the initiation of hypoxemia, and others to receive, in addition to dextrose, 30 min of FiO_2 1.0 following the hypoxic–ischemic event. Other treatment arms included sham (no hypoxemic period), 100% oxygen only, and combinations that included epinephrine injection. Rats subjected to 30 min of hypoxemia that received dextrose during hypoxemia were found to maintain neurologic function similar to controls 1 month later, whereas those that did not receive dextrose or that received epinephrine, in addition to dextrose, fared worse. No measurements of BG concentration were made, and a single dextrose dose was used (no tailored treatments were evaluated). These studies favor dextrose support during resuscitation, though species (rodents), age (4 days vs. transitional), and condition (pure hypoxemia vs. newborn resuscitation) differed for each population, and the comparator was not targeted but rather was a lack of dextrose administration.

For the critical outcome of *survival to discharge*, we identified 1 clinical trial (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) that addressed the PICO question [309]. In this study, 41 nonvigorous, newborn triplet lambs were randomized to either dextrose gel or placebo gel application to buccal mucosa; the primary outcome was survival at 3 h. Application of dextrose gel did not improve 3-h survival compared to placebo; however, no posttreatment BG concentration measurements were reported; therefore, it is unclear whether the gel was absorbed systemically. Thus, species (sheep), intervention (parenteral vs. enteral dextrose), and comparator (not targeted dextrose treatment but rather "yes/no") were indirect, and lack of BG concentration measurements to ensure systemic absorption of dextrose introduces a risk of bias as pertains to this PICO question.

For the important outcomes of *hospital length of stay*, *surrogate markers of perfusion*, and *hypoglycemia*, we identified no studies that addressed the PICO question.

For the important outcome of *histopathologic damage*, we identified 6 experimental studies (very low quality of evidence, downgraded for very serious indirectness, imprecision, and inconsistency) that addressed the PICO question [305–308, 310, 311]. Four of these studies (discussed above in Outcome 1: Favorable neurologic outcome) showed improved brain histopathologic outcomes when dextrose (0.5 g/kg IP) was administered at the initiation of hypoxemia [305–308]. However, a different study in 7-day-old rats showed that administration of a very high dose of dextrose (2.5 g/kg) IP following 2.5 h of normothermic hypoxia resulted in more severe histopathologic brain lesions compared to rats treated with placebo; BG concentration was measured in this study, which showed dextrose-administered rats achieved BG concentrations of 200–240 mg/dL (11.1–13.3 mmol/L), while

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those receiving saline placebo were severely hypoglycemic (20–40 mg/dL [1.1–2.2 mmol/L]) [310]. Finally, a study in 3- to 5-day-old puppies showed that treatment with a very high dose of dextrose (2.5 g/kg IV to achieve a BG concentration of ~600 mg/dL [33.3 mmol/L]) prior to KCl-induced, hypothermic CPA of 1.75-h duration worsened histopathologic damage to the caudate and amygdaloid nuclei and brainstem [311]. Other studies identified for this PICO were not summarized here, as treatment recommendations could be made based on these 6 studies combined with evidence evaluated for a higher priority outcome (favorable neurologic outcome).

7.3.3 | Treatment Recommendations

In newborn puppies and kittens that require prolonged resuscitation, we suggest measuring a BG concentration (weak recommendation, expert opinion).

In hypoglycemic newborn puppies and kittens that require resuscitation (with or without CPA), we recommend dextrose supplementation with a slow bolus of 0.25 g/kg dextrose (e.g., 0.5 mL/100 g of 5% dextrose solution over 5 min) IV, IO, or IP (strong recommendation, very low quality of evidence).

In hypoglycemic newborn puppies and kittens in which IV/IO or IP access is not possible, we suggest topical sublingual mucosal administration of dextrose at 0.5 g/kg (e.g., 0.1 mL/100 g of 50% dextrose solution) (weak recommendation, expert opinion).

In newborn puppies and kittens undergoing prolonged resuscitation (e.g., >10 min) that are not responding to standard measures (e.g., PPV, rewarming, stimulation) and in which BG concentrations cannot be measured, we suggest dextrose supplementation (weak recommendation, expert opinion).

7.3.4 | Justification of Treatment Recommendation

No literature was found to answer the PICO question regarding routine (standard) versus targeted parenteral dextrose administration in newborn puppies and kittens that require resuscitation (with or without CPA). All evidence was highly indirect, often in population (species, life stage, condition requiring resuscitation), and always in intervention and comparator. Thus, treatment recommendations were developed based on information known under these indirect circumstances in combination with expert opinion.

It is known in infants with HIE that hypoglycemia is an important risk factor for brain injury with long-term effects [312–314]. Neonatal hypoglycemia is independently associated with death in puppies [65], in piglets [315], and in foals [316]. These findings suggest hypoglycemia should be avoided in newborn puppies and kittens requiring resuscitation. However, studies using very large doses of dextrose (~2.5 g/kg) caused hyperglycemia that was shown to be detrimental in neonatal rats and dogs [310, 311]. Hyperglycemia has also been associated with poor neurologic outcomes in piglets [315]; both hyperglycemia and wide fluctuations in BG concentration have been associated with poorer neurologic outcomes in human infants with encephalopathy [314, 317]. Thus, given the limited information available, we believe the optimal strategy for dextrose treatment in newborn puppies and kittens requiring resuscitation is one that provides some, but not excessive, dextrose support to avoid wide fluctuations in BG concentration. Hypoglycemia should be considered a contributing factor where the newborn remains nonvigorous despite at least 5–10 min of resuscitation. To target dextrose administration to hypoglycemic newborns specifically, and to avoid hyperglycemia, we suggest determining BG concentration by paw pad puncture, which is feasible in many clinical contexts [318]. It is unclear what constitutes clinically significant hypoglycemia in newborn puppies and kittens, and there was variability among Domain Chairs, Co-Chairs, and subject matter experts regarding a BG concentration below which to administer dextrose. However, the majority indicated a cutoff of 3.0 mmol/L (54 mg/dL), with a BG concentration of <2.2 mmol/l (<40 mg/dL) interpreted as life-threatening hypoglycemia. As CRIs are not feasible in most contexts during resuscitation of newborn puppies and kittens, we recommend a slow bolus of 0.25 g/kg dextrose IV or IO, or less preferably IP. The IP route is used commonly by some subject matter experts and is considered practical, effective, and safe if executed correctly, which includes maintenance of strict asepsis. Where parenteral administration cannot be accomplished, oral administration of 0.5 g/kg dextrose (e.g., 0.1 mL/100 g of 50% dextrose) serves as an alternative. Oral administration can be executed as a topical sublingual mucosal application of dextrose, although some uncertainty regarding the efficacy of this route exists, and an increase in BG concentration will typically occur after >15 min of treatment [319]. It is, therefore, best suited for mild hypoglycemia, while IV/IO dextrose is required for life-threatening, clinical (tremors, seizures) hypoglycemia.

7.3.5 | Knowledge Gaps

Blood glucose concentrations in newborn dogs and cats receiving resuscitative measures at birth are unknown, and thus, the value of BG concentration measurement in this population is unknown. The optimal strategy for dextrose supplementation in newborn puppies and kittens requiring resuscitation has not been examined.

7.4 | Glucose Management After Resuscitation—NB-26

In newborn dogs and cats after ROSC (P), how does routine parenteral administration of glucose (I), compared with targeted administration of glucose (C), improve outcome (O)?

7.4.1 | Introduction

When newborn puppies and kittens that have experienced CPA achieve ROSC, it is unknown how routine or standard-dose parenteral dextrose administration compares to dextrose administration targeted to a specific BG concentration. Hypoglycemia may occur in distressed newborn puppies and kittens due to lack of glycogen stores and delayed nursing, and hypoglycemia independently predicts nonsurvival in neonatal puppies [65].

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Additionally, it has been established that hyperglycemia may cause brain injury in newborn piglets after a period of hypoxia–ischemia, so dextrose administration cannot be considered safe at every dose [304]. Following newborn resuscitation, recent human guidelines recommend monitoring BG concentration, avoiding hypo- and hyperglycemia, avoiding wide variation in BG concentration, and having protocols in place to manage unstable BG concentration [9]; additionally, one may consider dextrose administration by CRI to avoid hypoglycemia [8, 9]. This PICO question was designed to determine whether standard-dose dextrose (i.e., 0.25–0.5 g/kg) should be supplemented routinely to all newborn puppies and kittens following ROSC, or whether dextrose should be given to target a specific BG concentration.

7.4.2 | Consensus on Science

For the most critical outcome *of favorable neurologic outcome*, we identified one experimental study (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) that addressed the PICO question [320]. In this study, 43 piglets, aged 0–3 days, were subjected to hypoxic brain injury through a combination of carotid artery clamping, controlled hemorrhage, and decreased FiO_2. All piglets had been pretreated with 2 U/kg insulin to prevent stress-related hyperglycemia. After 30 min of cerebral hypoxia, the carotid arteries were unclamped, removed blood was reinfused, and piglets received oxygen at FiO_2 1.0. Following brain re-oxygenation, piglets were randomized to receive either dextrose 1 g/kg IV bolus followed by 1 g/kg/h IV for 2 more hours or an equal volume of saline. Dextrose-treated piglets experienced marked hyperglycemia, while placebo-treated piglets appeared to experience euglycemia to mild hypoglycemia. No difference was found between the 2 groups' neurologic examination scores 1 day later. This study suggests no effect of routine dextrose administration following resuscitation of neonatal pigs, though the dextrose dose was higher than those commonly used in small animal veterinary practice.

For the critical outcome of *survival to discharge* and the important outcomes of *hospital length of stay* and *complications*, no studies pertaining to the PICO question were identified.

For the important outcome of *histopathologic damage*, we identified three experimental studies (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, imprecision, and inconsistency) that addressed the PICO question [310, 320, 321]. The study from LeBlanc et al., already summarized in the paragraph above, evaluated the effect of routine dextrose administration following 30 min of cerebral hypoxia in newborn piglets (age: 0–3 days) and found no difference in brain section pathological examination scores for those treated with dextrose compared with those that received placebo [320]. Sheldon et al. studied the effect of a high dose of dextrose (2.5 g/kg IP) following 2.5 h of normothermic hypoxia on histopathologic brain lesions in 7-day-old rats and revealed more severe neuronal damage in the brains of dextrose-treated rats compared to those treated with placebo [310]. However, another experimental study in 7-day-old rats undergoing 1 h of cerebral hypoxia–ischemia (ligated left carotid artery, 1 h at FiO_2 0.08) found that animals treated immediately following the hypoxic period with dextrose IP showed less widespread and less severe histopathologic brain damage at sacrifice 72 h later than rats treated with 0.9% NaCl placebo [321]. These 3Hypoxic-ischemic encephalopathy studies reveal contradictory information regarding histopathologic outcomes in animals treated with dextrose versus placebo immediately following reoxygenation; no study identified evaluated the effect of routine dextrose versus BG-targeted dextrose administration following ROSC in any species.

7.4.3 | Treatment Recommendations

In newborn puppies and kittens that are nonvigorous and not nursing after ROSC, we suggest measuring a BG concentration (weak recommendation, expert opinion).

In hypoglycemic newborn puppies and kittens after ROSC, we suggest supplementing dextrose by CRI (e.g., 2.5% dextrose in isotonic crystalloid fluids given at a physiologic rate IV or IO) rather than by bolus injection (weak recommendation, very low quality of evidence).

In hypoglycemic newborn puppies and kittens after ROSC, we recommend dextrose supplementation with a slow bolus of 0.25 g/kg dextrose (e.g., 0.5 mL/100 g of 5% dextrose solution over 5 min) IV, IO, or IP, if an IV or IO CRI is not feasible (strong recommendation, very low quality of evidence).

In hypoglycemic newborn puppies and kittens after ROSC in which IV, IO, or IP administration are not possible, we suggest oral administration of dextrose at 0.5 g/kg (e.g., 0.1 mL/100 g of 50% dextrose solution) (weak recommendation, expert opinion).

In newborn puppies and kittens that are nonvigorous and not nursing after resuscitation and in which BG concentrations cannot be measured, we suggest dextrose supplementation (weak recommendation, expert opinion).

7.4.4 | Justification of Treatment Recommendation

No literature was found to answer the PICO question regarding routine (standard) versus targeted parenteral dextrose administration in newborn puppies and kittens after ROSC. All evidence was highly indirect in population (species, life stage, scenario), intervention, and comparator. Thus, treatment recommendations were developed based on information known under these indirect circumstances in combination with expert opinion.

Hypoglycemia is an important risk factor for brain injury with long-term effects in newborn infants with HIE [312–314]. It was shown to be independently associated with death in several species, including puppies [65], piglets [315], and foals [322]. Thus, hypoglycemia should be avoided in newborn puppies and kittens following ROSC. Hyperglycemia was also shown to be detrimental in studies where very large doses of dextrose (~2.5 g/kg) were given to newborn rats and puppies [310, 311]. High BG concentration has also been associated with poor neurologic outcomes in piglets [315]. In newborn infants with HIE, both hyperglycemia

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and wide fluctuations in BG concentration have been associated with worse neurologic outcome [314, 317]. Thus, given the limited information available, we believe a safe and effective strategy for dextrose treatment in newborn puppies and kittens following ROSC is founded in first determining the BG concentration. A blood sample can be feasibly obtained by puncture of the paw pad in most newborns [318]. If the animal is hypoglycemic (i.e., BG < 3.0 mmol/L; <5 mg/dL), a sensible strategy is one that provides some, but not excessive, dextrose support as a CRI to avoid wide fluctuations in BG concentration. If a CRI is not possible, we recommend 0.25 g/kg dextrose IV/IO by slow bolus administration with the intention to avoid life-threatening hypoglycemia (e.g., BG < 2.2 mmol/L; <40 mg/dL) and marked iatrogenic hyperglycemia (e.g., BG > 11 mmol/L; >200 mg/dL). While IV/IO is the preferred route, some subject matter experts routinely administer an isotonic dextrose solution IP. Adequate technique to avoid organ injury and septic peritonitis is required to use this route. The frequency of intermittent administration may be determined by serial BG concentration sampling or by clinical response. In clinical contexts where parenteral administration of dextrose is not possible, we suggest oral administration. Dextrose (50%) can be applied topically on the sublingual mucosa, although absorption will be slow [319, 323]. Dextrose administration by orogastric tube is another possibility after ROSC as long as it is performed by skilled personnel to minimize the risk of injury to the newborn [318]. Alert newborns can be encouraged to swallow the dextrose solution by syringe administration. We generally suggest against routine dextrose administration without documented hypoglycemia; however, if the animal remains nonvigorous and not nursing after resuscitation (e.g., newborn with now adequate ventilation and circulation), hypoglycemia could contribute to the newborn's impairment, and we agreed that empirical administration of dextrose is reasonable under these circumstances.

7.4.5 | Knowledge Gaps

The optimal strategy for dextrose supplementation, including the range of acceptable BG concentration, in newborn puppies and kittens following ROSC, is unknown. The reference interval for BG concentration and cutoff point(s) for clinically relevant hypoglycemia at birth in newborn puppies and kittens are uncertain.

7.5 | Temperature Management of Newborns With Signs of HIE—NB-27

In newborn dogs and cats with ROSC that remain comatose (P), how does permissive hypothermia to maintain core temperature below normal (I), compared with active warming to maintain or achieve normothermia (C), improve outcome (O)?

7.5.1 | Introduction

Hypoxic-ischemic encephalopathy in the newborn occurs as a consequence of ante-, peri-, or postpartum asphyxiation and can lead to severe short- and long-term neurological dysfunction [267]. Criteria to identify HIE are not specifically described for newborn puppies and kittens but have been well delineated in infants and foals [324, 325]. Clinical signs vary with severity and include lethargy to stupor/coma, decreased to no activity, extensor rigidity to decerebrate posture, hypotonia to flaccidity, weak or absent sucking reflex, constricted or dilated pupils with absent pupillary light reflex, low HR, and intermittent breathing or apnea. The diagnosis of HIE in newborn infants is made based on the identification of a sentinel event (e.g., prolapse of the umbilical cord), perinatal bradycardia, need for resuscitation at birth, severe acidosis, very low Apgar score 10 min after birth, and the development of the above clinical signs suggestive of encephalopathy shortly after birth [267]. As the underlying brain injury progresses, there is a critical window of opportunity shortly after the hypoxic insult to influence the neurological outcome through timely intervention (i.e., neuroprotection) [326]. Temperature management, including deliberate maintenance of hypothermia, is a suggested intervention in adult people, dogs, and cats that remain comatose after resuscitation from CPA, owing to its multiple beneficial neuroprotective effects [12, 327, 328]. TH (33°C–34°C for 72 h, started within 6 h of birth) has been recommended for newborn infants with moderate to severe HIE for more than 15 years [126]. We herein examine the question of whether temperature management, specifically permissive hypothermia, should be practiced in newborn puppies and kittens with signs of HIE.

7.5.2 | Consensus on Science

For the most critical outcome of *favorable neurologic outcome*, we located 8 clinical trials (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) [329–336] and 4 experimental studies (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) that addressed the PICO question [337–340]. The downgrading originated from a lack of blinding, species other than dogs and cats, and studies evaluating the effect of active cooling methodologies in a neonatal intensive care setting rather than permissive hypothermia in a veterinary setting. The clinical trials are all RCTs including newborn, near-term, or term infants with moderate to severe HIE that were randomized within 6 h of birth to treatment with TH or to standard care with normothermia. Hypothermia was implemented as selective head cooling in 2 studies [331, 335] and global hypothermia in the remaining 6 trials [329, 330, 332–334, 336]. A rectal temperature of 34°C–35°C and 33°C–34°C was targeted during selective head cooling and global hypothermia, respectively. The duration of hypothermia was 72 h in all but one study (48 h) [330]. The majority (5/8) of studies demonstrated a significant benefit of cooling on the composite outcome of death or severe neurological disability [329, 330, 333–335], while 2 studies showed a trend toward benefit [331, 332]. These 7 studies taken together include 1313 infants and suggest an overall benefit of TH to reduce the risk of poor functional outcome (death or severe disability) (RR 0.75, 95% CI 0.68–0.83); also, infants with moderate HIE benefited more than those with severe HIE. While these studies were all conducted in high-income countries, one more recent multicenter RCT was conducted in low- and middle-income countries [336]. This study, including 394 term infants with moderate to severe HIE, found no reduction in the incidence of death or severe disability with TH when compared to normothermia

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(RR 1.06, 95% CI 0.87–1.3), indicating that TH might not have the same effect in a resource-restricted environment. Importantly, the intensity of care that was delivered to the infants in this study was still far superior to what is currently accomplished in a clinical veterinary setting. Four experimental animal studies using a variety of asphyxial models in rats, mice, and piglets showed either improved neurological function with HT or no effect compared to normothermia [337–340].

For the critical outcome of *survival to discharge*, we identified 10 clinical trials (low quality of evidence, downgraded for serious risk of bias and serious indirectness) [329–336, 341, 342] and 2 experimental studies (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [337, 343]. Most of the clinical trials are the same as those listed for favorable neurologic outcome, and data for survival to discharge were available for all but one study. While only 2 trials showed an increase in survival to discharge with TH [329, 334], when considering the data pooled from all studies ($n = 1983$), cooling led to a small but significant improvement in survival (TH: 73%, normothermia: 68%; RR 1.01, 95% CI 1.01–1.13). However, the largest study by Thayyil et al., a multicenter RCT including cases from several low- and middle-income countries ($n = 408$), demonstrated a reduction in survival to discharge with TH (64%) compared to normothermia (76%) (RR 0.84, 95% CI 0.74–0.96) [336]. Survival data from 2 experimental studies, none in target species and with significant indirectness in model and outcome, suggested no effect of cooling on survival to the study endpoint in one study and increased mortality with TH in another [337, 343].

For the important outcome of *complications* associated with TH, we located 8 clinical trials (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and inconsistency) [329, 332–336, 341, 342], 4 observational studies (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) [344–347], and 1 experimental study (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) [348]. The majority of the clinical trials either showed a protective effect of TH on markers of kidney [341] and cardiac injury [342] or revealed similar incidence of adverse events (e.g., hypotension, prolonged coagulation times, thrombocytopenia, intracranial bleeding, lung injury, GI and hepatic dysfunction, arrhythmias, or sepsis) when TH was instituted compared to normothermia [329, 332–335]. Moreover, complications were common in both TH and normothermia, with persistent hypotension, prolonged coagulation times, and thrombocytopenia occurring in 40%–80% of infants [332]. In contrast to these studies, the RCT conducted in low- and middle-income countries demonstrated consistently higher incidence of adverse events with TH, including coagulopathy, thrombocytopenia, hypotension, cardiac arrhythmias, and persistent acidosis [336]. Multiple small observational studies including near-term or term infants reported adverse events associated with TH, including prolonged bleeding times and bradycardia, but also found a reduction in kidney injury or no association with organ or metabolic dysfunction when compared to normothermia [344–347]. A single experimental study involving 1-day-old asphyxiated piglets did not reveal any significant hematological or biochemical changes aside from the need for more dextrose and oxygen administration during TH compared to normothermic controls [348].

For the important outcome of *seizure reduction* with TH, we located 1 clinical trial (very low quality of evidence, downgraded for serious risk of bias, very serious indirectness, and imprecision) [329], 1 observational study (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) [349], and 4 experimental studies (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, imprecision, and inconsistency) [338, 343, 350, 351]. In term infants ($n = 111$) with moderate to severe HIE, TH at 33.5°C for 72 h led to a significant reduction in seizure activity during the intervention period ($n = 17$, 27%) compared to standard care with normothermia ($n = 31$, 49%, $p = 0.004$) [329]. Similarly, the findings in a small observational study ($n = 69$) of newborn infants with moderate HIE demonstrated an association between seizure reduction and TH, while no such association was noted in infants with severe HIE [349]. The impact of TH on seizure reduction was tested in multiple animal studies with mixed results, which may be ascribed to the vastly different animal models employed. One of the studies utilizing a fetal sheep model showed that post-asphyxial TH for 48 h significantly reduced the seizure burden (70 ± 39 min of seizures) compared to normothermia (300 ± 199 min, $p < 0.05$) over the study period [350]. The remaining studies in newborn piglets and mouse pups did not identify any effect of TH on seizure mitigation [338, 343, 350, 351].

For the important outcome of *hospital length of stay*, we located 4 clinical trials (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) [330, 332, 333, 336] and 1 observational study (very low quality of evidence, downgraded for serious risk of bias, serious indirectness, and imprecision) [346]. In the three RCTs conducted in high-income countries that together encompassed 595 infants, the duration of hospitalization was similar in TH and normothermia groups and averaged 2–3 weeks [330, 332, 333], while TH led to longer hospitalization (i.e., 2 days more) in the RCT in low- and middle-income countries [336]. Likewise, in a small observational study ($n = 38$) conducted in Marrakech, hospital length of stay was longer in infants undergoing TH (mean, 12.4 days) versus normothermia (mean, 6.7 days) [346].

For the important outcome of *histopathologic damage*, we located 13 experimental studies (very low quality of evidence, downgraded for serious risk of bias and very serious indirectness) pertinent to the PICO question [338–340, 348, 350–358]. Across multiple asphyxial models encompassing several species, the preponderance of studies suggests a reduction in tissue injury with TH, specifically in the brain [339, 340, 350, 352, 353, 355–358] and the heart [354], while others found no protective effect of TH but also no harm [338, 348, 351]. Histologically apparent heart, liver, lung, kidney, and gastrointestinal pathology was common regardless of temperature management strategy [348].

7.5.3 | Treatment Recommendations

In newborn puppies and kittens with signs of acute HIE, we suggest permitting the animal to remain at a low normal temperature for newborn puppies and kittens (i.e., 35°C, 95°F) for 24 h after birth (weak recommendation, expert opinion).

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7.5.4 | Justification of Treatment Recommendation

While we did not identify any evidence to address the PICO question directly in newborn puppies and kittens, the evidence we did find consistently suggested that HIE is modifiable and that TH is beneficial in improving outcomes from HIE in clinical and experimental studies across multiple settings and species. Taken together, there is adequate certainty that hypothermia of sufficient depth (i.e., 33°C–35°C), initiated early in the evolution of HIE and maintained for a sufficient duration (typically 48–72 h), is beneficial in newborn infants with HIE. As this applies to any HIE of the newborn and not just to those that underwent CPR, we removed the term "ROSC" from the treatment recommendation and generalized this recommendation to newborn puppies and kittens with clinical signs of HIE.

Evidence from human RCTs has shown that infants with moderate HIE benefit more from TH than infants with mild or severe HIE [329, 331, 333–335]. In newborn infants, clinical signs of moderate HIE include lethargy, reduced but present activity, hypotonia, weak but present sucking reflex, bradycardia, and irregular (but present) spontaneous breathing [359]. Because HIE has not been defined clinically for newborn puppies and kittens, we suggest applying this treatment recommendation to any newborn puppy or kitten with clinical signs consistent with HIE in newborn infants.

Additionally, TH is unlikely to be effective in cases of HIE due to longer durations of hypoxia, such as from antenatal or chronic intrauterine hypoxia, and thus is preferentially applied to newborn infants with *acute* perinatal hypoxic insult. For this reason, we included the term "acute" in the current treatment recommendations' population description, though the acuteness is often unknown. The high proportion of prenatal insults (as opposed to acute periparturient hypoxic events) in the trial by Thayyil et al., which was conducted in low- and middle-income countries, was considered the reason for the lack of benefit of TH in this cohort [336]. TH is recommended for newborn infants with moderate to severe evolving HIE in low- and middle-income countries based on data from multiple RCTs not included in our evidence analysis [327]. However, ILCOR warns that the adoption of TH without close monitoring, following of treatment protocols, and access to comprehensive neonatal intensive care may be associated with harm [327].

While TH is the standard of care in newborn infants with HIE, several challenges exist in implementing TH in small animal veterinary practice. The management of newborns with TH is resource intensive and highly technical, in part due to the cooling itself and in part due to the severity of illness of HIE patients, who often experience pulmonary, cardiac, kidney, hematologic, and metabolic instability [360]. In human medicine, a neonatal ICU is a precondition for successful implementation of TH, since a high percentage of these infants are critically ill, are mechanically ventilated, receive EEG and MRI monitoring, and are hospitalized for 2 or more weeks [327, 360, 361]. To our knowledge, such resources are not available for newborn puppies and kittens in the veterinary setting. In addition, newborn puppies and kittens have a need distinct from human infants for early passive transfer of immunoglobulins through colostrum (ideally in the first 8 h after birth) to avoid short- and long-term immune system compromise that would require additional intensive management in colostrum-deprived newborns [362, 363]. However, we believe that allowing newborn puppies and kittens to sustain the naturally present low body temperature at birth without aggressive rewarming, while preventing more significant hypothermia (i.e., <34°C) and its associated adverse effects (i.e., hypoglycemia), is reasonable and feasible to support those with signs of acute HIE. In newborn puppies, the rectal temperature at birth was 33.7 ± 1.4°C after C-section and 33.1 ± 3.1°C with eutocia; was 35.1 ± 1.8°C and 33.2 ± 4.7°C, respectively, after 1 h; and increased to a median temperature of 36.6°C (range, 35.9°C–37.2°C) after 24 h [18, 75]. We therefore decided on a target rectal temperature of approximately 35°C.

Taken together, there is a complex interaction between the severity of HIE, time to cooling, degree of cooling, and duration of TH [364]. In animals with more severe HIE, longer duration of TH is associated with increased preservation of neurological integrity [365, 366]; however, animal studies also provide evidence for a neuroprotective effect after cooling periods of 24 h or less [367–369]. Given the limited resources available in veterinary medicine that restrict care to newborn puppies and kittens with low severity of HIE, we considered a 24-h duration of permissive hypothermia to be a pragmatic approach to balance risk, benefit, and feasibility of TH until more clinical veterinary data are available.

7.5.5 | Knowledge Gaps

There are no criteria in place to identify and categorize the severity of HIE in newborn puppies and kittens. There are no studies in newborn puppies or kittens regarding the effect of TH or permissive hypothermia on survival, ideal case selection for TH or permissive hypothermia, optimal temperature and duration, or the feasibility of permissive hypothermia in the resource-limited veterinary environment. There are no studies on the adverse effects of permissive hypothermia in newborn puppies or kittens.

7.6 | Rewarming Rate of Newborns With and Without Signs of HIE—NB-28

In newborn dogs and cats with ROSC that are spontaneously hypothermic (P), how does rewarming at a rate greater than 1°C/h (I), compared with rewarming at a rate of ≤1°C/h (C), improve outcome (O)?

7.6.1 | Introduction

Newborn puppies and kittens are commonly hypothermic after birth (i.e., in puppies: 33.7 ± 1.4°C after C-section and 33.1 ± 3.1°C with eutocia) and thus they might be particularly vulnerable to low body temperature if undergoing resuscitative measures [75]. Establishing normothermia (35.0°C–37.2°C; 95°F–99°F for newborns) by utilizing passive and active temperature control measures is recommended during resuscitation of newborn puppies and kittens (see *NB-11*) and infants [8]. However, after a hypoxic–ischemic insult, evidence suggests that hypothermia is neuroprotective and that it should be maintained by active cooling (i.e., TH) or permissively in newborns with HIE

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(see *NB-27*) [8, 327]. The current RECOVER treatment recommendation in adult dogs and cats with ROSC suggests slow rewarming (0.25°C/h to 0.5°C/h) and recommends against fast rewarming (e.g., >1°C/h) [12, 370]. This question asks whether slow rewarming is beneficial over fast rewarming (e.g., >1°C) in newborn puppies and kittens that experienced a significant hypoxic–ischemic insult at birth (e.g., CPA) and that are hypothermic.

7.6.2 | Consensus on Science

We identified no studies addressing the question for the critical outcome of *favorable neurologic outcome* and *survival to discharge* and the important outcome of *surrogate markers of perfusion*.

For the important outcome of *complications*, we identified 1 experimental study (very low quality of evidence, downgraded for very serious indirectness and imprecision) pertinent to the PICO question [371]. In an HIE model in near-term fetal lambs, cerebral ischemia of 30 min was followed by 48 h of hypothermia and either fast (5°C/h, $n = 8$) or slow (0.2°C/h, $n = 8$) rewarming. While seizure activity was extensive during ischemia and effectively suppressed during hypothermia, rapid rewarming resulted in no significant effect on EEG-documented seizure burden (e.g., no rebound seizures) [371].

For the important outcome of *histopathologic damage*, we identified 5 experimental studies (very low quality of evidence, downgraded for very serious indirectness and imprecision) pertinent to the PICO question [371–375]. The same near-term fetal HIE model described above was used in 3 studies examining the effect of slow (0.2°C/h to 0.5°C/h) versus fast rewarming (4°C/h to 5°C/h) on neuronal cell death and apoptosis as well as white matter changes (oligodendrocyte reduction, astrocytosis, microgliosis) [371, 374, 375]. For the majority of outcomes, slow rewarming had no protective effect over fast rewarming. Only 1 study found a reduction in astrocyte proliferation, a marker of brain injury, with slow rewarming [374]. It remains open whether this was a direct benefit of slow rewarming itself or due to the associated extension of hypothermia. Two studies were conducted using the same newborn swine asphyxial cardiac arrest model with animals undergoing CPR, 18 h of hypothermia, and rewarming at either 0.5°C/h (slow, $n = 8$) or 4°C/h (fast, $n = 8$) [372, 373]. Fast rewarming did not lead to any differences in neuronal cell death but was associated with increased apoptosis in the cortex but not in subcortical white matter [372, 373].

7.6.3 | Treatment Recommendations

In newborn puppies and kittens that are hypothermic at birth and have evidence of H, we suggest rewarming at a rate no faster than 1°C/h to achieve normothermia (35.0°C–37.2°C; 95°F–99°F) while avoiding accidental hyperthermia (weak recommendation, very low quality of evidence).

In newborn puppies and kittens that are hypothermic at birth without signs of HIE, we suggest actively rewarming newborns over 1–2 h to reach normothermia (35.0°C–37.2°C; 95°F–99°F), avoiding accidental hyperthermia (weak recommendation, expert opinion).

7.6.4 | Justification of Treatment Recommendation

There are 2 scenarios in which rewarming is relevant in the context of newborn resuscitation of puppies and kittens. One concerns those animals with unintended hypothermia at birth that otherwise transition normally and for which establishing normothermia is important (see *NB-11*). The other scenario concerns animals with acute signs of HIE that are deliberately treated with permissive hypothermia for a period of time and might require rewarming by external heat administration at the end of that period to achieve normothermia (see *NB-27*). The current PICO question primarily relates to the latter scenario. The studies identified report only lower priority outcomes, and the study findings do not demonstrate consistent, if any, benefit of slow over fast rewarming on the outcomes that were examined. This lack of differential effect occurred despite a 10- to 20-fold difference between slow and fast rewarming rates [371–375]. Moreover, slower rewarming will lead to longer exposure to hypothermia, which could be the reason for the beneficial effects observed in some studies [371, 374]. Studies that did not qualify for inclusion in the evidence evaluation here, 1 case report and 1 observational study without a control group, reported a risk of hypotension with rapid rewarming and the possibility for rebound seizure activity during rewarming [376, 377]. In addition, multiple experimental animal studies of HIE for other reasons than periparturient asphyxiation demonstrate harm with fast (i.e., >1°C/h) rewarming rates [378–383]. For precautionary reasons, the recommendation for newborn infants undergoing TH is to rewarm over at least 4 h, or at a rate of 0.5°C/h or less, which was the case in most clinical TH trials [126, 327, 330, 332–334, 336]. Fast rewarming rates through external heat administration also carry the theoretical risk of overshoot hyperthermia. All taken together, we believe that it is prudent to avoid rapid rewarming of hypothermic newborn puppies and kittens with signs of acute HIE and thus suggest a rewarming rate of 1°C/h or less.

We did not systematically review the evidence on optimal rewarming rates for newborn puppies and kittens that are unintentionally hypothermic at birth but are otherwise normal or require only low levels of support. The most recent treatment recommendation for temperature management of newborn hypothermic infants emphasizes the need for establishing normothermia but does not stipulate any specific rewarming rate due to a lack of evidence [8]. Observational and interventional studies in newborn infants involving very-low-birthweight to normal full-term infants and rewarming rates ranging from 0.1°C/h to 5°C/h did not document an association between rewarming rate and a variety of outcomes, including mortality [384–388]. One observational study identified an association between higher rewarming rates and the risk of hyperthermia [387]. We did not identify any studies in newborn puppies and kittens pertaining to the topic. Thus, we recommend establishing normothermia over a few hours (e.g., 1–2 h) and maintaining normothermia (see *NB-11*). Avoidance of hyperthermia with exposure to external heat sources through appropriate monitoring

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is of central importance, as temperature overshoot is likely the biggest risk with rapid rewarming rates and can be detrimental [389].

7.6.5 | Knowledge Gaps

The benefits and risks of fast versus slow rewarming after intended hypothermia in newborn puppies and kittens with HIE have not been studied, and no safe protocols have been established. Concerns of particular interest are the occurrence of hypoglycemia with prolonged hypothermia and slow rewarming, as well as the risk of seizure activity or overshoot hyperthermia with faster rewarming strategies.

8 | Discussion

This article describes the development, substance, and rationale of the first evidence- and consensus-based treatment recommendations for resuscitation of newborn puppies and kittens and is an addition to the series of RECOVER CPR guidelines for adult dogs and cats [11, 17, 204, 248, 390]. This series of guidelines is an important element in the pathway from scientific knowledge to clinical decision-making, which spans from generating evidence from research, synthesizing that evidence to generate guidelines, and finally applying the guidelines in practice to inform clinical decisions.

In this process, we extracted a large amount of scientific information from the peer-reviewed literature to address a prioritized list of clinical questions pertaining to the resuscitation of newborn puppies and kittens. The resulting treatment recommendations can serve as the foundation for uniform training of the veterinary community in resuscitation of newborn puppies and kittens and, as such, can lead to a positive clinical impact. To increase accessibility of this information to veterinary professionals in the clinic, a concise summary is important; such a clinical reference is available in a companion article, the RECOVER Newborn Resuscitation Guidelines [19].

We used a similar methodology to develop the current treatment recommendations as was previously employed to generate the most recent RECOVER CPR guidelines for adult dogs and cats, with the exception of an added consensus step [17]. This additional consensus step included a group of subject matter experts in the field of small animal theriogenology and reproduction medicine, as the RECOVER Initiative expected to identify very low quality of evidence or no evidence regarding many of the PICO questions. Indeed, 47% ($n = 28$) of all recommendations were developed based on expert opinion, and 44% ($n = 26$) were based on very low quality of evidence. We identified significant knowledge gaps for nearly all PICO questions. The writing group also depended moderately on expert opinion during the evidence evaluation process for the CPR treatment recommendations in adult dogs and cats for both the 2012 and 2024 RECOVER guidelines [204, 248, 370, 390–394]. Much of the uncertainty in the evidence was the consequence of the very serious indirectness of species, and in fact, we only located 1Dr RCT in transitional newborn puppies [275]. This staggering lack of research data in newborn puppies and kittens needs urgent addressing if higher certainty treatment recommendations are to be devised for this patient set. Until then, most clinical decision-making in newborn puppies and kittens will continue to originate from clinical trials in newborn infants and experimental animal studies using transitional newborn models [205]. It is our hope that the many knowledge gaps that emerged in the process will serve as a basis for broad, collaborative clinical research initiatives to gather evidence in the field of veterinary newborn resuscitation. It is expected that the RECOVER Newborn Resuscitation treatment recommendations will be updated once significant new information becomes available.

Despite the lack of evidence in many cases, we provide treatment recommendations because of the need for clear, consistent standards for resuscitative measures in newborn puppies and kittens. The uncertainty that plagues almost all treatment recommendations is reflected in their wording as weak recommendations (i.e., to "suggest" for or against an intervention) and as such is clearly identifiable to the reader. While the strength of a recommendation typically echoes the quality of evidence (i.e., a weak recommendation for low or very low quality of evidence; a strong recommendation for high or moderate quality of evidence), we allowed deviations where deemed appropriate and provided reasoning for this in the justification section of each PICO question. An example is the emphasis on PPV with severe bradycardia that is founded on the knowledge of asphyxiation as the source problem for low HR in transitional newborns. However, there are no clinical trials or experimental studies directly comparing PPV to placebo in nonvigorous, bradycardic newborns that are apneic or gasping, and such studies would not be considered ethical. There are also no studies that compare specific HR cutoffs as triggers to escalate or deescalate interventions. To provide recommendations that are clinically actionable, we provided cutoff values reasoned by physiologic scientific knowledge and validated the cutoffs by consensus. Moreover, the feasibility of an intervention in the veterinary clinical context also influenced the wording of recommendations. ET intubation, for example, while alleviating many issues associated with bag–mask ventilation such as gastric inflation and inadequacy of minute ventilation, is technically challenging and can cause severe upper airway injury. In addition, the intubation process precludes concurrent PPV and might distract rescuers from conducting other interventions, all of which can expose the newborn to additional harm. Because of these tangible clinical concerns, we suggest ET intubation in animals that are not responding to at least 60 s of PPV with bag–mask ventilation only if it is feasible in the context of a particular resuscitation environment. If we raised significant concerns about the undesirable effects of an intervention, we recommended against or suggested against that intervention. For example, we suggest against the use of atropine in bradycardic newborns at birth and also in those undergoing CPR, as there is significant concern about increasing the HR in the face of severe hypoxemia [395]; a low heart rate is likely protective of the myocardium byreducing myocardial oxygen consumption, and vital organ blood flow is maintained through compensatory mechanisms unless bradycardia is extreme and prolonged [196]. This should, however, not preclude clinicians from administering atropine in special circumstances where they perceive that atropine may be beneficial. To emphasize this point, we typically recommended or suggested against "routine" administration of an intervention.

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The broad strokes of the treatment recommendations herein are in line with previously published clinical guides on newborn resuscitation in puppies and kittens [13, 16]. These publications similarly recommend tactile stimulation, maintenance of normothermia, consideration of bradycardia for decision-making, and prioritization of airway management and PPV with a tight-fitting mask, and suggest the administration of drugs (e.g., epinephrine, doxapram, reversal drugs) or advise against them (atropine). Where the RECOVER treatment recommendations differ is in the cutoffs for timelines (e.g., time intervals from PPV to expected response of newborn until next action), the delineation of a clear sequence from birth to PPV to chest compressions, the inclusion of clear operational definitions for HR changes to guide action (e.g., HR < 50/min to start chest compressions), the de-emphasis of routine administration of doxapram, reversals and GV 26 stimulation, and some changes in dosing (e.g., lower dose of epinephrine).

We were not able to consider all topics relevant to the resuscitation of newborn puppies and kittens due to the limited resources available for this extended and complex evidence evaluation process. For example, the administration of caffeine might be used by some clinicians in nonvigorous, bradypneic newborns instead of doxapram. Umbilical cord milking with delayed cord clamping might be practiced by some veterinary surgeons during C-section and is recommended in term newborn infants not expected to require resuscitation [327]. As more direct veterinary evidence is published to address these and other questions, integrating such topics in future rounds of evidence evaluation is warranted.

Currently, significant uncertainty remains regarding most resuscitative interventions in newborn puppies and kittens at birth. However, through a comprehensive evaluation of the evidence and a consensus process that included considerations of feasibility, the treatment recommendations herein lay the foundation for clear, actionable guidance in small animal newborn resuscitation. In addition, a list of prioritized knowledge gaps emerged from this project and can serve to guide collaborative clinical research to overcome the lack of veterinary scientific data at present.

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Conflicts of Interest

Dr Burkitt-Creedon is the Editor of the Journal but only participated in the review process as an author. The authors declare no other conflicts of interest.

Endnotes

[a] Boller, Manuel, Jamie Burkitt-Creedon, and Daniel J. Fletcher. 2025. "RECOVER Newborn Guidelines 2025." OSF. June 14. https://osf.io/wxzqa/ (accessed on June 14, 2025).

[b] https://nowcomment.com (accessed on May 14, 2025).

References

1. A. Katheria and N. N. Finer, "Newborn Resuscitation," in *Avery's Diseases of the Newborn*, 10th ed., ed. C. A. Gleason and S. E. Juul (Elsevier, 2018), 273–288.

2. S. B. Hooper, M. J. Kitchen, G. R. Polglase, et al., "The Physiology of Neonatal Resuscitation," *Current Opinion in Pediatrics* 30, no. 2 (2018): 187–191.

3. A. Finnemore and A. Groves, "Physiology of the Fetal and Transitional Circulation," *Seminars in Fetal & Neonatal Medicine* 20, no. 4 (2015): 210–216.

4. P. F. Moon, H. N. Erb, J. W. Ludders, et al., "Perioperative Risk Factors for Puppies Delivered by Cesarean Section in the United States and Canada," *Journal of the American Animal Hospital Association* 36, no. 4 (2000): 359–368.

5. A. J. Cornelius, R. Moxon, J. Russenberger, et al., "Identifying Risk Factors for Canine Dystocia and Stillbirths," *Theriogenology* 128 (2019): 201–206.

6. R. Tønnessen, K. S. Borge, A. Nødtvedt, and A. Indrebø, "Canine Perinatal Mortality: A Cohort Study of 224 Breeds," *Theriogenology* 77, no. 9 (2012): 1788–1801.

7. A. Fournier, M. Masson, F. Corbière, et al., "Epidemiological Analysis of Reproductive Performances and Kitten Mortality Rates in 5,303 Purebred Queens of 45 Different Breeds and 28,065 Kittens in France," *Reproduction in Domestic Animals = Zuchthygiene* 52 (2017): 153–157.

8. M. H. Wyckoff, J. Wyllie, K. Aziz, et al., "Neonatal Life Support: 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations," *Circulation* 142, no. 16_suppl_1 (2020): S185–S221.

9. J. Madar, C. C. Roehr, S. Ainsworth, et al., "European Resuscitation Council Guidelines 2021: Newborn Resuscitation and Support of Transition of Infants at Birth," *Resuscitation* 161 (2021): 291–326.

10. N. K. Yamada, E. Szyld, M. L. Strand, et al., "2023 American Heart Association and American Academy of Pediatrics Focused Update on Neonatal Resuscitation: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care," *Circulation* 149, no. 1 (2024): e157–e166.

11. J. M. Burkitt-Creedon, M. Boller, D. J. Fletcher, et al., "2024 RECOVER Guidelines: Updated Treatment Recommendations for CPR in Dogs and Cats," *Journal of Veterinary Emergency and Critical Care* 34, no. Suppl 1 (2024): 104–123.

12. D. J. Fletcher, M. Boller, B. M. Brainard, et al., "RECOVER Evidence and Knowledge Gap Analysis on Veterinary CPR. Part 7: Clinical Guidelines," *Journal of Veterinary Emergency and Critical Care* 22, no. Suppl (2012): S102–S131.

13. A. M. Traas, "Resuscitation of Canine and Feline Neonates," *Theriogenology* 70, no. 3 (2008): 343–348.

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14. P. F. Moon, B. J. Massat, and P. J. Pascoe, "Neonatal Critical Care," *Veterinary Clinics of North America: Small Animal Practice* 31, no. 2 (2001): 343–367.

15. A. A. Cavanagh, "Neonatal Resuscitation," *Veterinary Team Brief* 5, no. 5 (2017): 27–28.

16. A. P. Davidson, "Neonatal Resuscitation: Improving the Outcome," *Veterinary Clinics of North America: Small Animal Practice* 44, no. 2 (2014): 191–204.

17. D. J. Fletcher, M. Boller, J. M. Burkitt-Creedon, et al., "2024 RECOVER Guidelines: Methods, Evidence Identification, Evaluation, and Consensus Process for Development of Treatment Recommendations," *Journal of Veterinary Emergency and Critical Care* 34, no. Suppl 1 (2024): 3–15.

18. S. A. Grundy, "Clinically Relevant Physiology of the Neonate," *Veterinary Clinics of North America: Small Animal Practice* 36, no. 3 (2006): 443–459.

19. M. B. Boller, "RECOVER Guidelines: Newborn Resuscitation in Dogs and Cats. Clinical Guidelines," *Journal of Veterinary Emergency and Critical Care* (2025).

20. O. D. Saugstad, T. Rootwelt, and O. Aalen, "Resuscitation of Asphyxiated Newborn Infants With Room Air or Oxygen: An International Controlled Trial: The Resair 2 Study," *Pediatrics* 102, no. 1 (1998): e1.

21. S. Ramji, S. Ahuja, S. Thirupuram, et al., "Resuscitation of Asphyxie Newborn Infants With Room Air or 100% Oxygen," *Pediatric Research* 34, no. 6 (1993): 809–812.

22. S. Ramji, R. Rasaily, P. K. Mishra, et al., "Resuscitation of Asphyxiated Newborns With Room Air or 100% Oxygen at Birth: A Multicentric Clinical Trial," *Indian Pediatrics* 40, no. 6 (2003): 510–517.

23. N. Bajaj, R. H. Udani, and R. N. Nanavati, "Room Air vs. 100 Per Cent Oxygen for Neonatal Resuscitation: A Controlled Clinical Trial," *Journal of Tropical Pediatrics* 51, no. 4 (2005): 206–211.

24. G. H. Guyatt, A. D. Oxman, R. Kunz, et al., "GRADE: Going From Evidence to Recommendations," *BMJ* 336, no. 7652 (2008): 1049–1051.

25. J. McGowan, M. Sampson, D. M. Salzwedel, et al., "PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement," *Journal of Clinical Epidemiology* 75 (2016): 40–46.

26. R. Boulkedid, H. Abdoul, M. Loustau, et al., "Using and Reporting the Delphi Method for Selecting Healthcare Quality Indicators: A Systematic Review," *PLoS ONE* 6, no. 6 (2011): e20476.

27. R. Guinsburg, M. F. B. de Almeida, E. Finan, et al., "Tactile Stimulation in Newborn Infants With Inadequate Respiration at Birth: A Systematic Review," *Pediatrics* 149, no. 4 (2022): e2021055067, https://doi.org/10.1542/peds.2021-055067.

28. H. L. Ersdal, E. Mduma, E. Svensen, and J. M. Perlman, "Early Initiation of Basic Resuscitation Interventions Including Face Mask Ventilation May Reduce Birth Asphyxia Related Mortality in Low-Income Countries: A Prospective Descriptive Observational Study," *Resuscitation* 83, no. 7 (2012): 869–873.

29. N. Baik-Schneditz, B. Urlesberger, B. Schwaberger, et al., "Tactile Stimulation During Neonatal Transition and Its Effect on Vital Parameters in Neonates During Neonatal Transition," *Acta Paediatrica* 107, no. 6 (2018): 952–957.

30. E. M. Scarpelli, S. Condorelli, and E. V. Cosmi, "Cutaneous Stimulation and Generation of Breathing in the Fetus," *Pediatric Research* 11, no. Pt 1 (1977): 24–28.

31. E. E. Faridy, "Instinctive Resuscitation of the Newborn Rat," *Respiration Physiology* 51, no. 1 (1983): 1–19.

32. J. Dekker, T. Martherus, S. J. E. Cramer, et al., "Tactile Stimulation to Stimulate Spontaneous Breathing During Stabilization of Preterm Infants at Birth: A Retrospective Analysis," *Frontiers in Pediatrics* 5 (2017): 61.

33. R. S. Bloom, *Textbook of Neonatal Resuscitation*, 3rd ed. (American Heart Association/American Academy of Pediatrics, 1994).

34. S. Niermeyer, J. Kattwinkel, P. Van Reempts, et al., "International Guidelines for Neonatal Resuscitation: An Excerpt From the Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care: International Consensus on Science. Contributors and Reviewers for the Neonatal Resuscitation Guidelines," *Pediatrics* 106, no. 3 (2000): E29.

35. M. H. Wyckoff, K. Aziz, M. B. Escobedo, et al., "Part 13: Neonatal Resuscitation: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care," *Circulation* 132, no. 18 Suppl 2 (2015): S543–S560.

36. S. Chettri, B. Adhisivam, and B. V. Bhat, "Endotracheal Suction for Nonvigorous Neonates Born Through Meconium Stained Amniotic Fluid: A Randomized Controlled Trial," *Journal of Pediatrics* 166, no. 5 (2015): 1208.e1–1213.e1.

37. S. Nangia, S. Sunder, R. Biswas, and A. Saili, "Endotracheal Suction in Term Non Vigorous Meconium Stained Neonates—A Pilot Study," *Resuscitation* 105 (2016): 79–84.

38. A. Kumar, P. Kumar, and S. Basu, "Endotracheal Suctioning for Prevention of Meconium Aspiration Syndrome: A Randomized Controlled Trial," *European Journal of Pediatrics* 178, no. 12 (2019): 1825–1832.

39. P. Ting and J. P. Brady, "Tracheal Suction in Meconium Aspiration," *American Journal of Obstetrics and Gynecology* 122, no. 6 (1975): 767–771.

40. N. E. Vain, E. G. Szyld, L. M. Prudent, et al., "Oropharyngeal and Nasopharyngeal Suctioning of Meconium-Stained Neonates Before Delivery of Their Shoulders: Multicentre, Randomised Controlled Trial," *Lancet* 364, no. 9434 (2004): 597–602.

41. S. Goericke-Pesch and A. Wehrend, "New Method for Removing Mucus From the Upper respiratory Tract of Newborn Puppies Following Caesarean Section," *The Veterinary Record* 170, no. 11 (2012): 289, https://doi.org/10.1136/vr.100625.

42. S. Lakshminrusimha, B. Mathew, J. Nair, et al., "Tracheal Suctioning Improves Gas Exchange but Not Hemodynamics in Asphyxiated Lambs With Meconium Aspiration," *Pediatric Research* 77, no. 2 (2015): 347–355.

43. M. Pocivalnik, B. Urlesberger, E. Ziehenberger, et al., "Oropharyngeal Suctioning in Neonates Immediately After Delivery: Influence on Cerebral and Peripheral Tissue Oxygenation," *Early Human Development* 91, no. 2 (2015): 153–157.

44. P. A. Waltman, J. M. Brewer, B. P. Rogers, and W. L. May, "Building Evidence for Practice: A Pilot Study of Newborn Bulb Suctioning at Birth," *Journal of Midwifery & Women's Health* 49, no. 1 (2004): 32–38.

45. S. Gungor, E. Kurt, and E. Teksoz, "Oronasopharyngeal Suction Versus No Suction in Normal and Term Infants Delivered by Elective Cesarean Section: A Prospective Randomized Controlled Trial," *Gynecologic and Obstetric Investigation* 61, no. 1 (2006): 9–14.

46. S. Gungor, E. Teksoz, T. Ceyhan, et al., "Oronasopharyngeal Suction Versus No Suction in Normal, Term and Vaginally Born Infants: A Prospective Randomised Controlled Trial," *Australian and New Zealand Journal of Obstetrics and Gynaecology* 45, no. 5 (2005): 453–456.

47. A. Bancalari, V. Díaz, and H. Araneda, "Effects of Pharyngeal Suction on the Arterial Oxygen Saturation and Heart Rate in Healthy Newborns Delivered by Elective Cesarean Section," *Journal of Neonatal-Perinatal Medicine* 12, no. 3 (2019): 271–276.

48. V. Modarres Nejad, R. Hosseini, A. Sarrafi Nejad, and G. Shafiee, "Effect of Oronasopharyngeal Suction on Arterial Oxygen Saturation in Normal, Term Infants Delivered Vaginally: A Prospective Randomised Controlled Trial," *Journal of Obstetrics and Gynaecology* 34, no. 5 (2014): 400–402.

49. M. Bruckner and G. M. Schmölzer, "Physiologic Changes During Neonatal Transition and the Influence of Respiratory Support," *Clinics in Perinatology* 48, no. 4 (2021): 697–709.

50. M. Carrasco, M. Martell, and P. C. Estol, "Oronasopharyngeal Suction at Birth: Effects on Arterial Oxygen Saturation," *Journal of Pediatrics* 130, no. 5 (1997): 832–834.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70012, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

51. P. C. Estol, H. Piriz, S. Basalo, et al., "Oro-Naso-Pharyngeal Suction at Birth: Effects on Respiratory Adaptation of Normal Term Vaginally Born Infants," *Journal of Perinatal Medicine* 20, no. 4 (1992): 297–305.

52. J. Kelleher, R. Bhat, A. A. Salas, et al., "Oronasopharyngeal Suction Versus Wiping of the Mouth and Nose at Birth: A Randomised Equivalency Trial," *Lancet* 382, no. 9889 (2013): 326–330.

53. V. R. Viraraghavan, S. Nangia, B. H. Prathik, et al., "Yield of Meconium in Non-Vigorous Neonates Undergoing Endotracheal Suctioning and Profile of all Neonates Born Through Meconium-Stained Amniotic Fluid: A Prospective Observational Study," *Paediatrics and International Child Health* 38, no. 4 (2018): 266–270.

54. T. F. Baskett and F. Nagele, "Bernhard Schultze and the Swinging Neonate," *Resuscitation* 51, no. 1 (2001): 3–6.

55. S. A. Grundy, S. M. Liu, and A. P. Davidson, "Intracranial Trauma in a Dog due to Being "Swung" at Birth," *Top Companion Anim Med* 24, no. 2 (2009): 100–103.

56. K. Lunze, D. E. Bloom, D. T. Jamison, and D. H. Hamer, "The Global Burden of Neonatal Hypothermia: Systematic Review of a Major Challenge for Newborn Survival," *BMC Medicine* 11, no. 1 (2013): 24, https://doi.org/10.1186/1741-7015-11-24.

57. B. Reyes-Sotelo, D. Mota-Rojas, J. Martínez-Burnes, et al., "Thermal Homeostasis in the Newborn Puppy: Behavioral and Physiological Responses," *Journal of Animal Behaviour and Biometeorology* 9, no. 3 (2020): e2112, https://doi.org/10.31893/jabb.21012.

58. G. W. Crighton and R. Pownall, "The Homeothermic Status of the Neonatal Dog," *Nature* 251, no. 5471 (1974): 142–144.

59. J. M. Perlman, J. Wyllie, J. Kattwinkel, et al., "Part 7: Neonatal Resuscitation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations," *Circulation* 132, no. 16 Suppl 1 (2015): S204–S241.

60. V. V. Ramaswamy, M. F. de Almeida, J. A. Dawson, et al., "Maintaining Normal Temperature Immediately After Birth in Late Preterm and Term Infants: A Systematic Review and Meta-Analysis," *Resuscitation* 180 (2022): 81–98.

61. M. P. Meyer, M. J. Payton, A. Salmon, et al., "A Clinical Comparison of Radiant Warmer and Incubator Care for Preterm Infants From Birth to 1800 Grams," *Pediatrics* 108, no. 2 (2001): 395–401.

62. M. C. Reilly, S. Vohra, V. E. Rac, et al., "Randomized Trial of Occlusive Wrap for Heat Loss Prevention in Preterm Infants," *Journal of Pediatrics* 166, no. 2 (2015): 262.e2–268.e2.

63. S. Vohra, G. Frent, V. Campbell, et al., "Effect of Polyethylene Occlusive Skin Wrapping on Heat Loss in Very Low Birth Weight Infants at Delivery: A Randomized Trial," *Journal of Pediatrics* 134, no. 5 (1999): 547–551.

64. S. Vohra, R. S. Roberts, B. Zhang, et al., "Heat Loss Prevention (HeLP) in the Delivery Room: A Randomized Controlled Trial of Polyethylene Occlusive Skin Wrapping in Very Preterm Infants," *Journal of Pediatrics* 145, no. 6 (2004): 750–753.

65. H. Mila, A. Grellet, M. Delebarre, et al., "Monitoring of the Newborn Dog and Prediction of Neonatal Mortality," *Preventive Veterinary Medicine* 143 (2017): 11–20.

66. A. R. Laptook, W. Salhab, and B. Bhaskar, "Admission Temperature of Low Birth Weight Infants: Predictors and Associated Morbidities," *Pediatrics* 119, no. 3 (2007): e643–e649.

67. L. C. Mullany, J. Katz, S. K. Khatry, et al., "Risk of Mortality Associated With Neonatal Hypothermia in Southern Nepal," *Archives of Pediatrics & Adolescent Medicine* 164, no. 7 (2010): 650–656.

68. A. L. Kent and J. Williams, "Increasing Ambient Operating Theatre Temperature and Wrapping in Polyethylene Improves Admission Temperature in Premature Infants," *Journal of Paediatrics and Child Health* 44, no. 6 (2008): 325–331.

69. S. S. Miller, H. C. Lee, and J. B. Gould, "Hypothermia in Very Low Birth Weight Infants: Distribution, Risk Factors and Outcomes," *Journal of Perinatology* 31, no. Suppl 1 (2011): S49–S56.

70. C. V. Rohlicek, C. Saiki, T. Matsuoka, and J. P. Mortola, "Cardiovascular and Respiratory Consequences of Body Warming During Hypoxia in Conscious Newborn Cats," *Pediatric Research* 40, no. 1 (1996): 1–5.

71. C. Uystepruyst, J. Coghe, T. Dorts, et al., "Effect of Three Resuscitation Procedures on Respiratory and Metabolic Adaptation to Extra Uterine Life in Newborn Calves," *Veterinary Journal* 163, no. 1 (2002): 30–44.

72. K. Haaland, E. M. Løberg, P. A. Steen, et al., "The Effect of Mild Post-Hypoxic Hypothermia on Organ Pathology in a Piglet Survival Model of Global Hypoxia," *Prenatal and Neonatal Medicine* 2, no. 4 (1997): 329–337.

73. S. A. Abd-El Hamid, M. M. Badr-El Din, N. I. Dabous, and K. M. Saad, "Effect of the Use of a Polyethylene Wrap on the Morbidity and Mortality of Very Low Birth Weight Infants in Alexandria University Children's Hospital," *Journal of the Egyptian Public Health Association* 87, no. 5-6 (2012): 104–108.

74. R. Lenclen, M. Mazraani, M. Jugie, et al., "Use of a Polyethylene Bag: A Way to Improve the Thermal Environment of the Premature Newborn at the Delivery Room," *Archives De Pediatrie* 9, no. 3 (2002): 238–244.

75. F. G. Vassalo, C. R. B. Simões, M. J. Sudano, et al., "Topics in the Routine Assessment of Newborn Puppy Viability," *Topics in Companion Animal Medicine* 30, no. 1 (2015): 16–21.

76. B. A. Shah, A. G. Wlodaver, M. B. Escobedo, et al., "Impact of Electronic Cardiac (ECG) Monitoring on Delivery Room Resuscitation and Neonatal Outcomes," *Resuscitation* 143 (2019): 10–16.

77. A. Katheria, K. Arnell, M. Brown, et al., "A Pilot Randomized Controlled Trial of EKG for Neonatal Resuscitation," *PLoS ONE* 12, no. 11 (2017): e0187730.

78. M. C. Murphy, L. De Angelis, L. K. McCarthy, and C. P. F. O'Donnell, "Comparison of Infant Heart Rate Assessment by Auscultation, ECG and Oximetry in the Delivery Room," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 103, no. 5 (2018): F490–F492.

79. A. Dyson, M. Jeffrey, and M. Kluckow, "Measurement of Neonatal Heart Rate Using Handheld Doppler Ultrasound," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 102, no. 2 (2017): F116–F119.

80. B. Iglesias, M. A. J. Rodri Guez, E. Aleo, et al., "3-Lead Electrocardiogram Is More Reliable Than Pulse Oximetry to Detect Bradycardia During Stabilisation at Birth of Very Preterm Infants," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 103, no. 3 (2018): F233–F237.

81. G. Agrawal, A. Kumar, S. Wazir, et al., "A Comparative Evaluation of Portable Doppler Ultrasound Versus Electrocardiogram in Heart-Rate Accuracy and Acquisition Time Immediately After Delivery: A Multicenter Observational Study," *The Journal of Maternal-Fetal & Neonatal Medicine* 34, no. 13 (2019): 2053–2060.

82. C. O. F. Kamlin, C. P. F. O'Donnell, and N. J. Everest, "Accuracy of Clinical Assessment of Infant Heart Rate in the Delivery Room," *Resuscitation* 71, no. 3 (2006): 319–321.

83. A. Katheria, W. Rich, and N. Finer, "Electrocardiogram Provides a Continuous Heart Rate Faster Than Oximetry During Neonatal Resuscitation," *Pediatrics* 130, no. 5 (2012): e1177–e1181.

84. R. Shimabukuro, K. Takase, S. Ohde, and I. Kusakawa, "Handheld Fetal Doppler Device for Assessing Heart Rate in Neonatal Resuscitation," *Pediatrics International* 59, no. 10 (2017): 1069–1073.

85. J. J. Van Vonderen, S. B. Hooper, J. K. Kroese, et al., "Pulse Oximetry Measures a Lower Heart Rate at Birth Compared With Electrocardiography," *Journal of Pediatrics* 166, no. 1 (2015): 49–53.

86. N. Morina, P. A. Johnson, and M. O'Reilly, "Doppler Ultrasound for Heart Rate Assessment in a Porcine Model of Neonatal Asphyxia," *Frontiers in Pediatrics* 8 (2020): 18, https://doi.org/10.3389/fped.2020.00018.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70012, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

87. D. H. Luong, P.-Y. Cheung, and M. O'Reilly, "Electrocardiography vs. Auscultation to Assess Heart Rate During Cardiac Arrest With Pulseless Electrical Activity in Newborn Infants," *Frontiers in Pediatrics* 6 (2018): 366, https://doi.org/10.3389/fped.2018.00366.

88. L. M. Walter, B. Ahmed, A. Odoi, et al., "Bradycardias Are Associated With More Severe Effects on Cerebral Oxygenation in Very Preterm Infants Than in Late Preterm Infants," *Early Human Development* 127 (2018): 33–41.

89. M. C. Murphy, L. De Angelis, L. K. McCarthy, and C. P. F. O'Donnell, "Randomised Study Comparing Heart Rate Measurement in Newly Born Infants Using a Monitor Incorporating Electrocardiogram and Pulse Oximeter Versus Pulse Oximeter Alone," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 104, no. 5 (2019): F547–F550.

90. H. Mizumoto, S. Tomotaki, H. Shibata, et al., "Electrocardiogram Shows Reliable Heart Rates Much Earlier Than Pulse Oximetry During Neonatal Resuscitation," *Pediatrics International* 54, no. 2 (2012): 205–207.

91. C. P. F. O'Donnell, C. O. F. Kamlin, P. G. Davis, and C. J. Morley, "Feasibility of and Delay in Obtaining Pulse Oximetry During Neonatal Resuscitation," *Journal of Pediatrics* 147, no. 5 (2005): 698–699.

92. B. Ström Holst and J. Frössling, "The Swedish Breeding Cat: Population Description, Infectious Diseases and Reproductive Performance Evaluated by a Questionnaire," *Journal of Feline Medicine and Surgery* 11, no. 10 (2009): 793–802.

93. K. S. Borge, R. Tønnessen, A. Nødtvedt, and A. Indrebø, "Litter Size at Birth in Purebred Dogs—A Retrospective Study of 224 Breeds," *Theriogenology* 75, no. 5 (2011): 911–919.

94. D. A. Giussani, J. A. Spencer, P. J. Moore, et al., "Afferent and Efferent Components of the Cardiovascular Reflex Responses to Acute Hypoxia in Term Fetal Sheep," *The Journal of Physiology* 461, no. 1 (1993): 431–449.

95. S. Badurdeen, P. G. Davis, S. B. Hooper, et al., "Physiologically Based Cord Clamping for Infants ≥32+0 Weeks Gestation: A Randomised Clinical Trial and Reference Percentiles for Heart Rate and Oxygen Saturation for Infants ≥35+0 Weeks Gestation," *PLoS Medicine* 19, no. 6 (2022): e1004029.

96. J. E. Linde, J. Schulz, J. M. Perlman, et al., "Normal Newborn Heart Rate in the First Five Minutes of Life Assessed by Dry-Electrode Electrocardiography," *Neonatology* 110, no. 3 (2016): 231–237.

97. D. Groppetti, A. Pecile, A. P. Del Carro, et al., "Evaluation of Newborn Canine Viability by Means of Umbilical Vein Lactate Measurement, Apgar Score and Uterine Tocodynamometry," *Theriogenology* 74, no. 7 (2010): 1187–1196.

98. M. Batista, C. Moreno, J. Vilar, et al., "Neonatal Viability Evaluation by Apgar Score in Puppies Delivered by Cesarean Section in Two Brachycephalic Breeds (English and French Bulldog)," *Animal Reproduction Science* 146, no. 3-4 (2014): 218–226.

99. M. C. Veronesi, "Assessment of Canine Neonatal Viability—The Apgar Score," *Reproduction in Domestic Animals = Zuchthygiene* 51 (2016): 46–50.

100. M. L. Espinoza, P.-Y. Cheung, T.-F. Lee, et al., "Heart Rate Changes During Positive Pressure Ventilation After Asphyxia-Induced Bradycardia in a Porcine Model of Neonatal Resuscitation," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 104, no. 1 (2019): F98–F101.

101. H. Kirpalani, S. J. Ratcliffe, M. Keszler, et al., "Effect of Sustained Inflations vs Intermittent Positive Pressure Ventilation on Bronchopulmonary Dysplasia or Death Among Extremely Preterm Infants: The SAIL Randomized Clinical Trial," *JAMA* 321, no. 12 (2019): 1165–1175.

102. P. Jiravisitkul, S. Rattanasiri, and P. Nuntnarumit, "Randomised Controlled Trial of Sustained Lung Inflation for Resuscitation of Preterm Infants in the Delivery Room," *Resuscitation* 111 (2017): 68–73.

103. G. Lista, P. Fontana, F. Castoldi, et al., "Does Sustained Lung Inflation at Birth Improve Outcome of Preterm Infants at Risk for Respiratory Distress Syndrome?," *Neonatology* 99, no. 1 (2011): 45–50.

104. J. J. van Vonderen, S. B. Hooper, H. D. Hummler, et al., "Effects of a Sustained Inflation in Preterm Infants at Birth," *Journal of Pediatrics* 165, no. 5 (2014): 903.e1–908.e1.

105. D. G. Tingay, A. Togo, P. M. Pereira-Fantini, et al., "Aeration Strategy at Birth Influences the Physiological Response to Surfactant in Preterm Lambs," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 104, no. 6 (2019): F587–F593.

106. C. Klingenberg, K. S. Sobotka, T. Ong, et al., "Effect of Sustained Inflation Duration; Resuscitation of Near-Term Asphyxiated Lambs," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 98, no. 3 (2013): F222–F227.

107. D. G. Tingay, G. R. Polglase, R. Bhatia, et al., "Pressure-Limited Sustained Inflation vs. Gradual Tidal Inflations for Resuscitation in Preterm Lambs," *Journal of Applied Physiology* 118, no. 7 (2015): 890–897.

108. M. E. Probyn, S. B. Hooper, P. A. Dargaville, et al., "Positive End Expiratory Pressure During Resuscitation of Premature Lambs Rapidly Improves Blood Gases Without Adversely Affecting Arterial Pressure," *Pediatric Research* 56, no. 2 (2004): 198–204.

109. C. Grasso, P. Sciacca, V. Giacchi, et al., "Effects of Sustained Lung Inflation, a Lung Recruitment Maneuver in Primary Acute Respiratory Distress Syndrome, in Respiratory and Cerebral Outcomes in Preterm Infants," *Early Human Development* 91, no. 1 (2015): 71–75.

110. M. S. El-Chimi, H. A. Awad, T. M. El-Gammasy, et al., "Sustained Versus Intermittent Lung Inflation for Resuscitation of Preterm Infants: A Randomized Controlled Trial," *The Journal of Maternal-Fetal & Neonatal Medicine* 30, no. 11 (2017): 1273–1278.

111. S. K. Griffiths and J. P. Campbell, "Placental Structure, Function and Drug Transfer," *BJA Education* 15, no. 2 (2015): 84–89.

112. J. E. Brice, T. A. Moreland, and C. H. Walker, "Effects of Pethidine and Its Antagonists on the Newborn," *Archives of Disease in Childhood* 54, no. 5 (1979): 356–361.

113. B. W. Bonta, J. V. Gagliardi, V. Williams, and J. B. Warshaw, "Naloxone Reversal of Mild Neurobehavioral Depression in Normal Newborn Infants After Routine Obstetric Analgesia," *Journal of Pediatrics* 94, no. 1 (1979): 102–105.

114. W. Dick, E. Knoche, and E. Traub, "Clinical Investigations of the Influence of Various Naloxone Doses on the Newborn," *Journal of Perinatal Medicine* 6, no. 2 (1978): 95–101.

115. J. M. Evans, M. I. Hogg, and M. Rosen, "Reversal of Narcotic Depression in the Neonate by Nalozone," *BMJ* 2, no. 6044 (1976): 1098–1100.

116. P. C. Wiener, M. I. Hogg, and M. Rosen, "Effects of Naloxone on Pethidine-Induced Neonatal Depression. Part I—Intravenous Naloxone," *BMJ* 2 (1977): 228–229.

117. P. C. Wiener, M. I. Hogg, and M. Rosen, "Effects of Naloxone on Pethidine-Induced Neonatal Depression. Part II—Intramuscular Naloxone," *BMJ* 2 (1977): 229–231.

118. T. Gerhardt, E. Bancalari, H. Cohen, and L. F. Rocha, "Use of Naloxone to Reverse Narcotic Respiratory Depression in the Newborn Infant," *Journal of Pediatrics* 90, no. 6 (1977): 1009–1012.

119. D. Box and D. Cochran, "Safe Reduction in Administration of Naloxone to Newborn Infants: An Observational Study," *Acta Paediatrica* 95, no. 9 (2006): 1083–1086.

120. C. Wang, S. Liu, C. Han, et al., "Effect and Placental Transfer of Dexmedetomidine During Caesarean Section Under Epidural Anaesthesia," *Journal of International Medical Research* 45, no. 3 (2017): 964–972.

121. S. D. Roy and G. L. Flynn, "Solubility and Related Physicochemical Properties of Narcotic Analgesics," *Pharmaceutical Research* 5, no. 9 (1988): 580–586.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70012, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

122. V. Chernick, J. Manfreda, V. D. Booy, et al., "Clinical Trial of Naloxone, in Birth Asphyxia," *Journal of Pediatrics* 113, no. 3 (1988): 519–525.

123. V. Chernick, D. L. Madansky, and E. E. Lawson, "Naloxone Decreases the Duration of Primary Apnea With Neonatal Asphyxia," *Pediatric Research* 14, no. 4 (1980): 357–359.

124. A. Martinez, J. Padbury, L. Shames, et al., "Naloxone Potentiates Epinephrine Release During Hypoxia in Fetal Sheep: Dose Response and Cardiovascular Effects," *Pediatric Research* 23, no. 4 (1988): 343–347.

125. R. M. de-Castro, J. E. Cabral-Filho, J. A. Costa, et al., "Neonatal Treatment With Naloxone Causes Permanent Hyperalgesia in Rats," *Brazilian Journal of Medical and Biological Research* 26, no. 7 (1993): 747–751.

126. J. M. Perlman, J. Wyllie, J. Kattwinkel, et al., "Part 11: Neonatal Resuscitation: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations," *Circulation* 122, no. 16 SUPPL. 2 (2010): S516–S538.

127. A. M. Cone, S. Nadel, and B. Sweeney, "Flumazenil Reverses Diazepam-Induced Neonatal Apnoea and Hypotonia," *European Journal of Pediatrics* 152, no. 5 (1993): 458–459.

128. P. Richard, E. Autret, J. Bardol, et al., "The Use of Flumazenil in a Neonate," *Journal of Toxicology Clinical Toxicology* 29, no. 1 (1991): 137–140.

129. J. C. Dixon, B. D. Speidel, and J. J. Dixon, "Neonatal Flumazenil Therapy Reverses Maternal Diazepam," *Acta Paediatrica* 87, no. 2 (1998): 225–226.

130. J. Shin, "Anesthetic Management of the Pregnant Patient: Part 2," *Anesthesia Progress* 68, no. 2 (2021): 119–127.

131. M. Mandelli, P. L. Morselli, S. Nordio, et al., "Placental Transfer of Diazepam and Its Disposition in the Newborn," *Clinical Pharmacology & Therapeutics* 17, no. 5 (1975): 564–572.

132. K. G. M. De Cramer, K. E. Joubert, and J. O. Nöthling, "Puppy Survival and Vigor Associated With the Use of Low Dose Medetomidine Premedication, Propofol Induction and Maintenance of Anesthesia Using Sevoflurane Gas-Inhalation for Cesarean Section in the Bitch," *Theriogenology* 96 (2017): 10–15.

133. D. Groppetti, F. Di Cesare, A. Pecile, et al., "Maternal and Neonatal Wellbeing During Elective C-Section Induced With a Combination of Propofol and Dexmedetomidine: How Effective Is the Placental Barrier in Dogs?," *Theriogenology* 129 (2019): 90–98.

134. P. F. Moon, H. N. Erb, J. W. Ludders, et al., "Perioperative Management and Mortality Rates of Dogs Undergoing Cesarean Section in the United States and Canada," *Journal of the American Veterinary Medical Association* 213, no. 3 (1998): 365–369.

135. J. Cain and A. Davidson, "Canine Cesarean Section: Emergency and Elective," *Veterinary Clinics of North America: Small Animal Practice* 53, no. 5 (2023): 1123–1146.

136. R. Huupponen, S. Karhuvaara, M. Anttila, et al., "Buccal Delivery of an Alpha 2-Adrenergic Receptor Antagonist, Atipamezole, in Humans," *Clinical Pharmacology & Therapeutics* 58, no. 5 (1995): 506–511.

137. F. M. Oliver, T. W. Sweatman, J. H. Unkel, et al., "Comparative Pharmacokinetics of Submucosal vs. intravenous Flumazenil (Romazicon) in an Animal Model," *Pediatric Dentistry* 22, no. 6 (2000): 489–493.

138. A. L. Portbury, R. Chandra, M. Groelle, et al., "Catecholamines Act via a β-Adrenergic Receptor to Maintain Fetal Heart Rate and Survival," *American Journal of Physiology - Heart and Circulatory Physiology* 284, no. 6 (2003): H2069–H2077.

139. A. M. Walker, J. P. Cannata, M. H. Dowling, et al., "Age-Dependent Pattern of Autonomic Heart Rate Control During Hypoxia in Fetal and Newborn Lambs," *Biology of the Neonate* 35, no. 3/4 (1979): 198–208.

140. P. Danilo, Jr., M. R. Rosen, and A. J. Hordof, "Effects of Acetylcholine on the Ventricular Specialized Conducting System of Neonatal and Adult Dogs," *Circulation Research* 43, no. 5 (1978): 777–784.

141. R. C. Goodlin and H. C. Haesslein, "Fetal Reacting Bradycardia," *American Journal of Obstetrics and Gynecology* 129, no. 8 (1977): 845–856.

142. E. Balıkcı and A. Yıldız, "Effects on Arterial Blood Gases and Some Clinical Parameters of Caffeine, Atropine Sulphate or Doxapram Hydrochloride in Calves With Neonatal Asphyxia," *Revue de Medecine Veterinaire* 160, no. 6 (2009): 282–287.

143. S. E. Mace and M. N. Levy, "Neural Control of Heart Rate: A Comparison Between Puppies and Adult Animals," *Pediatric Research* 17, no. 6 (1983): 491–495.

144. A. Bashir, B. Bird, L. Wu, et al., "Neonatal Outcomes Based on Mode and Intensity of Delivery Room Resuscitation," *Journal of Perinatology* 37, no. 10 (2017): 1103–1107.

145. X.-Y. Zhu, B.-C. Lin, Q.-S. Zhang, et al., "A Prospective Evaluation of the Efficacy of the Laryngeal Mask Airway During Neonatal Resuscitation," *Resuscitation* 82, no. 11 (2011): 1405–1409.

146. L. Armstrong, N. Caulkett, S. Boysen, et al., "Assessing the Efficacy of Ventilation of Anesthetized Neonatal Calves Using a Laryngeal Mask Airway or Mask Resuscitator," *Frontiers in Veterinary Science* 5 (2018): 292.

147. M. Vento, J. Sastre, M. A. Asensi, and J. Viña, "Room-Air Resuscitation Causes Less Damage to Heart and Kidney Than 100% Oxygen," *American Journal of Respiratory and Critical Care Medicine* 172, no. 11 (2005): 1393–1398.

148. A. Mrelashvili, J. B. Russ, D. M. Ferriero, and C. J. Wusthoff, "The Sarnat Score for Neonatal Encephalopathy: Looking Back and Moving Forward," *Pediatric Research* 88, no. 6 (2020): 824–825.

149. P. Y. Cheung, L. Obaid, M. Emara, et al., "Cardio-Renal Recovery of Hypoxic Newborn Pigs After 18%, 21% and 100% Reoxygenation," *Intensive Care Medicine* 34, no. 6 (2008): 1114–1121.

150. E. Smit, X. Liu, H. Gill, et al., "The Effect of Resuscitation in 100% Oxygen on Brain Injury in a Newborn Rat Model of Severe Hypoxic-Ischaemic Encephalopathy," *Resuscitation* 96 (2015): 214–219.

151. M. Vento, M. Asensi, J. Sastre, et al., "Six Years of Experience With the Use of Room Air for the Resuscitation of Asphyxiated Newly Born Term Infants," *Biology of the Neonate* 79, no. 3-4 (2001): 261–267.

152. M. Vento, M. Asensi, J. Sastre, et al., "Oxidative Stress in Asphyxiated Term Infants Resuscitated With 100% Oxygen," *Journal of Pediatrics* 142, no. 3 (2003): 240–246.

153. J. M. Goplerud, S. Kim, and M. Delivoria-Papadopoulos, "The Effect of Post-Asphyxial Reoxygenation With 21% vs. 100% Oxygen on Na+, K+-ATPase Activity in Striatum of Newborn Piglets," *Brain Research* 696, no. 1-2 (1995): 161–164.

154. T. Rootwelt, J. P. Odden, C. Hall, and O. D. Saugstad, "Regional Blood Flow During Severe Hypoxemia and Resuscitation With 21% or 100% O2 in Newborn Pigs," *Journal of Perinatal Medicine* 24, no. 3 (1996): 227–236.

155. E. Haase, D. L. Bigam, Q. B. Nakonechny, et al., "Resuscitation With 100% Oxygen Causes Intestinal Glutathione Oxidation and Reoxygenation Injury in Asphyxiated Newborn Piglets," *Annals of Surgery* 240, no. 2 (2004): 364–373.

156. D. Fugelseth, W. B. Børke, K. Lenes, et al., "Restoration of Cardiopulmonary Function With 21% Versus 100% Oxygen After Hypoxaemia in Newborn Pigs," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 90, no. 3 (2005): F229–F234.

157. J. P. Stevens, E. Haase, T. Churchill, et al., "Resuscitation With 21% or 100% Oxygen Is Equally Effective in Restoring Perfusion and Oxygen Metabolism in the Liver of Hypoxic Newborn Piglets," *Shock* 27, no. 6 (2007): 657–662.

158. J. P. Stevens, T. Churchill, K. Fokkelman, et al., "Oxidative Stress and Matrix Metalloproteinase-9 Activity in the Liver After Hypoxia and Reoxygenation With 21% or 100% Oxygen in Newborn Piglets," *European Journal of Pharmacology* 580, no. 3 (2008): 385–393.

159. P.-Y. Cheung, J. ST, L. Obaid, et al., "The Systemic, Pulmonary and Regional Hemodynamic Recovery of Asphyxiated Newborn Piglets

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70012, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Resuscitated With 18%, 21% and 100% Oxygen," *Resuscitation* 76, no. 3 (2008): 457–464.

160. A. L. Solevåg, I. Dannevig, B. Nakstad, and O. D. Saugstad, "Resuscitation of Severely Asphyctic Newborn Pigs With Cardiac Arrest by Using 21% or 100% Oxygen," *Neonatology* 98, no. 1 (2010): 64–72.

161. A. L. Solevag, C. Garcia-Hidalgo, P.-Y. Cheung, et al., "Ventilation With 18, 21, or 100% Oxygen During Cardiopulmonary Resuscitation of Asphyxiated Piglets: A Randomized Controlled Animal Trial," *Neonatology* 117, no. 1 (2020): 102–110.

162. R. Solberg, M. Longini, F. Proietti, et al., "Resuscitation With Supplementary Oxygen Induces Oxidative Injury in the Cerebral Cortex," *Free Radical Biology and Medicine* 53, no. 5 (2012): 1061–1067.

163. S. Lakshminrusimha, R. H. Steinhorn, S. Wedgwood, et al., "Pulmonary Hemodynamics and Vascular Reactivity in Asphyxiated Term Lambs Resuscitated With 21 and 100% Oxygen," *Journal of Applied Physiology* 111, no. 5 (2011): 1441–1447.

164. E. Haase, D. L. Bigam, Q. B. Nakonechny, et al., "Cardiac Function, Myocardial Glutathione, and Matrix Metalloproteinase-2 Levels in Hypoxic Newborn Pigs Reoxygenated by 21%, 50%, or 100% Oxygen," *Shock* 23, no. 4 (2005): 383–389.

165. C. O. Chua, G. Vinukonda, F. Hu, et al., "Effect of Hyperoxic Resuscitation on Propensity of Germinal Matrix Haemorrhage and Cerebral Injury," *Neuropathology and Applied Neurobiology* 36, no. 5 (2010): 448–458.

166. V. H. Kumar, A. Patel, D. D. Swartz, et al., "Exposure to Supplemental Oxygen and Its Effects on Oxidative Stress and Antioxidant Enzyme Activity in Term Newborn Lambs," *Pediatric Research* 67, no. 1 (2010): 66–71.

167. S. Kutzsche, P. Ilves, O. J. Kirkeby, and O. D. Saugstad, "Hydrogen Peroxide Production in Leukocytes During Cerebral Hypoxia and Reoxygenation With 100% or 21% Oxygen in Newborn Piglets," *Pediatric Research* 49, no. 6 (2001): 834–842.

168. J. P. Poulsen, S. Oyasaeter, and O. D. Saugstad, "Hypoxanthine, Xanthine, and Uric Acid in Newborn Pigs During Hypoxemia Followed by Resuscitation With Room Air or 100% Oxygen," *Critical Care Medicine* 21, no. 7 (1993): 1058–1065.

169. T. Rootwelt, E. M. Loberg, A. Moen, et al., "Hypoxemia and Reoxygenation With 21% or 100% Oxygen in Newborn Pigs: Changes in Blood Pressure, Base Deficit, and Hypoxanthine and Brain Morphology," *Pediatric Research* 32, no. 1 (1992): 107–113.

170. M. M. Tyree, C. Dalgard, and J. T. O'Neill, "Impact of Room Air Resuscitation on Early Growth Response Gene-1 in a Neonatal Piglet Model of Cerebral Hypoxic Ischemia," *Pediatric Research* 59, no. 3 (2006): 423–427.

171. H. H. Odland, G. A. B. Kro, T. Edvardsen, et al., "Impaired Diastolic Function and Disruption of the Force-Frequency Relationship in the Right Ventricle of Newborn Pigs Resuscitated With 100% Oxygen," *Neonatology* 101, no. 2 (2012): 147–153.

172. W. B. Borke, B. H. Munkeby, B. Halvorsen, et al., "Increased Myocardial Matrix Metalloproteinases in Hypoxic Newborn Pigs During Resuscitation: Effects of Oxygen and Carbon Dioxide," *European Journal of Clinical Investigation* 34, no. 7 (2004): 459–466.

173. V. Fanos, A. Noto, T. Xanthos, et al., "Metabolomics Network Characterization of Resuscitation After Normocapnic Hypoxia in a Newborn Piglet Model Supports the Hypothesis That Room Air Is Better," *BioMed Research International* 2014 (2014): 731620, https://doi.org/10.1155/2014/731620.

174. P. A. Tølløfsrud, A. B. Solås, and O. D. Saugstad, "Newborn Piglets With Meconium Aspiration Resuscitated With Room Air or 100% Oxygen," *Pediatric Research* 50, no. 3 (2001): 423–429.

175. K. H. Bockhorst, P. A. Narayana, J. Dulin, et al., "Normobaric Hyperoximia Increases Hypoxia-Induced Cerebral Injury: DTI Study in Rats," *Journal of Neuroscience Research* 88, no. 5 (2010): 1146–1156.

176. I. Chapados, C. L. Chik, and P.-Y. Cheung, "Plasma Cortisol Response to ACTH Challenge in Hypoxic Newborn Piglets Resuscitated With 21% and 100% Oxygen," *Shock* 33, no. 5 (2010): 519–525.

177. G. Faa, V. Fanos, D. Fanni, et al., "Reoxygenation of Asphyxiated Newborn Piglets: Administration of 100% Oxygen Causes Significantly Higher Apoptosis in Cortical Neurons, as Compared to 21%," *BioMed Research International* 2014 (2014): 476349, https://doi.org/10.1155/2014/476349.

178. R. Solberg, J. H. Andresen, R. Escrig, et al., "Resuscitation of Hypoxic Newborn Piglets With Oxygen Induces a Dose-Dependent Increase in Markers of Oxidation," *Pediatric Research* 62, no. 5 (2007): 559–563.

179. B. H. Munkeby, W. B. Børke, K. Bjørnland, et al., "Resuscitation of Hypoxic Piglets With 100% O2 Increases Pulmonary Metalloproteinases and IL-8," *Pediatric Research* 58, no. 3 (2005): 542–548.

180. B. H. Munkeby, W. B. Børke, K. Bjørnland, et al., "Resuscitation With 100% O2 Increases Cerebral Injury in Hypoxemic Piglets," *Pediatric Research* 56, no. 5 (2004): 783–790.

181. W. B. Børke, B. H. Munkeby, L. Mørkrid, et al., "Resuscitation With 100% O 2 Does Not Protect the Myocardium in Hypoxic Newborn Piglets," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 89, no. 2 (2004): F156–F160.

182. K. Fokkelman, E. Haase, J. Stevens, et al., "Tissue-Specific Changes in Glutathione Content of Hypoxic Newborn Pigs Reoxygenated With 21% or 100% Oxygen," *European Journal of Pharmacology* 562, no. 1-2 (2007): 132–137.

183. B. A. Feet, X. Q. Yu, T. Rootwelt, et al., "Effects of Hypoxemia and Reoxygenation With 21% or 100% Oxygen in Newborn Piglets: Extracellular Hypoxanthine in Cerebral Cortex and Femoral Muscle," *Critical Care Medicine* 25, no. 8 (1997): 1384–1391.

184. K. S. Sobotka, C. Morley, T. Ong, et al., "Circulatory Responses to Asphyxia Differ If the Asphyxia Occurs in Utero or Ex Utero in Near-Term Lambs," *PLoS ONE* 9, no. 11 (2014): e112264.

185. A. Kibsgaard, H. Ersdal, J. T. Kvaløy, et al., "Newborns Requiring Resuscitation: Two Thirds Have Heart Rate ≥100 Beats/Minute in the First Minute After Birth," *Acta Paediatrica* 112, no. 4 (2023): 697–705.

186. C. H. Yam, J. A. Dawson, G. M. Schmolzer, et al., "Heart Rate Changes During Resuscitation of Newly Born Infants <30 Weeks Gestation: An Observational Study," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 96, no. 2 (2011): F102–F107.

187. P. A. Bjorland, K. Oymar, H. L. Ersdal, and S. I. Rettedal, "Incidence of Newborn Resuscitative Interventions at Birth and Short-Term Outcomes: A Regional Population-Based Study," *BMJ Paediatrics Open* 3, no. 1 (2019): e000592.

188. E. E. Foglia, B. A. Shah, and E. Szyld, "Positive Pressure Ventilation at Birth," *Seminars in Perinatology* 46, no. 6 (2022): 151623.

189. P. Kapadia, C. Hurst, D. Harley, et al., "Trends in Neonatal Resuscitation Patterns in Queensland, Australia—A 10-Year Retrospective Cohort Study," *Resuscitation* 157 (2020): 126–132.

190. G. R. Polglase, T. Ong, and N. H. Hillman, "Cardiovascular Alterations and Multiorgan Dysfunction After Birth Asphyxia," *Clinics in Perinatology* 43, no. 3 (2016): 469–483.

191. S. Ramachandran, M. Bruckner, M. H. Wyckoff, and G. M. Schmölzer, "Chest Compressions in Newborn Infants: A Scoping Review," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 108, no. 5 (2023): 442–450.

192. M. Binkhorst, E. van Elsäcker, R. P. Matthijsse, et al., "Threshold to Initiate Chest Compressions for Bradycardia at Birth: A Narrative Review," *Journal of Perinatology* ahead of print, May 13, 2025, https://doi.org/10.1038/s41372-025-02320-2.

193. J. A. Dawson, C. O. F. Kamlin, C. Wong, et al., "Changes in Heart Rate in the First Minutes After Birth," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 95, no. 3 (2010): F177–F181.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70012, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

194. Z. Alhassen, P. Vali, A. Lesneski, et al., "What Is the Optimal Heart Rate Cut-Off for Initiating Chest Compressions in Neonatal Bradycardia?," *Pediatrics* 147 (2021): 753–753.

195. P. Chandrasekharan, S. Gugino, C. Koenigsknecht, et al., "Chest Compressions During Neonatal Bradycardia Do Not Enhance Flow to Vital Organs but Reduce Inherent Cardiac Activity," *Pediatrics* 149 (2022): 654–654.

196. V. Agrawal, S. Lakshminrusimha, and P. Chandrasekharan, "Chest Compressions for Bradycardia During Neonatal Resuscitation—Do We Have Evidence?," *Children* 6, no. 11 (2019).

197. C. F. Babbs, A. Meyer, and V. Nadkarni, "Neonatal CPR: Room at the Top—A Mathematical Study of Optimal Chest Compression Frequency Versus Body Size," *Resuscitation* 80, no. 11 (2009): 1280–1284.

198. E. S. Li, P.-Y. Cheung, T.-F. Lee, et al., "Return of Spontaneous Circulation Is Not Affected by Different Chest Compression Rates Superimposed With Sustained Inflations During Cardiopulmonary Resuscitation in Newborn Piglets," *PLoS ONE* 11, no. 6 (2016): e0157249.

199. J. T. Hamrick, J. L. Hamrick, U. Bhalala, et al., "End-Tidal CO2-Guided Chest Compression Delivery Improves Survival in a Neonatal Asphyxial Cardiac Arrest Model," *Pediatric Critical Care Medicine* 18, no. 11 (2017): e575–e584.

200. S. Patel, P.-Y. Cheung, T.-F. Lee, et al., "Asynchronous Ventilation at 120 Compared With 90 or 100 Compressions per Minute Improves Haemodynamic Recovery in Asphyxiated Newborn Piglets," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 105 (2020): 357–363.

201. M. Bruckner, M. Neset, and M. O'Reilly, "Haemodynamic Changes With Varying Chest Compression Rates in Asphyxiated Piglets," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 108, no. 2 (2023): 200–203.

202. S. Yu, C. Wu, Y. Zhu, et al., "Rat Model of Asphyxia-Induced Cardiac Arrest and Resuscitation," *Frontiers in Neuroscience* 16 (2023): 1087725.

203. L. Lamoureux, J. Radhakrishnan, and R. J. Gazmuri, "A Rat Model of Ventricular Fibrillation and Resuscitation by Conventional Closed-Chest Technique," *Journal of Visualized Experiments: JoVE* no. 98 (2015): 52413, https://doi.org/10.3791/52413.

204. K. Hopper, S. E. Epstein, J. M. Burkitt-Creedon, et al., "2024 RECOVER Guidelines: Basic Life Support. Evidence and Knowledge Gap Analysis With Treatment Recommendations for Small Animal CPR," *Journal of Veterinary Emergency and Critical Care* 34, no. Suppl 1 (2024): 16–43.

205. S. B. Hooper, A. B. te Pas, G. R. Polglase, and M. Wyckoff, "Animal Models in Neonatal Resuscitation Research: What Can They Teach Us?," *Seminars in Fetal & Neonatal Medicine* 23, no. 5 (2018): 300–305.

206. J. P. Mortola and J. T. Fisher, "Mouth and Nose Resistance in Newborn Kittens and Puppies," *Journal of Applied Physiology, Respiratory, Environmental and Exercise Physiology* 51, no. 3 (1981): 641–645.

207. A. Mugnier, H. Mila, F. Guiraud, et al., "Birth Weight as a Risk Factor for Neonatal Mortality: Breed-Specific Approach to Identify At-Risk Puppies," *Preventive Veterinary Medicine* 171 (2019): 104746.

208. A. Mugnier, T. Cane, V. Gaillard, et al., "Birth Weight in the Feline Species: Description and Factors of Variation in a Large Population of Purebred Kittens," *Theriogenology* 190 (2022): 32–37.

209. K. O. Maher, R. A. Berg, C. W. Lindsey, et al., "Depth of Sternal Compression and Intra-Arterial Blood Pressure During CPR in Infants Following Cardiac Surgery," *Resuscitation* 80, no. 6 (2009): 662–664.

210. A. Meyer, V. Nadkarni, A. Pollock, et al., "Evaluation of the Neonatal Resuscitation Program's Recommended Chest Compression Depth Using Computerized Tomography Imaging," *Resuscitation* 81, no. 5 (2010): 544–548.

211. J. A. van Eijk, L. C. Doeleman, S. A. Loer, et al., "Ventilation During Cardiopulmonary Resuscitation: A Narrative Review," *Resuscitation* 203 (2024): 110366.

212. A. L. Solevag, I. Dannevig, M. Wyckoff, et al., "Extended Series of Cardiac Compressions During CPR in a Swine Model of Perinatal Asphyxia," *Resuscitation* 81, no. 11 (2010): 1571–1576.

213. A. L. Solevåg, I. Dannevig, M. Wyckoff, et al., "Return of Spontaneous Circulation With a Compression:Ventilation Ratio of 15:2 Versus 3:1 in Newborn Pigs With Cardiac Arrest due to Asphyxia," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 96, no. 6 (2011): F417–F421.

214. M. P. Pasquin, P.-Y. Cheung, S. Patel, et al., "Comparison of Different Compression to Ventilation Ratios (2:1, 3:1, and 4:1) During Cardiopulmonary Resuscitation in a Porcine Model of Neonatal Asphyxia," *Neonatology* 114, no. 1 (2018): 37–45.

215. I. Dannevig, A. L. Solevåg, O. D. Saugstad, and B. Nakstad, "Lung Injury in Asphyxiated Newborn Pigs Resuscitated From Cardiac Arrest—The Impact of Supplementary Oxygen, Longer Ventilation Intervals and Chest Compressions at Different Compression-to-Ventilation Ratios," *Open Respiratory Medicine Journal* 6, no. 1 (2012): 89–96.

216. A. M. Boldingh, A. L. Solevag, E. Aasen, and B. Nakstad, "Resuscitators Who Compared Four Simulated Infant Cardiopulmonary Resuscitation Methods Favoured the Three-to-One Compression-to-Ventilation Ratio," *Acta Paediatrica* 105, no. 8 (2016): 910–916.

217. R. J. Hemway, C. Christman, and J. Perlman, "The 3:1 Is Superior to a 15:2 Ratio in a Newborn manikin Model in Terms of Quality of Chest Compressions and Number of Ventilations," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 98, no. 1 (2013): F42–F45.

218. A. L. Solevag, J. M. Madland, E. Gjaerum, and B. Nakstad, "Minute Ventilation at Different Compression to Ventilation Ratios, Different Ventilation Rates, and Continuous Chest Compressions With Asynchronous Ventilation in a Newborn Manikin," *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* 20 (2012): 73.

219. S. K. Srikantan, R. A. Berg, T. Cox, et al., "Effect of One-Rescuer Compression/Ventilation Ratios on Cardiopulmonary Resuscitation in Infant, Pediatric, and Adult Manikins," *Pediatric Critical Care Medicine* 6, no. 3 (2005): 293–297.

220. R. Moshiro, P. Mdoe, and J. M. Perlman, "A Global View of Neonatal Asphyxia and Resuscitation," *Frontiers in Pediatrics* 7 (2019): 489, https://doi.org/10.3389/fped.2019.00489.

221. A. B. te Pas, P. G. Davis, S. B. Hooper, and C. J. Morley, "From Liquid to Air: Breathing After Birth," *Journal of Pediatrics* 152, no. 5 (2008): 607–611.

222. G. M. Schmolzer, M. O'Reilly, and J. Labossiere, "3:1 Compression to Ventilation Ratio Versus Continuous Chest Compression With Asynchronous Ventilation in a Porcine Model of Neonatal Resuscitation," *Resuscitation* 85, no. 2 (2014): 270–275.

223. M. R. Mendler, C. Weber, M. A. Hassan, et al., "Effect of Different Respiratory Modes on Return of Spontaneous Circulation in a Newborn Piglet Model of Hypoxic Cardiac Arrest," *Neonatology* 109, no. 1 (2016): 22–30.

224. A. Aggelina, I. Pantazopoulos, G. Giokas, et al., "Continuous Chest Compressions With Asynchronous Ventilation Improve Survival in a Neonatal Swine Model of Asphyxial Cardiac Arrest," *American Journal of Emergency Medicine* 48 (2021): 60–66.

225. P. Vali, A. Lesneski, M. Hardie, et al., "Continuous Chest Compressions With Asynchronous Ventilations Increase Carotid Blood Flow in the Perinatal Asphyxiated Lamb Model," *Pediatric Research* 90, no. 4 (2021): 752–758.

226. M. R. Mendler, M. Maurer, M. A. Hassan, et al., "Different Techniques of Respiratory Support Do Not Significantly Affect Gas Exchange During Cardiopulmonary Resuscitation in a Newborn Piglet Model," *Neonatology* 108, no. 1 (2015): 73–80.

227. C. Morin, T.-F. Lee, and M. O'Reilly, "Cardiopulmonary Resuscitation With 3:1 Compression:Ventilation or Continuous Compression With Asynchronized Ventilation in Infantile Piglets," *Pediatric Research* 96, no. 5 (2024): 1235–1242.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70012, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

228. G. M. Schmolzer, M. O'Reilly, and J. Labossiere, "Cardiopulmonary Resuscitation With Chest Compressions During Sustained Inflations: A New Technique of Neonatal Resuscitation That Improves Recovery and Survival in a Neonatal Porcine Model," *Circulation* 128, no. 23 (2013): 2495–2503.

229. E. S. Li, I. Gorens, P.-Y. Cheung, et al., "Chest Compressions During Sustained Inflations Improve Recovery When Compared to a 3:1 Compression:Ventilation Ratio During Cardiopulmonary Resuscitation in a Neonatal Porcine Model of Asphyxia," *Neonatology* 112, no. 4 (2017): 337–346.

230. G. M. Schmolzer, M. O Reilly, and C. Fray, "Chest Compression During Sustained Inflation Versus 3:1 Chest Compression:Ventilation Ratio During Neonatal Cardiopulmonary Resuscitation: A Randomised Feasibility Trial," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 103, no. 5 (2018): F455–F460.

231. P. Vali, P. Chandrasekharan, M. Rawat, et al., "Continuous Chest Compressions During Sustained Inflations in a Perinatal Asphyxial Cardiac Arrest Lamb Model," *Pediatric Critical Care Medicine* 18, no. 8 (2017): e370–e377.

232. J. Mustofa, P. Y. Cheung, S. Patel, et al., "Effects of Different Durations of Sustained Inflation During Cardiopulmonary Resuscitation on Return of Spontaneous Circulation and Hemodynamic Recovery in Severely Asphyxiated Piglets," *Resuscitation* 129 (2018): 82–89.

233. G. M. Schmölzer, G. Pichler, A. L. Solevåg, et al., "Sustained Inflation and Chest Compression Versus 3:1 Chest Compression to Ventilation Ratio During Cardiopulmonary Resuscitation of Asphyxiated Newborns (SURV1VE): A Cluster Randomised Controlled Trial," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 109, no. 4 (2024): 428–435.

234. D. J. Mujsce, J. Towfighi, and R. C. Vannucci, "Physiologic and Neuropathologic Aspects of Hypothermic Circulatory Arrest in Newborn Dogs," *Pediatric Research* 28, no. 4 (1990): 354–360.

235. D. J. Mujsce, J. Towfighi, J. Y. Yager, and R. C. Vannucci, "Neuropathologic Aspects of Hypothermic Circulatory Arrest in Newborn Dogs," *Acta Neuropathologica* 85, no. 2 (1993): 190–198.

236. S. K. Berkelhamer, P. Vali, J. Nair, et al., "Inadequate Bioavailability of Intramuscular Epinephrine in a Neonatal Asphyxia Model," *Frontiers in Pediatrics* 10 (2022): 828130.

237. J. de Jager, R. Pothof, K. J. Crossley, et al., "Evaluating the Efficacy of Endotracheal and Intranasal Epinephrine Administration in Severely Asphyxic Bradycardic Newborn Lambs: A Randomised Preclinical Study," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 110, no. 2 (2025): 207–212.

238. J. Nair, P. Vali, S. F. Gugino, et al., "Bioavailability of Endotracheal Epinephrine in an Ovine Model of Neonatal Resuscitation," *Early Human Development* 130 (2019): 27–32.

239. G. R. Polglase, Y. Brian, D. Tantanis, et al., "Endotracheal Epinephrine at Standard Versus High Dose for Resuscitation of Asystolic Newborn Lambs," *Resuscitation* 198 (2024): 110191.

240. M. Rawat, S. Gugino, C. Koenigsknecht, et al., "Masked Randomized Trial of Epinephrine Versus Vasopressin in an Ovine Model of Perinatal Cardiac Arrest," *Children* 10, no. 2 (2023): 349.

241. C. T. Roberts, S. Klink, G. M. Schmölzer, et al., "Comparison of Intraosseous and Intravenous Epinephrine Administration During Resuscitation of Asphyxiated Newborn Lambs," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 107, no. 3 (2022): 311–316.

242. N. T. Songstad, C. Klingenberg, E. V. McGillick, et al., "Efficacy of Intravenous, Endotracheal, or Nasal Adrenaline Administration During Resuscitation of Near-Term Asphyxiated Lambs," *Frontiers in Pediatrics* 8 (2020): 262.

243. P. Vali, P. Chandrasekharan, M. Rawat, et al., "Evaluation of Timing and Route of Epinephrine in a Neonatal Model of Asphyxial Arrest," *Journal of the American Heart Association* 6, no. 2 (2017): e004402.

244. C. Halling, J. E. Sparks, L. Christie, and M. H. Wyckoff, "Efficacy of Intravenous and Endotracheal Epinephrine During Neonatal Cardiopulmonary Resuscitation in the Delivery Room," *The Journal of Pediatrics* 185 (2017): 232–236.

245. C. A. Barber and M. H. Wyckoff, "Use and Efficacy of Endotracheal Versus Intravenous Epinephrine During Neonatal Cardiopulmonary Resuscitation in the Delivery Room," *Pediatrics* 118, no. 3 (2006): 1028–1034.

246. J. M. Perlman and R. Risser, "Cardiopulmonary Resuscitation in the Delivery Room: Associated Clinical Events," *Archives of Pediatrics & Adolescent Medicine* 149, no. 1 (1995): 20–25.

247. D. E. Niles, C. Cines, E. Insley, et al., "Incidence and Characteristics of Positive Pressure Ventilation Delivered to Newborns in a US Tertiary Academic Hospital," *Resuscitation* 115 (2017): 102–109.

248. J. Wolf, G. J. Buckley, E. A. Rozanski, et al., "2024 RECOVER Guidelines: Advanced Life Support. Evidence and Knowledge Gap Analysis With Treatment Recommendations for Small Animal CPR," *Journal of Veterinary Emergency and Critical Care* 34, no. Suppl 1 (2024): 44–75.

249. R. A. Berg, C. W. Otto, K. B. Kern, et al., "A Randomized, Blinded Trial of High-Dose Epinephrine Versus Standard-Dose Epinephrine in a Swine Model of Pediatric Asphyxial Cardiac Arrest," *Critical Care Medicine* 24, no. 10 (1996): 1695–1700.

250. M. B. M. Perondi, A. G. Reis, E. F. Paiva, et al., "A Comparison of High-Dose and Standard-Dose Epinephrine in Children With Cardiac Arrest," *New England Journal of Medicine* 350, no. 17 (2004): 1722–1730.

251. M. D. Patterson, D. A. Boenning, B. L. Klein, et al., "The Use of High-Dose Epinephrine for Patients With Out-of-Hospital Cardiopulmonary Arrest Refractory to Prehospital Interventions," *Pediatric Emergency Care* 21, no. 4 (2005): 227–237.

252. D. J. Burchfield, M. P. Preziosi, V. W. Lucas, and J. Fan, "Effects of Graded Doses of Epinephrine During Asphxia-Induced Bradycardia in Newborn Lambs," *Resuscitation* 25, no. 3 (1993): 235–244.

253. D. Sankaran, P. K. Chandrasekharan, S. F. Gugino, et al., "Randomised Trial of Epinephrine Dose and Flush Volume in Term Newborn Lambs," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 106, no. 6 (2021): 578–583.

254. D. Sankaran, M. Rawat, and S. Lakshminrusimha, "Optimal Oxygen Use in Neonatal Advanced Cardiopulmonary Resuscitation—A Literature Review," *Pediatric Medicine* 6 (2023): 16.

255. A. L. Solevag, G. M. Schmolzer, and M. O'Reilly, "Myocardial Perfusion and Oxidative Stress After 21% vs. 100% Oxygen Ventilation and Uninterrupted Chest Compressions in Severely Asphyxiated Piglets," *Resuscitation* 106 (2016): 7–13.

256. S. Nyame, P. Y. Cheung, T. F. Lee, et al., "A Randomized, Controlled Animal Study: 21% or 100% Oxygen During Cardiopulmonary Resuscitation in Asphyxiated Infant Piglets," *Children* 9, no. 11 (2022): 1601.

257. M. Rawat, P. Chandrasekharan, S. Gugino, et al., "Oxygenation and Hemodynamics During Chest Compressions in a Lamb Model of Perinatal Asphyxia Induced Cardiac Arrest," *Children* 6, no. 4 (2019): 52.

258. D. Sankaran, E. M. Giusto, A. L. Lesneski, et al., "Randomized Trial of 21% Versus 100% Oxygen During Chest Compressions Followed by Gradual Versus Abrupt Oxygen Titration After Return of Spontaneous Circulation in Neonatal Lambs," *Children* 10, no. 3 (2023): 575.

259. A. M. Boldingh, T. H. Jensen, A. T. Bjorbekk, et al., "Rescuers' Physical Fatigue With Different Chest Compression to Ventilation Methods During Simulated Infant Cardiopulmonary Resuscitation," *The Journal of Maternal-Fetal & Neonatal Medicine* 29, no. 19 (2016): 3202–3207.

260. I. Dannevig, A. L. Solevag, T. Sonerud, et al., "Brain Inflammation Induced by Severe Asphyxia in Newborn Pigs and the Impact of Alternative Resuscitation Strategies on the Newborn central Nervous System," *Pediatric Research* 73, no. 2 (2013): 163–170.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70012, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

261. S. Badurdeen, A. W. Gill, M. Kluckow, et al., "Excess Cerebral Oxygen Delivery Follows Return of Spontaneous Circulation in Near-Term Asphyxiated Lambs," *Scientific Reports* 10, no. 1 (2020): 16443.

262. H. Steiner and G. Neligan, "Perinatal Cardiac Arrest. Quality of the Survivors," *Archives of Disease in Childhood* 50, no. 9 (1975): 696–702.

263. H. Patel and P. J. Beeby, "Resuscitation Beyond 10 Minutes of Term Babies Born Without Signs of Life," *Journal of Paediatrics and Child Health* 40, no. 3 (2004): 136–138.

264. E. Kasdorf, A. Laptook, D. Azzopardi, et al., "Improving Infant Outcome With a 10 Min Apgar of 0," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 100, no. 2 (2015): F102–F105.

265. T. Sproat, R. Hearn, and S. Harigopal, "Outcome of Babies With no Detectable Heart Rate Before 10 Minutes of Age, and the Effect of Gestation," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 102, no. 3 (2017): F262–F265.

266. J. Shibasaki, T. Mukai, K. Tsuda, et al., "Outcomes Related to 10-min Apgar Scores of Zero in Japan," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 105, no. 1 (2020): 64–68.

267. E. Chakkarapani, L. S. de Vries, D. M. Ferriero, and A. J. Gunn, "Neonatal Encephalopathy and Hypoxic-Ischemic Encephalopathy: The state of the Art," *Pediatric Research* ahead of print, March 24, 2025, https://doi.org/10.1038/s41390-025-03986-2.

268. C. S. Yost, "A New Look at the Respiratory Stimulant Doxapram," *CNS Drug Reviews* 12, no. 3-4 (2006): 236–249.

269. J. R. Holladay, "Routine Use of Doxapram Hydrochloride in Neonatal Pups Delivered by Cesarean Section," *Veterinary Medicine, Small Animal Clinician* 66, no. 1 (1971): 28.

270. V. Rickard, "Birth and the First 24 Hours," in *Small Animal Pediatrics*, ed. M. E. Peterson and M. A. Kutzler (Saunders, 2011), 11–19.

271. J. A. Budde and D. M McCluskey, *Plumb's Veterinary Drug Handbook* (Wiley-Blackwell, 2023).

272. O. S. Bamford, G. S. Dawes, M. A. Hanson, and R. A. Ward, "The Effects of Doxapram on Breathing, Heart Rate and Blood Pressure in Fetal Lambs," *Respiration Physiology* 66, no. 3 (1986): 387–396.

273. C. H. Ten Hove, R. J. Vliegenthart, A. B. Te Pas, et al., "Long-Term Neurodevelopmental Outcome After Doxapram for Apnea of Prematurity," *Neonatology* 110, no. 1 (2016): 21–26.

274. T. Yamazaki, M. Kajiwara, K. Itahashi, and M. Fujimura, "Low-Dose Doxapram Therapy for Idiopathic Apnea of Prematurity," *Pediatrics International* 43, no. 2 (2001): 124–127.

275. T. H. Hyndman, S. Fretwell, R. S. Bowden, et al., "The Effect of Doxapram on Survival and APGAR Score in Newborn Puppies Delivered by Elective Caesarean: A Randomized Controlled Trial," *Journal of Veterinary Pharmacology and Therapeutics* 46, no. 6 (2023): 353–364.

276. C. Czaba-Hnizdo, M. Olischar, Z. Rona, et al., "Amplitude-Integrated Electroencephalography Shows That Doxapram Influences the Brain Activity of Preterm Infants," *Acta Paediatrica* 103, no. 9 (2014): 922–927.

277. C. Sreenan, P. C. Etches, N. Demianczuk, and C. M. T. Robertson, "Isolated Mental Developmental Delay in Very Low Birth Weight Infants: Association With Prolonged Doxapram Therapy for Apnea," *Journal of Pediatrics* 139, no. 6 (2001): 832–837.

278. U. Bleul, B. Bircher, R. S. Jud, and A. P. N. Kutter, "Respiratory and Cardiovascular Effects of Doxapram and Theophylline for the Treatment of Asphyxia in Neonatal Calves," *Theriogenology* 73, no. 5 (2010): 612–619.

279. U. Bleul and T. Bylang, "Effects of Doxapram, Prethcamide and Lobeline on Spirometric, Blood Gas and Acid-Base Variables in Healthy New-Born Calves," *Veterinary Journal* 194, no. 2 (2012): 240–246.

280. C. F. Poets, S. Darraj, and B. Bohnhorst, "Effect of Doxapram on Episodes of Apnoea, Bradycardia and Hypoxaemia in Preterm Infants," *Biology of the Neonate* 76, no. 4 (1999): 207–213.

281. H. Uehara, H. Yoshioka, H. Nagai, et al., "Doxapram Accentuates White Matter Injury in Neonatal Rats Following Bilateral Carotid Artery Occlusion," *Neuroscience Letters* 281, no. 2-3 (2000): 191–194.

282. R. B. Flint, W. Wv, S. Voller, et al., "Big Data Analyses for Continuous Evaluation of Pharmacotherapy: A Proof of Principle With Doxapram in Preterm Infants," *Current Pharmaceutical Design* 23, no. 38 (2017): 5919–5927.

283. A. Bairam, M. Faulon, P. Monin, and P. Vert, "Doxapram for the Initial Treatment of Idiopathic Apnea of Prematurity," *Biology of the Neonate* 61, no. 4 (1992): 209–213.

284. K. J. Barrington, N. N. Finer, G. Torok-Both, et al., "Dose-Response Relationship of Doxapram in the Therapy for Refractory Idiopathic Apnea of Prematurity," *Pediatrics* 80, no. 1 (1987): 22–27.

285. M. A. Beaudry, J. M. Bradley, L. M. Gramlich, and D. LeGatt, "Pharmacokinetics of Doxapram in Idiopathic Apnea of Prematurity," *Developmental Pharmacology and Therapeutics* 11, no. 2 (1988): 65–72.

286. A. Cote, P. W. Blanchard, and B. Meehan, "Metabolic and Cardiorespiratory Effects of Doxapram and Theophylline in Sleeping Newborn Piglets," *Journal of Applied Physiology* 72, no. 2 (1992): 410–415.

287. S. Giguere, L. C. Sanchez, A. Shih, et al., "Comparison of the Effects of Caffeine and Doxapram on Respiratory and Cardiovascular Function in Foals With Induced respiratory Acidosis," *American Journal of Veterinary Research* 68, no. 12 (2007): 1407–1416.

288. S. Giguere, J. K. Slade, and L. C. Sanchez, "Retrospective Comparison of Caffeine and Doxapram for the Treatment of Hypercapnia in Foals With Hypoxic-Ischemic Encephalopathy," *Journal of Veterinary Internal Medicine* 22, no. 2 (2008): 401–405.

289. E. Sagi, F. Eyal, G. Alpan, et al., "Idiopathic Apnoea of Prematurity Treated With Doxapram and Aminophylline," *Archives of Disease in Childhood* 59, no. 3 (1984): 281–283.

290. S. A. Prins, S. J. A. Pans, M. M. van Weissenbruch, et al., "Doxapram Use for Apnoea of Prematurity in Neonatal Intensive Care," *International Journal of Pediatrics* 2013 (2013): 251047.

291. N. N. Finer, K. J. Barrington, B. J. Hayes, and A. Hugh, "Obstructive, Mixed, and Central Apnea in the Neonate: Physiologic Correlates," *Journal of Pediatrics* 121, no. 6 (1992): 943–950.

292. J. W. Ward, D. L. Gilbert, B. V. Franko, et al., "Toxicologic Studies of Doxapram Hydrochloride," *Toxicology and Applied Pharmacology* 13, no. 2 (1968): 242–250.

293. R. J. S. Vliegenthart, C. H. Ten Hove, W. Onland, and A. Van Kaam, "Doxapram Treatment for Apnea of Prematurity: A Systematic Review," *Neonatology* 111, no. 2 (2017): 162–171.

294. A. Bairam, F. Marchal, J. P. Crance, et al., "Effects of Doxapram on Carotid Chemoreceptor Activity in Newborn Kittens," *Biology of the Neonate* 64, no. 1 (1993): 26–35.

295. A. Bairam, F. Marchal, B. Hannhart, et al., "Carotid Chemosensory Response to Doxapram in the Newborn Kitten," *Advances in Experimental Medicine and Biology* 337 (1993): 381–385.

296. V. Y. Hibaru, K. Pereira, K. D. M. Fuchs, et al., "Topics in the Routine Assessment of Newborn Kitten Vitality: Apgar Score, Reflexes and Complementary Assessments," *Journal of Feline Medicine and Surgery* 24, no. 6 (2022): e34–e42.

297. R. A. Abreu, L. L. Almeida, and R. R. D. Rosa Filho, "Canine Pulmonary Clearance During Feto-Neonatal Transition According to the Type of Delivery," *Theriogenology* 224 (2024): 156–162.

298. W.-W. Chan, K.-Y. Chen, H. Liu, et al., "Acupuncture for General Veterinary Practice," *Journal of Veterinary Medical Science* 63, no. 10 (2001): 1057–1062.

299. S. G. Dill, R. Gleed, N. S. Matthews, et al., "Cardiovascular Effects of Acupuncture Stimulation at Point Governing Vessel 26 in Halothane-Anesthetized Ponies," *American Journal of Veterinary Research* 49, no. 10 (1988): 1708–1712.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70012, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

300. A. C. G. Graboschii, C. Lira, J. L. F. Lins, et al., "Acupuncture in the Anesthetic Recovery of Bitches Submitted to Ovariohysterectomy," *Journal of Acupuncture and Meridian Studies* 16, no. 3 (2023): 95–100.

301. R. T. Skarda, "Anesthesia Case of the Month. Dystocia, Cesarean Section and Acupuncture Resuscitation of Newborn Kittens," *Journal of the American Veterinary Medical Association* 214, no. 1 (1999): 37–39.

302. C. Matterberger, N. Baik-Schneditz, B. Schwaberger, et al., "Blood Glucose and Cerebral Tissue Oxygenation Immediately After Birth—An Observational Study," *Journal of Pediatrics* 200 (2018): 19–23.

303. R. C. Vannucci, E. E. Nardis, S. J. Vannucci, and P. A. Campbell, "Cerebral Carbohydrate and Energy Metabolism During Hypoglycemia in Newborn Dogs," *American Journal of Physiology* 240, no. 3 (1981): R192–R199.

304. W. S. Park, Y. S. Chang, and M. Lee, "Effects of Hyperglycemia or Hypoglycemia on Brain Cell Membrane Function and Energy Metabolism During the Immediate Reoxygenation–Reperfusion Period After Acute Transient Global Hypoxia–Ischemia in the Newborn Piglet," *Brain Research* 901, no. 1 (2001): 102–108.

305. T. R. Anju, P. K. Korah, S. Jayanarayanan, and C. S. Paulose, "Enhanced Brain Stem 5HT(2)A Receptor Function Under Neonatal Hypoxic Insult: Role of Glucose, Oxygen, and Epinephrine Resuscitation," *Molecular and Cellular Biochemistry* 354, no. 1-2 (2011): 151–160.

306. T. R. Anju, J. Mathew, S. Jayanarayanan, and C. S. Paulose, "Cerebellar 5HT2A Receptor Function Under Hypoxia in Neonatal Rats: Role of Glucose, Oxygen, and Epinephrine Resuscitation," *Respiratory Physiology & Neurobiology* 172, no. 3 (2010): 147–153.

307. T. R. Anju, S. Smijin, R. Chinthu, and C. S. Paulose, "Decreased Cholinergic Function in the Cerebral Cortex of Hypoxic Neonatal Rats: Role of Glucose, Oxygen and Epinephrine Resuscitation," *Respiratory Physiology & Neurobiology* 180, no. 1 (2012): 8–13.

308. F. Chathu, A. Krishnakumar, and C. S. Paulose, "Acetylcholine Esterase Activity and Behavioral Response in Hypoxia Induced Neonatal Rats: Effect of Glucose, Oxygen and Epinephrine Supplementation," *Brain and Cognition* 68, no. 1 (2008): 59–66.

309. J. E. Hegarty, J. E. Harding, M. H. Oliver, et al., "Oral Dextrose Gel to Improve Survival in Less Vigorous Newborn Triplet Lambs: A Randomised Controlled Trial," *New Zealand Journal of Agricultural Research* 60, no. 1 (2017): 54–69.

310. R. A. Sheldon, J. C. Partridge, and D. M. Ferriero, "Postischemic Hyperglycemia Is Not Protective to the Neonatal Rat Brain," *Pediatric Research* 32, no. 4 (1992): 489–493.

311. R. C. Vannucci, A. Rossini, and J. Towfighi, "Effect of Hyperglycemia on Ischemic Brain Damage During Hypothermic Circulatory Arrest in Newborn Dogs," *Pediatric Research* 40, no. 2 (1996): 177–184.

312. W. A. Salhab, M. H. Wyckoff, A. R. Laptook, and J. M. Perlman, "Initial Hypoglycemia and Neonatal Brain Injury in Term Infants With Severe Fetal Acidemia," *Pediatrics* 114, no. 2 (2004): 361–366.

313. M. Nadeem, D. M. Murray, G. B. Boylan, et al., "Early Blood Glucose Profile and Neurodevelopmental Outcome at Two Years in Neonatal Hypoxic-Ischaemic Encephalopathy," *BMC Pediatrics* 11 (2011): 10, https://doi.org/10.1186/1471-2431-11-10.

314. S. K. Basu, J. R. Kaiser, D. Guffey, et al., "Hypoglycaemia and Hyperglycaemia Are Associated With Unfavourable Outcome in Infants With Hypoxic Ischaemic Encephalopathy: A Post Hoc Analysis of the CoolCap Study," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 101, no. 2 (2016): F149–F155.

315. A. Panzardi, M. L. Bernardi, A. P. Mellagi, et al., "Newborn Piglet Traits Associated With Survival and Growth Performance Until Weaning," *Preventive Veterinary Medicine* 110, no. 2 (2013): 206–213.

316. A. R. Hollis, R. C. Boston, and K. T. T. Corley, "Plasma Aldosterone, Vasopressin and Atrial Natriuretic Peptide in Hypovolaemia: A Preliminary Comparative Study of Neonatal and Mature Horses," *Equine Veterinary Journal* 40, no. 1 (2008): 64–69.

317. E. F. Pinchefsky, C. D. Hahn, D. Kamino, et al., "Hyperglycemia and Glucose Variability Are Associated With Worse Brain Function and Seizures in Neonatal Encephalopathy: A Prospective Cohort Study," *The Journal of Pediatrics* 209 (2019): 23–32.

318. F. KdM, P. KHNP, and G. M. Xavier, "Neonatal Hypoglycemia in Dogs—Pathophysiology, Risk Factors, Diagnosis and Treatment," *Frontiers in Veterinary Science* 11 (2024): 1345933, https://doi.org/10.3389/fvets.2024.1345933.

319. R. L. Holt, J. M. Gordon, and C. Ruaux, "Immediate Effect of Transmucosal Application of Corn Syrup or 50% Dextrose Solution on Blood Glucose Concentrations in Healthy Dogs," *Journal of Veterinary Emergency and Critical Care* 29, no. 6 (2019): 630–634.

320. M. H. LeBlanc, M. Huang, D. Patel, et al., "Glucose Given After Hypoxic Ischemia Does Not Affect Brain Injury in Piglets," *Stroke; A Journal of Cerebral Circulation* 25, no. 7 (1994): 1443–1447.

321. H. Hattori and C. G. Wasterlain, "Posthypoxic Glucose Supplement Reduces Hypoxic-Ischemic Brain Damage in the Neonatal Rat," *Annals of Neurology* 28, no. 2 (1990): 122–128.

322. A. R. Hollis, M. O. Furr, K. G. Magdesian, et al., "Blood Glucose Concentrations in Critically Ill Neonatal Foals," *Journal of Veterinary Internal Medicine* 22, no. 5 (2008): 1223–1227.

323. T. Edwards, G. Liu, M. Battin, et al., "Oral Dextrose Gel for the Treatment of Hypoglycaemia in Newborn Infants," *Cochrane Database of Systematic Reviews* 3, no. 3 (2022): Cd011027.

324. B. Lemyre and V. Chau, "Hypothermia for Newborns With Hypoxic-Ischemic Encephalopathy," *Paediatrics & Child Health* 23, no. 4 (2018): 285–291.

325. R. E. Toribio, "Equine Neonatal Encephalopathy: Facts, Evidence, and Opinions," *Veterinary Clinics of North America: Small Animal Practice* 35, no. 2 (2019): 363–378.

326. J. O. Davidson, F. Gonzalez, P. Gressens, and A. J. Gunn, "Update on Mechanisms of the Pathophysiology of Neonatal Encephalopathy," *Seminars in Fetal & Neonatal Medicine* 26, no. 5 (2021): 101267.

327. R. Greif, J. E. Bray, T. Djärv, et al., "2024 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations: Summary From the Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; Education, Implementation, and Teams; and First Aid Task Forces," *Circulation* 150, no. 24 (2024): e580–e687.

328. K. H. Polderman, "Mechanisms of Action, Physiological Effects, and Complications of Hypothermia," *Critical Care Medicine* 37, no. 7 (2009): S186–S202.

329. G. Simbruner, R. A. Mittal, F. Rohlmann, and R. Muche, "Systemic Hypothermia After Neonatal Encephalopathy: Outcomes of neo.nEURO.network RCT," *Pediatrics* 126, no. 4 (2010): e771–e778.

330. D. J. Eicher, C. L. Wagner, L. P. Katikaneni, et al., "Moderate Hypothermia in Neonatal Encephalopathy: Efficacy Outcomes," *Pediatric Neurology* 32, no. 1 (2005): 11–17.

331. P. D. Gluckman, J. S. Wyatt, D. Azzopardi, et al., "Selective Head Cooling With Mild Systemic Hypothermia After Neonatal Encephalopathy: Multicentre Randomised Trial," *Lancet* 365, no. 9460 (2005): 663–670.

332. D. V. Azzopardi, B. Strohm, A. D. Edwards, et al., "Moderate Hypothermia to Treat Perinatal Asphyxial Encephalopathy," *New England Journal of Medicine* 361, no. 14 (2009): 1349–1358.

333. S. Shankaran, A. R. Laptook, R. A. Ehrenkranz, et al., "Whole-Body Hypothermia for Neonates With Hypoxic-Ischemic Encephalopathy," *New England Journal of Medicine* 353, no. 15 (2005): 1574–1584.

334. S. E. Jacobs, C. J. Morley, T. E. Inder, et al., "Whole-Body Hypothermia for Term and Near-Term Newborns With Hypoxic-Ischemic Encephalopathy: A Randomized Controlled Trial," *Archives of Pediatrics & Adolescent Medicine* 165, no. 8 (2011): 692–700.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70012, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

335. Z. W-h, C. G-q, and S. X-m, "Selective Head Cooling With Mild Systemic Hypothermia After Neonatal Hypoxic-Ischemic Encephalopathy: A Multicenter Randomized Controlled Trial in China," *Journal of Pediatrics* 157, no. 3 (2010): 367–372, 372.e1–372.e3.

336. S. Thayyil, S. Pant, P. Montaldo, et al., "Hypothermia for Moderate or Severe Neonatal Encephalopathy in Low-Income and Middle-Income Countries (HELIX): A Randomised Controlled Trial in India, Sri Lanka, and Bangladesh," *The Lancet Global Health* 9, no. 9 (2021): e1273–e1285.

337. B. S. Lee, C.-W. Woo, S.-T. Kim, and K.-S. Kim, "Long-Term Neuroprotective Effect of Postischemic Hypothermia in a Neonatal Rat Model of Severe Hypoxic Ischemic Encephalopathy: A Comparative Study on the Duration and Depth of Hypothermia," *Pediatric Research* 68, no. 4 (2010): 303–308.

338. K. Haaland, E. M. Løberg, P. A. Steen, and M. Thoresen, "Posthypoxic Hypothermia in Newborn Piglets," *Pediatric Research* 41, no. 4 I (1997): 505–512.

339. H. Kida, S. Nomura, M. Shinoyama, et al., "The Effect of Hypothermia Therapy on Cortical Laminar Disruption Following Ischemic Injury in Neonatal Mice," *PLoS ONE* 8, no. 7 (2013): e68877, https://doi.org/10.1371/journal.pone.0068877.

340. J. Diaz, S. Abiola, N. Kim, et al., "Therapeutic Hypothermia Provides Variable Protection Against Behavioral Deficits After Neonatal Hypoxia-Ischemia: A Potential Role for Brain-Derived Neurotrophic Factor," *Developmental Neuroscience* 39, no. 1-4 (2017): 257–272.

341. V. Tanigasalam, V. Bhat, B. Adhisivam, and M. G. Sridhar, "Does Therapeutic Hypothermia Reduce Acute Kidney Injury Among Term Neonates With Perinatal Asphyxia?—A Randomized Controlled Trial," *The Journal of Maternal-Fetal & Neonatal Medicine* 29, no. 15 (2016): 2545–2548.

342. K. Rakesh, B. Vishnu Bhat, B. Adhisivam, and P. Ajith, "Effect of Therapeutic Hypothermia on Myocardial Dysfunction in Term Neonates With Perinatal Asphyxia—A Randomized Controlled Trial," *The Journal of Maternal-Fetal & Neonatal Medicine* 31, no. 18 (2018): 2418–2423.

343. N. Hoque, X. Liu, E. Chakkarapani, and M. Thoresen, "Minimal Systemic Hypothermia Combined With Selective Head Cooling Evaluated in a Pig Model of Hypoxia-Ischemia," *Pediatric Research* 77, no. 5 (2015): 674–680.

344. R. D. Christensen, M. J. Sheffield, D. K. Lambert, and V. L. Baer, "Effect of Therapeutic Hypothermia in Neonates With Hypoxic-Ischemic Encephalopathy on Platelet Function," *Neonatology* 101, no. 2 (2012): 91–94.

345. I. Nour, R. Elmaghraby, R. Shehata, et al., "Selective Head Cooling and Acute Kidney Injury in Neonates With Hypoxic Ischemic Encephalopathy," *Journal of Neonatal-Perinatal Medicine* 13, no. 1 (2020): 21–30.

346. F. M. R. Maoulainine, M. Elbaz, S. Elfaiq, et al., "Therapeutic Hypothermia in Asphyxiated Neonates: Experience From Neonatal Intensive Care Unit of University Hospital of Marrakech," *International Journal of Pediatrics* 2017, no. 2017: 3674140.

347. T. Abiramalatha, M. Kumar, S. Chandran, et al., "Troponin-T as a Biomarker in Neonates With Perinatal Asphyxia," *Journal of Neonatal-Perinatal Medicine* 10, no. 3 (2017): 275–280.

348. S. Satas, E. M. Løberg, H. Porter, et al., "Effect of Global Hypoxia-Ischaemia Followed by 24 h of Mild Hypothermia on Organ Pathology and Biochemistry in a Newborn Pig Survival Model," *Biology of the Neonate* 83, no. 2 (2003): 146–156.

349. P. Srinivasakumar, J. Zempel, M. Wallendorf, et al., "Therapeutic Hypothermia in Neonatal Hypoxic Ischemic Encephalopathy: Electrographic Seizures and Magnetic Resonance Imaging Evidence of Injury," *Journal of Pediatrics* 163, no. 2 (2013): 465–470.

350. J. O. Davidson, V. Draghi, S. Whitham, et al., "How Long Is Sufficient for Optimal Neuroprotection With Cerebral Cooling After Ischemia in Fetal Sheep?," *Journal of Cerebral Blood Flow and Metabolism* 38, no. 6 (2018): 1047–1059.

351. M. A. McNally, R. Chavez-Valdez, R. J. Felling, et al., "Seizure Susceptibility Correlates With Brain Injury in Male Mice Treated With Hypothermia After Neonatal Hypoxia-Ischemia," *Developmental Neuroscience* 40, no. 5-6 (2019): 576–585.

352. X.-Y. Xia and Y.-X. Xia, "Effects of Graded Hypothermia on Hypoxic-Ischemic Brain Damage in the Neonatal Rat," *Chinese Medical Sciences Journal* 26, no. 1 (2011): 49–53.

353. E. Koo, R. A. Sheldon, B. S. Lee, et al., "Effects of Therapeutic Hypothermia on White Matter Injury From Murine Neonatal Hypoxia-Ischemia," *Pediatric Research* 82, no. 3 (2017): 518–526.

354. X. Liu, J. Tooley, and E. M. Løberg, "Immediate Hypothermia Reduces Cardiac Troponin I After Hypoxic-Ischemic Encephalopathy in Newborn Pigs," *Pediatric Research* 70, no. 4 (2011): 352–356.

355. M. Thoresen, J. Penrice, A. Lorek, et al., "Mild Hypothermia After Severe Transient Hypoxia-Ischemia Ameliorates Delayed Cerebral Energy Failure in the Newborn Piglet," *Pediatric Research* 37, no. 5 (1995): 667–670.

356. K. Q. Zhou, V. Draghi, C. A. Lear, et al., "Protection of Axonal Integrity With 48 or 72 h of Cerebral Hypothermia in Near-Term Fetal Sheep," *Pediatric Research* 88 (2020): 48–56.

357. M. Xiong, L. X. Chen, S. M. Ma, et al., "Short-Term Effects of Hypothermia on Axonal Injury, Preoligodendrocyte Accumulation and Oligodendrocyte Myelination After Hypoxia-Ischemia in the Hippocampus of Immature Rat Brain," *Developmental Neuroscience* 35, no. 1 (2013): 17–27.

358. T. Wood, D. Osredkar, M. Puchades, et al., "Treatment Temperature and Insult Severity Influence the Neuroprotective Effects of Therapeutic Hypothermia," *Scientific Reports* 6 (2016): 23430.

359. H. B. Sarnat and M. S. Sarnat, "Neonatal Encephalopathy Following Fetal Distress: A Clinical and Electroencephalographic Study," *Archives of Neurology* 33, no. 10 (1976): 696–705.

360. T. Arnautovic, S. Sinha, and A. R. Laptook, "Neonatal Hypoxic-Ischemic Encephalopathy and Hypothermia Treatment," *Obstetrics and Gynecology* 143, no. 1 (2024): 67–81.

361. E. Jabbour, P. Wintermark, W. Basfar, et al., "Costs of Care for Neonates With Hypoxic-Ischemic Encephalopathy Treated With Therapeutic Hypothermia and Validation of the Canadian Neonatal Network Costing Algorithm," *Journal of Pediatrics: Clinical Practice* 14 (2024): 200124.

362. S. Chastant and H. Mila, "Passive Immune Transfer in Puppies," *Animal Reproduction Science* 207 (2019): 162–170.

363. J. K. Levy, P. C. Crawford, W. R. Collante, and M. G. Papich, "Use of Adult Cat Serum to Correct Failure of Passive Transfer in Kittens," *Journal of the American Veterinary Medical Association* 219, no. 10 (2001): 1401–1405.

364. J. O. Davidson, G. Wassink, L. G. van den Heuij, et al., "Therapeutic Hypothermia for Neonatal Hypoxic-Ischemic Encephalopathy—Where to From Here?," *Frontiers in Neurology* 6 (2015): 198.

365. F. Colbourne and D. Corbett, "Delayed and Prolonged Post-Ischemic Hypothermia Is Neuroprotective in the Gerbil," *Brain Research* 654, no. 2 (1994): 265–272.

366. D. L. Clark, M. Penner, I. M. Orellana-Jordan, and F. Colbourne, "Comparison of 12, 24 and 48 h of Systemic Hypothermia on Outcome After Permanent Focal Ischemia in Rat," *Experimental Neurology* 212, no. 2 (2008): 386–392.

367. D. M. Agnew, R. C. Koehler, A.-M. Guerguerian, et al., "Hypothermia for 24 Hours After Asphyxic Cardiac Arrest in Piglets Provides Striatal Neuroprotection That Is Sustained 10 Days after Rewarming," *Pediatric Research* 54, no. 2 (2003): 253–262.

368. A. R. Laptook, R. J. T. Corbett, R. Sterett, et al., "Modest Hypothermia Provides Partial Neuroprotection When Used for Immediate Resuscitation After Brain Ischemia," *Pediatric Research* 42, no. 1 (1997): 17–23.

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369. M. Thoresen, S. Satas, E. M. Løberg, et al., "Twenty-Four Hours of Mild Hypothermia in Unsedated Newborn Pigs Starting After a Severe Global Hypoxic-Ischemic Insult Is Not Neuroprotective," *Pediatric Research* 50, no. 3 (2001): 405–411.

370. S. D. Smarick, S. C. Haskins, M. Boller, et al., "RECOVER Evidence and Knowledge Gap Analysis on Veterinary CPR. Part 6: Post-Cardiac Arrest Care," *Journal of Veterinary Emergency and Critical Care* 22, no. Suppl 1 (2012): S85–S101.

371. J. O. Davidson, G. Wassink, V. Draghi, et al., "Limited Benefit of Slow Rewarming After Cerebral Hypothermia for Global Cerebral Ischemia in Near-Term Fetal Sheep," *Journal of Cerebral Blood Flow and Metabolism* 39, no. 11 (2019): 2246–2257.

372. B. Wang, J. S. Armstrong, J.-H. Lee, et al., "Rewarming From Therapeutic Hypothermia Induces Cortical Neuron Apoptosis in a Swine Model of Neonatal Hypoxic-Ischemic Encephalopathy," *Journal of Cerebral Blood Flow and Metabolism* 35, no. 5 (2015): 781–793.

373. B. Wang, J. S. Armstrong, M. Reyes, et al., "White Matter Apoptosis Is Increased by Delayed Hypothermia and Rewarming in a Neonatal Piglet Model of Hypoxic Ischemic Encephalopathy," *Neuroscience* 316 (2016): 296–310.

374. V. Draghi, G. Wassink, K. Q. Zhou, et al., "Differential Effects of Slow Rewarming After Cerebral Hypothermia on White Matter Recovery After Global Cerebral Ischemia in Near-Term Fetal Sheep," *Scientific Reports* 9, no. 1 (2019): 10142.

375. A. McDouall, K. Q. Zhou, A. Davies, et al., "Slow Rewarming After Hypothermia Does Not Ameliorate White Matter Injury After Hypoxia-Ischemia in Near-Term Fetal Sheep," *Pediatric Research* 97, no. 3 (2025): 1209–1219, https://doi.org/10.1038/s41390-024-03332-y.

376. M. Thoresen and A. Whitelaw, "Cardiovascular Changes During Mild Therapeutic Hypothermia and Rewarming in Infants With Hypoxic-Ischemic Encephalopathy," *Pediatrics* 106, no. Pt 1 (2000): 92–99.

377. M. Battin, L. Bennet, and A. J. Gunn, "Rebound Seizures During Rewarming," *Pediatrics* 114, no. 5 (2004): 1369–1369.

378. X. Lu, L. Ma, S. Sun, et al., "The Effects of the Rate of Postresuscitation Rewarming Following Hypothermia on Outcomes of Cardiopulmonary Resuscitation in a Rat Model," *Critical Care Medicine* 42, no. 2 (2014): e106–e113.

379. C. Berger, F. Xia, M. Köhrmann, and S. Schwab, "Hypothermia in Acute Stroke-Slow Versus Fast Rewarming. An Experimental Study in Rats," *Experimental Neurology* 204, no. 1 (2007): 131–137.

380. E. Suehiro, Y. Ueda, E. P. Wei, et al., "Posttraumatic Hypothermia Followed by Slow Rewarming Protects the Cerebral Microcirculation," *Journal of Neurotrauma* 20, no. 4 (2003): 381–390.

381. E. Suehiro and J. T. Povlishock, "Exacerbation of Traumatically Induced Axonal Injury by Rapid Posthypothermic Rewarming and Attenuation of Axonal Change by Cyclosporin A," *Journal of Neurosurgery* 94, no. 3 (2001): 493–498.

382. L. L. A. Bisschops, C. W. E. Hoedemaekers, T. E. Mollnes, and J. G. van der Hoeven, "Rewarming After Hypothermia After Cardiac Arrest Shifts the Inflammatory Balance," *Critical Care Medicine* 40, no. 4 (2012): 1136–1142.

383. S.-Z. Zhu, Y. Gu, Z. Wu, et al., "Hypothermia Followed by Rapid Rewarming Exacerbates Ischemia-Induced Brain Injury and Augments Inflammatory Response in Rats," *Biochemical and Biophysical Research Communications* 474, no. 1 (2016): 175–181.

384. F. Rech Morassutti, F. Cavallin, and P. Zaramella, "Association of Rewarming Rate on Neonatal Outcomes in Extremely Low Birth Weight Infants With Hypothermia," *Journal of Pediatrics* 167, no. 3 (2015): 557.e2–561.e2.

385. A. Feldman, B. De Benedictis, G. Alpan, et al., "Morbidity and Mortality Associated With Rewarming Hypothermic Very Low Birth Weight Infants," *Journal of Neonatal-Perinatal Medicine* 9, no. 3 (2016): 295–302.

386. P. Jain, J. S. Dalal, and G. Gathwala, "Rapid vs. Slow Rewarming for Management of Moderate to Severe Hypothermia in Low-Birth-Weight Pre-Term Neonates—An Open Label Randomized Controlled Trial," *Journal of Tropical Pediatrics* 67, no. 1 (2021): fmaa098, https://doi.org/10.1093/tropej/fmaa098.

387. E. Rossi, D. M. Maziku, D. E. Leluko, et al., "Rewarming Rate of Hypothermic Neonates in a Low-Resource Setting: A Retrospective Single-Center Study," *Frontiers in Pediatrics* 11 (2023): 1113897.

388. K. J. Motil, M. G. Blackburn, and J. R. Pleasure, "The Effects of Four Different Radiant Warmer Temperature Set-Points Used for Rewarming Neonates," *Journal of Pediatrics* 85, no. 4 (1974): 546–550.

389. B. W. Christensen and H. N. Erb, "An Investigation of the Discrepancy Between Set and Actual Temperature of Neonatal Incubators: Concern for Hypothermia and Hyperthermia," *Journal of the American Veterinary Medical Association* 262, no. 1 (2024): 68–71.

390. B. M. Brainard, S. L. Lane, J. M. Burkitt-Creedon, et al., "2024 RECOVER Guidelines: Monitoring. Evidence and Knowledge Gap Analysis With Treatment Recommendations for Small Animal CPR," *Journal of Veterinary Emergency and Critical Care* 34, no. Suppl 1 (2024): 76–103.

391. B. M. Brainard, M. Boller, D. J. Fletcher, and R. Authors, "RECOVER Evidence and Knowledge Gap Analysis on Veterinary CPR. Part 5: Monitoring," *Journal of Veterinary Emergency and Critical Care* 22, no. Suppl 1 (2012): S65–S84.

392. K. Hopper, S. E. Epstein, D. J. Fletcher, et al., "RECOVER Evidence and Knowledge Gap Analysis on Veterinary CPR. Part 3: Basic Life Support," *Journal of Veterinary Emergency and Critical Care* 22, no. Suppl 1 (2012): S26–S43.

393. M. McMichael, J. Herring, D. J. Fletcher, et al., "RECOVER Evidence and Knowledge Gap Analysis on Veterinary CPR. Part 2: Preparedness and Prevention," *Journal of Veterinary Emergency and Critical Care* 22, no. Suppl 1 (2012): S13–S25.

394. E. A. Rozanski, J. E. Rush, G. J. Buckley, et al., "RECOVER Evidence and Knowledge Gap Analysis on Veterinary CPR. Part 4: Advanced Life Support," *Journal of Veterinary Emergency and Critical Care* 22, no. Suppl 1 (2012): S44–S64.

395. A. M. Scremin, O. U. Scremin, and T. Brechner, "Survival Under Hypoxia. Age Dependence and Effect of Cholinergic Drugs," *Stroke; A Journal of Cerebral Circulation* 11, no. 5 (1980): 548–552.

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SPECIAL ARTICLE OPEN ACCESS

RECOVER Guidelines: Newborn Resuscitation in Dogs and Cats. Clinical Guidelines

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ABSTRACT

Objective: To present evidence- and consensus-based guidelines for resuscitation of newborn puppies and kittens.

Design: Prioritized clinical questions pertaining to newborn resuscitation and in the Population–Intervention–Comparator–Outcome (PICO) format were used to inform systematic literature searches by information specialists, to extract research findings from relevant publications and synthesize them into evidence, to assess this evidence for quality, and, finally, to develop draft treatment recommendations. These steps were followed by a consensus process and a community commenting period prior to finalization of the project. These RECOVER Newborn Resuscitation Guidelines are a concise summary of the newborn resuscitation process to provide clear and actionable clinical instructions to veterinary professionals.

Setting: Transdisciplinary, international collaboration in university, specialty, and emergency practice.

Results: A total of 28 PICO questions pertaining to resuscitation of puppies and kittens at birth were addressed in this project. This resulted in 59 treatment recommendations that delineate an iterative approach to newborn resuscitation starting with airway clearance, tactile stimulation, and temperature control, as well as positive pressure ventilation, and instruct on more advanced measures such as CPR. An algorithm displays the flow of assessments and actions over the course of the resuscitation process.

Abbreviations: CPA, cardiopulmonary arrest; CRI, constant rate infusion; C-section, Cesarean section; EE, Evidence Evaluator; ET, endotracheal; GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; HIE, hypoxic–ischemic encephalopathy; HR, heart rate; IO, intraosseous; IQR, interquartile range; PEEP, positive end-expiratory pressure; PICO, Population–Intervention–Comparator–Outcome; PIP, peak inspiratory pressure; PPV, positive pressure ventilation; ROSC, return of spontaneous circulation; RR, respiratory rate; SI, sustained inflation.

Manuel Boller and Jamie M. Burkitt-Creedon contributed equally to this work.

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Conclusions: These RECOVER Newborn Resuscitation Guidelines present a concise and comprehensive framework for resuscitation of puppies and kittens at birth. These works serve to support veterinary professionals and breeders, educational systems, and research initiatives in conducting, implementing, and advancing newborn resuscitation in puppies and kittens.

1 | Introduction

At birth, newborn puppies and kittens undergo dramatic physiological changes that can lead to severe harm or even death if any of the involved critical processes fail [1]. Within minutes, the newborn must aerate its previously fluid-filled lungs to transition gas exchange from the now-removed placenta to the lungs, and simultaneously alter the way blood circulates through the heart and lungs in a fundamental way [1–3]. The goal of newborn resuscitation is to support animals at birth through their essential transition from intra- to extrauterine physiology. But how to do this best?

For several decades, the International Liaison Committee on Resuscitation (ILCOR) has provided evidence- and consensus-based treatment recommendations for resuscitation of newborn infants, empowering medical personnel around the world to deliver resuscitation measures rooted in systematic appraisal of scientific knowledge [4, 5]. In veterinary medicine, RECOVER published evidence- and consensus-based treatment recommendations for CPR in adult dogs and cats in 2012 and 2024, but these guidelines did not pertain to newborns [6, 7]. Also, while recommendations for the practical execution of CPR in neonates and newborns have been published previously, each has represented the expertise of individual subject matter experts in the field [8–11]. No evidence- and consensus-based guidelines have been available for resuscitation of newborn puppies and kittens in the first minutes after birth.

Physiology of the newborn is dynamic during transition and differs greatly from the adult. Given this difference, newborns require unique resuscitation methods that differ fundamentally from methods used to resuscitate post-transitional dogs and cats in distress or in cardiopulmonary arrest (CPA).

The goal of the RECOVER Newborn Resuscitation Guidelines project was to generate evidence- and consensus-based treatment recommendations for resuscitation of newborn puppies and kittens to arrive at a concise and actionable set of clinical instructions for veterinary professionals.

2 | Methods

2.1 | Definitions

"Newborn" herein is defined as a mammal such as a dog or cat from birth through the first few hours of life, spanning the transition from intrauterine, fetal life to extrauterine life. A "neonate" is a dog or cat from birth until initiation of weaning (approximately 4–5 weeks depending on species and breed), at which time it is referred to as "pediatric" until it reaches sexual maturity (e.g., approximately 6 months of age depending on species and breed).

"Newborn resuscitation" includes interventions delivered from birth through the first few hours after birth to support the establishment of breathing and postnatal circulation, and related emergency care. In most cases, these interventions will be applied in a measured fashion to support the newborn's independent efforts to transition from intrauterine to postnatal physiology. Thus, resuscitation in the newborn may be limited to single measures such as tactile stimulation, establishment of a patent airway (i.e., airway clearance), oxygen supplementation, or positive pressure ventilation (PPV), or may include all the above along with chest compressions (i.e., CPR).

"Cardiorespiratory transition at birth" describes the fundamental changes in respiratory and circulatory function that the newborn experiences at birth. In this process, fetal physiology, which entirely depends on placental gas exchange and has the right and left ventricles functioning in parallel, transitions to postnatal physiology where gas exchange is relegated entirely to the lungs and the right and left ventricles work in series to serve the pulmonary and systemic circulations, respectively (Figure 1). Supporting this transition from fetal to newborn life is the primary goal of newborn resuscitation.

"Aeration of the lungs" is a critical process at birth [12]. Lung aeration reduces pulmonary vascular resistance and is the foundation for circulatory transition (Figure 1) [13]. A significant percentage of the fluid in airways and lungs is expelled during labor and delivery due to uterine contractions, posture changes, abdominal contraction of the dam, and the passage of the fetus through the birth canal [2]. In addition, the pulmonary alveolar epithelium changes from a fluid-secreting (prenatal) to a fluid-absorbing phenotype (postnatal), a transition orchestrated by a multitude of coinciding factors, including catecholamine release during birth, other endocrine factors, and an increase in alveolar PO_2 with the first few breaths; these factors drive active sodium absorption through the alveolar membrane and thus clearance of alveolar fluid [14]. The very high transpulmonary pressure of 50 cm H_2O or more during the first inspirations also plays a key role and can lead to fluid clearance of the lungs on its own with little contribution from the aforementioned mechanisms [15, 16]. High transpulmonary pressure also leads to aeration of the peripheral lungs during inspiration and helps to establish functional residual capacity; the adduction of the glottis during exhalation, as well as vocalization (an expiratory phenomenon), furthers the retention of end-expiratory alveolar gas and supports the formation of functional residual capacity [16]. PPV and positive end-expiratory pressure (PEEP) can support lung aeration if the newborn animal is not breathing within the first minute of birth on its own, or after tactile stimulation.

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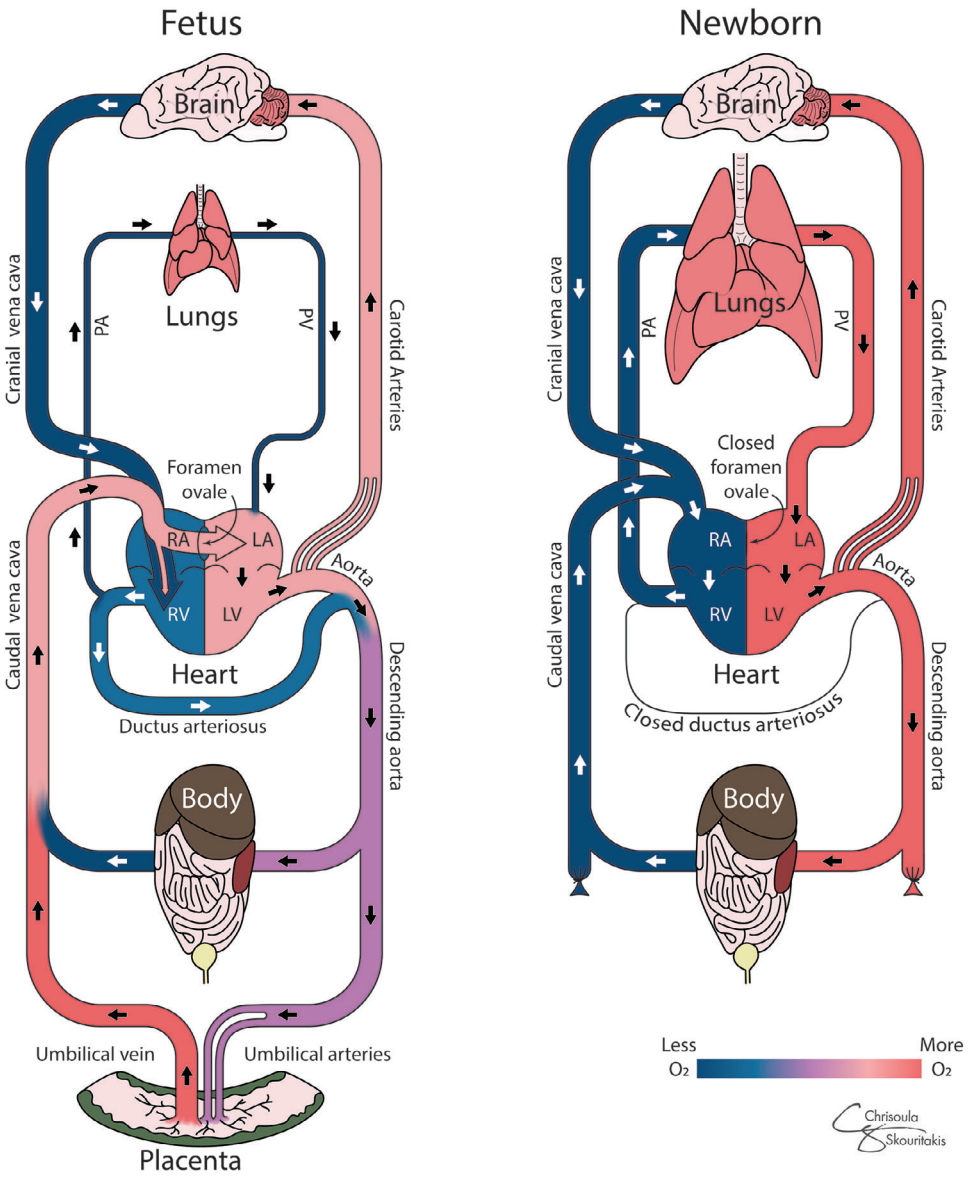


FIGURE 1 | Transition of the cardiorespiratory system at birth. (A) The cardiorespiratory system prior to birth. Gas exchange occurs exclusively in the placenta. Its vascular bed is of low vascular resistance and receives the majority of the fetus's aortic blood flow. The lung is filled with fluid and has high vascular resistance. This leads to a relatively higher pressure on the right side of the heart than on the left side. This pressure gradient drives approximately 50% of oxygenated caudal vena cava blood to transit directly through the foramen ovale into the left atrium. This well-oxygenated blood then perfuses the brain. The remaining 50% of caudal vena cava blood comingles with cranial vena cava blood that is of low oxygen saturation and leaves the right ventricle through the pulmonary artery, with most of it directly entering the descending aorta via the ductus arteriosus. As a consequence, the two ventricles function in parallel to generate aortic blood flow, with the preductal arterial oxygen saturation being markedly higher than the post-ductal arterial oxygen saturation. (B) After the completion of cardiorespiratory transition, hours following birth. At birth, the placenta is removed, and the lungs are aerated. The removal of the placenta increases peripheral vascular resistance and consequently pressures in the aorta and the left ventricle. In contrast, the vascular resistance in the now air-filled lungs decreases, pulmonary arterial blood flow through the lungs markedly increases, and blood flow through the ductus arteriosus ceases. This leads to an increase in left atrial pressure, to the functional closure of the foramen ovale, and to the cessation of the blood shunting from the right to the left atrium through it. Consequently, the two ventricles now function in series, with only the left ventricle generating aortic blood flow and with uniformly high oxygen saturation present throughout the arterial vascular system. PA, pulmonary artery; PV, pulmonary vein; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle. Artwork by Chrisoula Toupadakis Skouritakis, Ph.D., MediaLab Services Director, Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis. Copyright: The RECOVER Initiative 2025. All rights reserved.

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A "nonvigorous newborn puppy or kitten" is one that is not or is only weakly crying, has sluggish or no reflex irritability, and has low muscle tone or is flaccid. These newborns require resuscitative measures.

2.2 | Evidence Evaluation

This guidelines project followed the 2024 RECOVER guidelines methodology published in detail elsewhere [17]. In short, these RECOVER Newborn Resuscitation Guidelines were generated using a modified version of the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) system for guidelines generation in health care [18]. The process started with the generation of a list of prioritized clinical questions pertaining to newborn resuscitation in puppies and kittens, which was accomplished by the collaboration of newborn Domain Chairs and RECOVER Co-Chairs. Twenty-eight out of 40 initially proposed questions were included in the evidence evaluation.

These questions, written in the PICO (Population–Intervention–Comparator–Outcome) format, served as the foundation for information specialists to develop literature search strategies[a]. These search strategies were applied to PubMed, CAB Direct, and Scopus, and the resulting articles were uploaded to a systematic review tool[b] for identification of relevant articles. Two Evidence Evaluators (EEs) were allocated to each PICO question and conducted an initial culling process based on title and abstract review. The full-text version of articles was then uploaded to a purpose-built RECOVER GRADE site, and EEs decided based on full-text review whether to include an article for data extraction or to exclude it. The decision to include an article for full analysis was based on its relevance to components of the respective PICO question, including the study population, the intervention under evaluation, its comparator intervention, and the outcomes reported. Articles that were non-peer reviewed, non-English, reviews, meta-analyses, case reports or case series, and observational or experimental studies without control groups were excluded from further review.

The EEs then extracted from each publication and for each outcome therein relevant quality metrics, such as study design and risk of bias, indirectness regarding population, intervention, comparator and outcome, imprecision, inconsistency, and other characteristics, following a questionnaire embedded in the RECOVER GRADE site. From these assessments, an Evidence Summary Table was generated for each outcome of every PICO question, and RECOVER Domain Chairs and Co-Chairs used this information to further synthesize the evidence, to grade the overall quality of evidence for or against an intervention, and, ultimately, to draft treatment recommendations.

The quality of evidence was categorized as high, moderate, low, or very low, while evidence relevant to the most critical outcomes (e.g., survival to discharge) was prioritized over evidence found for lower priority outcomes (e.g., surrogate markers of perfusion). The quality of evidence was denoted as expert opinion if there was no evidence identified to develop a recommendation.

2.3 | Drafting Treatment Recommendations

We then used the quality of evidence to determine how certain we can be that the desirable effects of an intervention outweigh the undesirable effects. Consequently, and in accordance with GRADE, we either *recommended for* an intervention if the certainty for benefit > risk was supported by high or moderate quality of evidence or *suggested for* an intervention if we were less certain (e.g., low or very low quality of evidence). To indicate that undesirable effects outweigh desirable effects, we *recommended against* or *suggested against* an intervention. In other words, a *recommendation for* or *against* an intervention indicates there is clear benefit or harm expected with that intervention, while a *suggestion for* or *against* an intervention indicates that there is probably overall benefit or harm, or that the effect might be small. Due to the importance of generating treatment recommendations capable of informing decision-making in the clinical context, the committee further considered the feasibility (e.g., Can it be implemented?) and the ease or challenge (e.g., Is it worth the effort?) for implementation in a veterinary setting. Thus, the final strength of the recommendation for an intervention may be higher or lower than what the quality of evidence alone would indicate; detailed justification for each recommendation is provided in a companion article [19].

2.4 | Consensus Process

A team of subject matter experts in the field of small animal theriogenology and reproduction (A.D., C.L., G.B., M.V., S.G.), RECOVER Domain Chairs (C.B., K.F.), and RECOVER Co-Chairs (M.B., J.B., D.F.) then reviewed and commented on all draft treatment recommendations in a modified Delphi process for consensus finding [20]. After each round of commenting, treatment recommendations were refined as needed and were then voted on again, until the group reached consensus, defined a priori as at least 80% agreement with a recommendation. The Newborn Resuscitation Algorithm was included in the consensus process. The draft versions of newborn definitions, treatment recommendations, and the algorithm were then made accessible[c] to the EEs, subject matter experts, and the veterinary community at large for a 2-week commenting period. Comments were considered by the Co-Chairs and Domain Chairs, and relevant treatment recommendations were refined to create a finalized set of consensus guidelines for resuscitation of newborn puppies and kittens, which appear in this publication. The most important recommendations are listed in Box 1. The structured summary for each PICO question can be found in an accompanying manuscript [19], and the complete Evidence Profile Worksheets and supportive files can be accessed in a public repository[a].

3 | Treatment Recommendations for Resuscitation of Newborn Puppies and Kittens

Table 1 lists all the treatment recommendations for resuscitation of newborn puppies and kittens. The consensus on science, justification for the treatment recommendations, knowledge gaps for each PICO, and full references associated with these treatment recommendations are contained within the accom-

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BOX 1 Most important treatment recommendations for resuscitation of newborn dogs and cats

- Immediately after birth, these measures are provided to any newborn requiring resuscitation:
  - Drying and stimulating
  - Clearing the airway
  - Maintenance of normothermia
- Apex beat palpation, auscultation, ECG, and Doppler ultrasound are suitable for heart rate (HR) determination, while pulse oximetry alone is not.
- Positive pressure ventilation (PPV) is initiated in nonvigorous newborns with severe bradycardia (HR < 120/min).
- PPV is initiated as early as possible in nonvigorous, apneic, or gasping newborns.
- Appropriate reversal drugs are administered in newborns requiring resuscitation after a C-section.
- We did not reach consensus on the use of GV 26 acupoint stimulation in nonvigorous newborns.
- Doxapram is not routinely administered in all newborns requiring resuscitation but is used in those that fail to respond to other supportive measures.
- Chest compressions are started if there is no heartbeat at any time following birth.
- Chest compressions are also started in newborns with very severe bradycardia (HR < 50/min) that does not improve after 30–60 seconds of PPV.
- During CPR, four chest compressions are delivered at a rate of 150/min and alternate with one breath (compression:ventilation ratio = 4:1)
- Drugs during CPR:
  - Administer epinephrine at 0.01–0.03 mg/kg IV or IO
  - No atropine should be administered
  - 100% oxygen should be provided

panying paper on evidence and knowledge gap analysis for newborn resuscitation [19]. Additional information about the clinical application of select recommendations appears in the sections that follow. The sequence of newborn resuscitation measures and the decision points to direct interventions are presented in an algorithm (Figure 2). The RECOVER Newborn Resuscitation Algorithm was designed as a tool for prebriefing ahead of a birth to refresh the key decision points and interventions and to organize the resuscitation team. In contrast to CPA in adult dogs and cats, parturition is a more predictable event, which allows for preparation. Familiarization with an algorithm "just-in-time" and "just-in-place" before a delivery is a precondition for best use as a cognitive aid for real-time guidance during the resuscitation process [21]. The explanations that follow are intended to guide the reader through the algorithm; the complete set of treatment recommendations appears in Table 1.

4 | Newborns Requiring Resuscitation

Most newborn dogs and cats born by eutocia are not expected to require any human intervention at birth. Puppies and kittens born by normal parturition (e.g., vaginal eutocia) whose mother can provide immediate postpartum care and that are vigorous, breathing, and vocalizing immediately after birth do not require resuscitation. A vigorous newborn puppy or kitten is one that is breathing with a respiratory rate (RR) of at least 15/min, is vocalizing clearly, and displays adequate reflex irritability with strong spontaneous movements [22]. Newborns that do not require resuscitation should be left with, or immediately placed with, the dam and supervised to confirm she is aware, coordinated, and displaying adequate maternal behavior [23]. Routine postpartum management (i.e., umbilical care, weighing, physical examination for congenital defects) should be performed within 1 h of delivery (see below).

Apgar scoring as a method for newborn viability assessment was originally described for newborn infants and then modified for use in newborn puppies and kittens [24–28]. Scores of 0–2 are assigned to each parameter (heart rate [HR], respiratory effort, reflex irritability, motility, and mucous membrane color), with a lower score indicating more severe depression [26]. In newborn puppies, low modified Apgar scores obtained within 5 min were highly associated with early mortality and were significantly lower in puppies born by Cesarean section (C-section) than in those born by eutocia [24–26]. However, as an Apgar score cutoff indicating the need for resuscitative measures at birth has not been established, we suggest against using a specific Apgar score to trigger resuscitation measures at birth. That said, once a newborn is identified as not requiring resuscitation or is recovering from initial resuscitation, it should be monitored using serial Apgar scoring (e.g., at 5, 30, and 60 min after birth) to identify those at risk of deterioration. Vigorous newborns should be weighed and examined for congenital conditions [29, 30], and their umbilical cord should be ligated, trimmed to 1 cm, and disinfected with a 2% tincture of iodine. The puppy or kitten can then be united with the dam in a warm environment (29°C–32°C [84°F–89°F]) that supports newborn normothermia (i.e., 35°C–37°C [95°F–99°F]). We suggest determining the body weight every 12 h, expecting a daily weight gain of 10%.

Nonvigorous newborn puppies and kittens require resuscitative measures. All canine and feline newborns delivered by C-section, and especially those born by emergency C-section, require support at birth as (1) these animals are generally of lower vitality than those born by vaginal eutocia [24, 25, 31–33] and (2) the dam is unable to provide care for the newborns during the initial period after birth. Thus, veterinary professionals will probably use these RECOVER Newborn Resuscitation Guidelines most commonly in the context of C-section deliveries.

5 | The First Minute

The first resuscitation measures immediately after birth include drying and stimulating the newborn, clearing its airway, and

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TABLE 1 | Treatment recommendations for resuscitation of newborn puppies and kittens. This table contains all RECOVER Newborn Resuscitation treatment recommendations, listed in the order of appearance in the algorithm.

Treatment recommendation	Strength of recommendation	Quality of evidence	PICO
Airway clearance			
For newborn puppies and kittens that require resuscitation at birth but are vigorous, we suggest using a clean, dry cloth to carefully remove fluid from around the nostrils and mouth.	Weak	Expert opinion	NB-09
For newborn puppies and kittens that are nonvigorous with excessive oropharyngeal fluid (clear or meconium-stained), we suggest gentle nasal or oropharyngeal suctioning immediately followed by PPV.	Weak	Expert opinion	NB-09
For newborn puppies and kittens that are nonvigorous with excessive oropharyngeal fluid (clear or meconium-stained), we suggest against the routine use of endotracheal suctioning.	Weak	Very low	NB-09
We suggest against interventions other than suctioning to clear excessive upper airway fluid in newborn puppies and kittens.	Weak	Expert opinion	NB-10
We recommend against the removal of upper airway fluid in newborn puppies and kittens by swinging.	Strong	Expert opinion	NB-10
Tactile stimulation			
In newborn puppies and kittens that require resuscitation, we recommend the use of tactile stimulation (e.g., rubbing, drying) immediately after birth without delaying essential interventions such as PPV.	Strong	Very low	NB-15
Temperature control at birth			
In newborn puppies and kittens that require resuscitation, we recommend maintenance of normothermia (95°F–99°F [35°C–37.2°C]) compared to no temperature control.	Strong	Moderate	NB-11
In newborn puppies and kittens that are hypothermic at birth without signs of HIE, we suggest actively rewarming newborns over 1–2 h to reach normothermia (35.0°C–37.2°C; 95°F–99°F), avoiding accidental hyperthermia.	Weak	Expert opinion	NB-28
Reversal drugs after C-sections			
In newborn puppies and kittens that require resuscitation after a C-section for which the dam was administered an opioid, α_2-adrenoceptor agonist, or benzodiazepine, we recommend administration of the appropriate reversal drug.	Strong	Very low	NB-20
In newborn puppies and kittens that are vigorous at birth and in which the dam was administered an opioid, α_2-adrenoceptor agonist, or benzodiazepine, there is insufficient evidence to suggest for or against routine administration of reversal drugs.	Weak	Very low	NB-20
GV 26 acupoint stimulation			
We did not reach consensus on whether to suggest for or against GV 26 stimulation in newborn puppies and kittens with inadequate spontaneous ventilation at birth.	NA	Expert opinion	NB-08
Doxapram			
We recommend against the routine administration of doxapram in newborn puppies and kittens undergoing resuscitation.	Strong	Moderate	NB-07
In apneic or gasping newborn puppies and kittens that are not responding to PPV, we suggest doxapram administration.	Weak	Very low	NB-07
In newborn puppies and kittens that are bradypneic and that fail to respond to timely administration of other supportive measures, we suggest the use of doxapram.	Weak	Very low	NB-07

(Continues)

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TABLE 1 | (Continued)

Treatment recommendation	Strength of recommendation	Quality of evidence	PICO
Atropine for the treatment of bradycardia			
In newborn puppies and kittens that require resuscitation and that are bradycardic, we suggest against routine atropine administration.	Weak	Expert opinion	NB-23
Determination of HR			
In newborn puppies and kittens requiring resuscitation, we suggest estimating the HR using any of the following techniques: apex beat palpation, cardiac auscultation, ECG, or Doppler ultrasound probe applied to the thorax.	Weak	Very low	NB-04
In newborn puppies and kittens requiring resuscitation, we recommend against the use of pulse oximetry as the only method to evaluate HR.	Strong	Very low	NB-04
Positive pressure ventilation in newborns not in CPA			
We recommend initiating PPV in nonvigorous newborn puppies and kittens with cleared upper airways that are bradycardic.	Strong	Expert opinion	NB-01
We suggest using an HR below 120/min as the threshold for initiating PPV in nonvigorous newborn puppies and kittens with cleared upper airways.	Weak	Expert opinion	NB-01
We recommend starting PPV as early as possible in nonvigorous puppies and kittens that are gasping or are apneic, regardless of the HR.	Strong	Expert opinion	NB-01
We suggest the use of room air (21% oxygen) over 100% oxygen during early assisted ventilation of newborn puppies and kittens.	Weak	Very low	NB-03
We suggest the use of 100% oxygen in newborn puppies and kittens in which the HR fails to increase despite 1–2 min of PPV.	Weak	Expert opinion	NB-03
In newborn puppies and kittens without CPA that require PPV, we suggest the use of a tight-fitting facemask attached to a self-inflating resuscitator (i.e., "bag") to deliver positive pressure breaths within 60 s of birth.	Weak	Very low	NB-05
In newborn puppies and kittens without CPA undergoing PPV by facemask and that fail to respond within 60 s (e.g., HR remains <120/min despite intervention), we suggest endotracheal intubation for continued PPV if feasible.	Weak	Expert opinion	NB-05
In newborn puppies and kittens that require resuscitation with PPV, we suggest administering PPV with an inspiratory time of 1 s and a peak inspiratory pressure of 20–25 cm H_2O.	Weak	Very low	NB-06
In newborn puppies and kittens that require resuscitation with PPV, we suggest application of at least 4 and no more than 8 cm H_2O positive end-expiratory pressure.	Weak	Very low	NB-06
In newborn puppies and kittens with bradycardia, cyanosis, or inadequate breathing efforts that persist despite 30–60 s of standard PPV using 1 s inspiratory time at a peak inspiratory pressure of 20–25 cm H_2O, we suggest giving a single 30-s sustained inflation at 30–35 cm H_2O, followed by continued standard PPV if indicated.	Weak	Low	NB-06
Initiation of chest compressions with very severe bradycardia			
In very severely bradycardic newborn puppies and kittens that have received effective PPV and oxygen supplementation for at least 30 s, we recommend initiating chest compressions.	Strong	Expert opinion	NB-02
We suggest using an HR below 50/min as the threshold for initiating chest compressions in newborn puppies and kittens that have received effective PPV and oxygen supplementation for at least 30 s.	Weak	Expert opinion	NB-02

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TABLE 1 | (Continued)

Treatment recommendation	Strength of recommendation	Quality of evidence	PICO
Chest compression point and animal position			
In newborn puppies and kittens requiring chest compressions, we suggest application of chest compressions in the laterolateral direction.	Weak	Expert opinion	NB-16
In newborn puppies and kittens requiring chest compressions, we suggest ventrodorsal (sternal) chest compressions when additional resuscitation measures (e.g., umbilical cord cannulation, monitoring modalities) are facilitated by dorsal recumbency.	Weak	Expert opinion	NB-16
In newborn puppies and kittens requiring chest compressions in lateral recumbency, we recommend that one or two fingers be located over the heart to compress the chest toward the tabletop, or alternatively, that one or two fingers (index and middle finger) and the opposing thumb be used to compress the chest directly over the heart.	Strong	Expert	NB-16
In newborn puppies and kittens requiring chest compressions in which dorsal recumbency is preferred (e.g., for cannulation of the umbilical vein or pronounced wide-chested thorax conformation), we recommend that one or two fingers (index and middle finger) compress the sternum toward the tabletop to achieve the targeted chest compression depth.	Strong	Expert opinion	NB-16
Chest compression rate and technique			
We suggest delivering chest compressions in newborn puppies or kittens at 120–150 compressions per minute.	Weak	Very low	NB-12
In newborn puppies and kittens receiving chest compressions, we suggest a compression depth of one-third to one-half of the width of the chest for laterolateral compressions.	Weak	Very low	NB-17
In newborn puppies and kittens receiving chest compressions, we suggest a compression depth of one-third the anterior–posterior (AP) diameter of the chest for ventrodorsal (i.e., sternal) compressions.	Weak	Very low	NB-17
Coordination of chest compressions and ventilation			
In newborn puppies and kittens receiving chest compressions and PPV with a cuffed endotracheal tube in place, we suggest delivering breaths concurrently to chest compressions (asynchronized ventilation).	Weak	Very low	NB-14
In newborn puppies and kittens receiving chest compressions and PPV that are not intubated with a cuffed endotracheal tube, we recommend synchronized ventilation by pausing chest compressions to deliver breaths.	Strong	Expert opinion	NB-14
In newborn puppies and kittens receiving chest compressions and synchronized PPV, we suggest a compression:ventilation ratio of 4:1.	Weak	Expert opinion	NB-13
Oxygen supplementation during CPR			
In newborn puppies and kittens receiving chest compressions, we suggest PPV with 100% oxygen.	Weak	Very low	NB-18
Epinephrine during CPR			
In newborn puppies and kittens with a very low HR (i.e., HR < 50/min) despite 60 s of adequate PPV and chest compressions, we recommend administration of epinephrine.	Strong	Moderate	NB-21
In newborn puppies and kittens with very low HR (i.e., HR < 50/min) despite 60 s of adequate PPV and chest compressions, we recommend IV or intraosseous (IO) administration of epinephrine over intratracheal or intranasal administration.	Strong	Moderate	NB-21

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TABLE 1 | (Continued)

Treatment recommendation	Strength of recommendation	Quality of evidence	PICO
In newborn puppies and kittens with very low HR (i.e., HR < 50/min) despite adequate PPV and chest compressions, we suggest against IM administration of epinephrine (including intralingual IM administration).	Weak	Very low	NB-21
Epinephrine dose during CPR			
In newborn puppies and kittens that remain very severely bradycardic (i.e., HR < 50/min) despite 60 s of PPV and chest compressions, we recommend administration of 0.01–0.03 mg/kg epinephrine IV/IO.	Strong	Very low	NB-22
In newborn puppies and kittens that remain very severely bradycardic (i.e., HR < 50/min) despite 60 s of PPV and chest compressions, we recommend against high-dose (0.1 mg/kg) IV/IO epinephrine.	Strong	Very low	NB-22
In newborn puppies and kittens that remain very severely bradycardic (i.e., <50/min) despite 60 s of PPV and chest compressions, in which epinephrine is given endotracheally because IV/IO access is not possible or significantly delayed, we suggest 0.05–0.1 mg/kg epinephrine ET.	Weak	Very low	NB-22
Atropine during CPR			
In newborn puppies and kittens that require resuscitation and are in CPA, we suggest against the routine administration of atropine during CPR.	Weak	Expert opinion	NB-24
Dextrose during resuscitation with or without CPA			
In newborn puppies and kittens that require prolonged resuscitation, we suggest measuring the blood glucose concentration.	Weak	Expert opinion	NB-19
In hypoglycemic newborn puppies and kittens that require resuscitation (with or without CPA), we recommend dextrose supplementation with a slow bolus of 0.25 g/kg dextrose (e.g., 0.5 mL/100 g of 5% dextrose solution over 5 min) IV, IO, or IP.	Strong	Very low	NB-19
In hypoglycemic newborn puppies and kittens in which IV/IO or IP access is not possible, we suggest topical sublingual mucosal administration of dextrose at 0.5 g/kg (e.g., 0.1 mL/100 g of 50% dextrose solution).	Weak	Expert opinion	NB-19
In newborn puppies and kittens undergoing prolonged resuscitation (e.g., >10 min) that are not responding to standard measures (e.g., PPV, rewarming, stimulation) and in which BG concentrations cannot be measured, we suggest dextrose supplementation.	Weak	Expert opinion	NB-19
Termination of CPR			
In newborn puppies and kittens receiving chest compressions, we suggest continuation of CPR for at least 15 min before abandoning resuscitation efforts as long as such efforts do not detract from the necessary care of littermates with a better prognosis.	Weak	Very low	NB-25
Temperature management with HIE			
In newborn puppies and kittens with signs of acute HIE, we suggest permitting the animal to remain at a low normal temperature for newborn puppies and kittens (i.e., 35°C, 95°F) for 24 h after birth.	Weak	Expert opinion	NB-27
In newborn puppies and kittens that are hypothermic at birth and show evidence of HIE, we suggest rewarming at a rate no faster than 1°C/h to achieve normothermia (35.0°C–37.2°C; 95°F–99°F) while avoiding accidental hyperthermia.	Weak	Very low	NB-28
Blood glucose management after ROSC			
In newborn puppies and kittens after ROSC that are nonvigorous and not nursing, we suggest measuring the blood glucose concentration.	Weak	Expert opinion	NB-26

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TABLE 1 | (Continued)

Treatment recommendation	Strength of recommendation	Quality of evidence	PICO
In hypoglycemic newborn puppies and kittens after ROSC, we suggest supplementing dextrose by CRI (e.g., 2.5% dextrose in isotonic crystalloid fluids given at a physiologic rate IV or IO) rather than by bolus injection.	Weak	Very low	NB-26
In hypoglycemic newborn puppies and kittens after ROSC, we recommend dextrose supplementation with a slow bolus of 0.25 g/kg dextrose (e.g., 0.5 mL/100 g of 5% dextrose over 5 min) IV, IO, or IP, if an IV or IO CRI is not feasible.	Strong	Very low	NB-26
In hypoglycemic newborn puppies and kittens after ROSC in which IV, IO, or IP administrations are not possible, we suggest oral administration of dextrose at 0.5 g/kg (e.g., 0.1 mL/100 g of 50% dextrose).	Weak	Expert opinion	NB-26
In newborn puppies and kittens that are nonvigorous and not nursing after resuscitation and in which blood glucose concentrations cannot be measured, we suggest dextrose supplementation.	Weak	Expert opinion	NB-26

Abbreviations: ALS, advanced life support; CPA, cardiopulmonary arrest; CRI, constant rate infusion; ET, endotracheal; HIE, hypoxic–ischemic encephalopathy; HR, heart rate; IO, intraosseous; IP, intraperitoneal; PPV, positive pressure ventilation; ROSC, return of spontaneous circulation; RR, respiratory rate; TV, tidal volume.

initiating measures to maintain normothermia. In practice, these measures are initiated concurrently and do not follow a strict order. Once these measures have succeeded, rescuers should determine the HR and assess the respiratory function within the first minute after delivery. The newborn puppy or kitten is expected to start vocalizing and moving within moments after birth. If not, information on HR and respiratory function is used to guide the initiation of appropriate resuscitative measures in support of the respiratory transition in that first minute.

5.1 | Temperature Control at Birth

We recommend that all resuscitative measures be undertaken in a temperature-controlled environment. The newborn's lack of thermoregulatory competency exposes it to the risk of hypothermia unless it is maintained in an environment that mitigates temperature loss. While we found only limited evidence in newborn puppies and kittens, multiple studies in human infants establish a strong relationship between hypothermia in newborns and morbidity (e.g., dysglycemia, sepsis) and mortality [34–38]. Newborn puppies born by C-section were found to have a mean body temperature of 34.0°C (93.2°F) at birth, which further decreased to 32°C (89.6°F) after 20 min; hypothermia was mitigated but still significant in puppies born by vaginal eutocia (i.e., 36.2°C [97.2°C] at birth and 34.0°C [93.2°F] after 20 min) [32]. We therefore recommend undertaking measures to maintain normothermia (NB-11). We consider a newborn rectal temperature between 35°C and 37°C (95°F and 99°F) to be normal. A suitable temperature control system should not interfere with other resuscitation efforts. Immediate drying of the newborn puppy or kitten with warm towels serves as an early measure to limit heat loss and also provides an element of tactile stimulation. Further, we suggest positioning the newborn on a dry, warm surface (e.g., warm towels) to shield it from conductive heat loss. Radiant heat loss can be reduced by placing the newborn beneath an overhead heat source (e.g., radiating heat warmer) while the rescuer administers necessary interventions. Care must be taken to avoid hyperthermia or skin burns, particularly because even vigorous newborns cannot reliably move away from too-hot surfaces quickly enough to avoid hyperthermia or burns. High-quality incubators generate a warm environment through circulating air and humidity; they can be suitable for post-resuscitation maintenance of normothermia when set at 29°C–32°C (84°F–89°F). Adequate monitoring to avoid accidental hyperthermia is required to avoid harm [39].

When they have become hypothermic, we suggest actively rewarming newborn puppies and kittens relatively rapidly over 1–2 h (NB-28) as long as they do not display signs of hypoxic–ischemic injury (e.g., mental obtundation). In this healthier population, rewarming rates of up to 5°C/h (8°F/h) were not associated with harm in infants [40–44], though a higher risk for temperature overshoot was noted in one study, and close monitoring is warranted to avoid hyperthermia [43].

5.2 | Tactile Stimulation

We recommend the use of tactile stimulation, such as rubbing with a dry, clean cloth, in nonvigorous newborns immediately after birth, as long as this does not delay or interfere with time-sensitive resuscitation measures such as PPV (NB-15). Tactile stimulation is highly feasible and low-risk when performed in a gentle, nontraumatic manner. Although tactile stimulation of newborns is a very common practice to stimulate breathing in veterinary species and infants, evidence to support the practice is very limited but generally neutral or in favor of the intervention [45–47]. One observational study in newborn infants found that tactile stimulation was associated with a relative risk reduction for the need of endotracheal (ET) intubation of nearly 60% [48].

5.3 | Establishing a Patent Airway

The need to immediately remove fetal membranes to free the newborn's airways at birth is obvious, and accordingly, we did not

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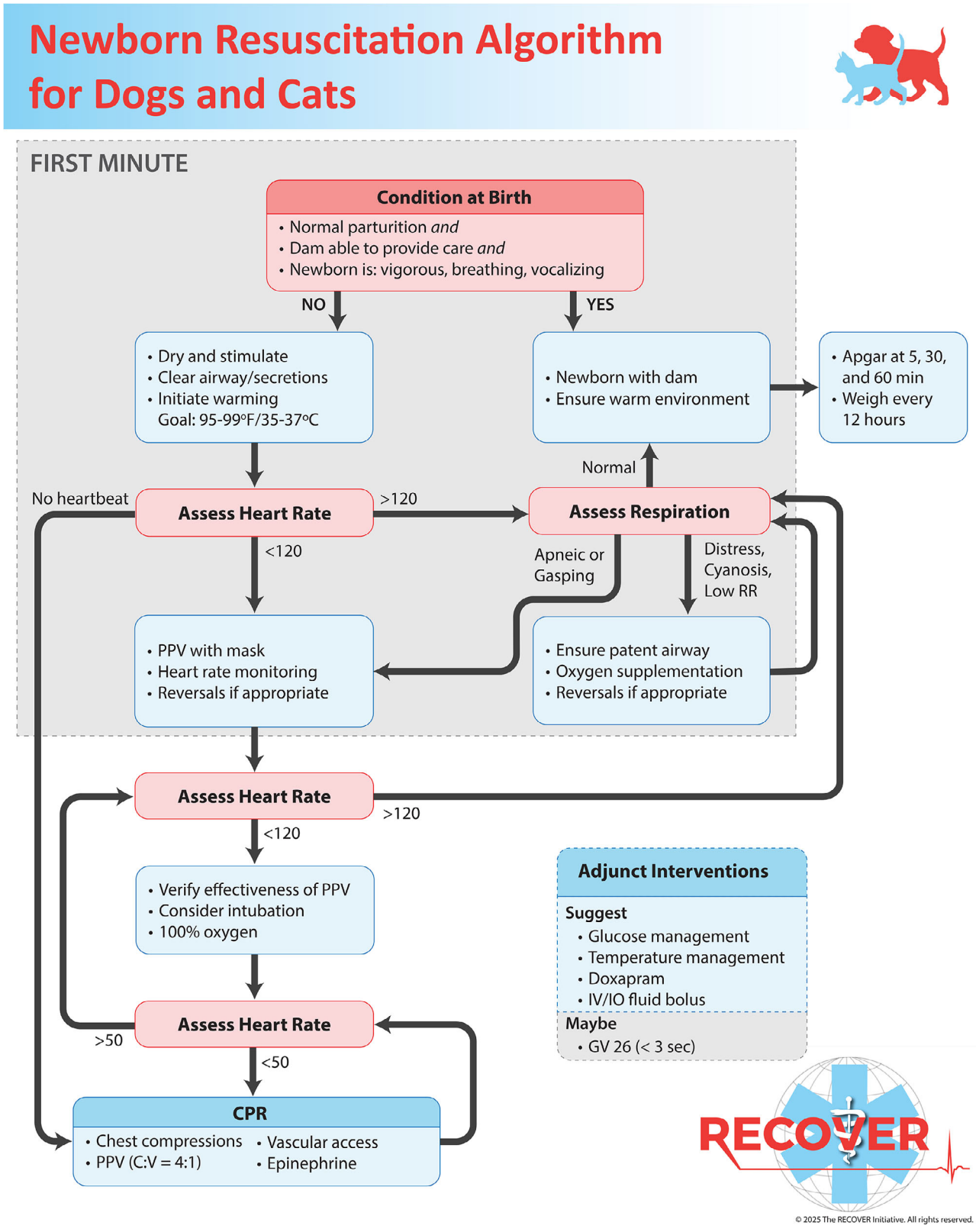


FIGURE 2 | Newborn resuscitation algorithm for puppies and kittens. C:V, compression:ventilation ratio during bag–mask ventilation and chest compressions during CPR; IO, intraosseous; GV 26, needle stimulation of the Governing Vessel 26 acupoint; PPV, positive pressure ventilation; RR, respiratory rate. Artwork by Chrisoula Toupadakis Skouritakis, Ph.D., MediaLab Services Director, Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis. Copyright: The RECOVER Initiative 2025. All rights reserved.

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evaluate any evidence to support this practice. Which measures to take, if any, to remove fluid from the newborn's airway, however, is less obvious. Fluid in the upper airways is typically cleared naturally and rapidly by the vigorous, vocalizing newborn without any external support required [12]. If the newborn is vigorous but needs support, for example, after a C-section, we suggest using a clean, dry cloth to gently remove excess fluid from around the nostrils and muzzle (NB-09). Suctioning exposes the airway to negative pressure and might counteract the goal of lung aeration, so it should not be done routinely. However, if the newborn puppy or kitten is nonvigorous, is not vocalizing loudly, and has excessive oropharyngeal fluid, whether clear or meconium stained, we suggest removal of that fluid by gentle, expedient nasal or oropharyngeal suctioning immediately followed by PPV (NB-09). For removal of fluid from nostrils and rostral oral cavity, a suction bulb can be used, while a mucus aspirator (e.g., DeLee suction catheter with mucous trap) allows for deeper oropharyngeal suctioning. Importantly, undue aspiration should be avoided as this could impede vitally important lung aeration.

Multiple studies in newborn infants and experimental animals have evaluated the effect of ET suctioning in the presence of excessive amniotic fluid and have not identified any benefit regardless of whether said fluid is meconium stained or not [49–53]. Compared to newborn infants, ET suction in newborn puppies and kittens is technically difficult to accomplish and exposes the animal to harm, including the risk of laryngeal swelling, lung derecruitment (reduced lung aeration) with severe desaturation, and compromise of life-saving measures such as PPV [53]. We therefore suggest against ET suctioning even if the oropharyngeal fluid is excessive and meconium stained (NB-09). Any fluid removal methodology should be brief and interfere as little as possible with the timely initiation of PPV, which is a priority intervention in nonvigorous newborn puppies and kittens that are apneic or gasping, breathing inadequately, or severely bradycardic.

We suggest against interventions other than suctioning to clear excessive upper airway fluid in newborns (NB-10). "Swinging" as a means to accelerate drainage of fluid from the newborn's airway by harnessing centrifugal force was historically advocated in human medicine over a century ago and has long been abandoned [54]. We recommend against this practice in newborn puppies and kittens due to the significant risk of intracranial hemorrhage, potential trauma, and aspiration of gastric contents (NB-10) [55]. Additionally, swinging delays the initiation of more effective resuscitative measures such as PPV.

5.4 | Heart Rate Assessment

The newborn's HR is a vital parameter used to guide resuscitation because it reflects the severity of hypoxemia; worsening bradycardia generally indicates the need for escalation of supportive measures, while an increase in HR suggests the possibility for de-escalation of care.

Bradycardia in the newborn is a consequence of hypoxemia and is mediated through vagal and nonvagal mechanisms [56]. As the bradycardia itself is a surrogate measure for the severity of hypoxemia and other factors concerning pulmonary aeration, it reflects the progress of the newborn's cardiorespiratory transition.

In newborn puppies and kittens requiring resuscitation, the goal is to obtain the first HR measurement within the first 60 s after birth, although this is not always feasible [57]. In late pregnancy, one small study found that normal fetal HR by echocardiogram was 218 ± 7/min in puppies ($n = 8$) and 228 ± 35/min for kittens ($n = 7$) [58]. In puppies experiencing normal birth (vaginal eutocia), the mean HR immediately after delivery was approximately 180/min, whereas it was approximately 165/min after C-section [32]. Puppies achieved a normal HR of 200–220/min after 5 min with eutocia and after 4 h following C-section [32].

We suggest estimating the HR using apex beat palpation, cardiac auscultation, ECG, or Doppler ultrasound probe and suggest against the use of pulse oximetry as the only method (NB-04). Although this has not been studied in newborn puppies and kittens, pulse oximetry was consistently inaccurate and slow at determining HR in newborn infants [59–62]. While dry-electrode ECG provided fast and accurate HR measurement in newborn infants, it is reasonable on practical grounds to obtain an initial HR by auscultation and only to escalate to continuous ECG monitoring when advanced resuscitation measures (e.g., prolonged PPV, CPR) are required.

We decided by consensus and based on expert opinion on specific, actionable HR cutoffs as decision markers to initiate certain resuscitative interventions. We suggest using an HR below 120/min as the threshold for initiating PPV when a newborn is also classified as nonvigorous, and the upper airway is clear (NB-07). In addition, an HR <120/min warrants administration of appropriate reversal drugs (i.e., naloxone, atipamezole, or flumazenil) if exposure to the respective agonist is documented (NB-20), such as during C-section.

If there is no heartbeat identified in a nonvigorous newborn puppy or kitten that is apneic or gasping, the newborn is in CPA, and CPR should be started without delay.

If the HR is found to be >120/min, we next recommend clinical assessment of the newborn's respiratory function.

5.5 | Respiratory Assessment

Normal RRs in newborns are generally >15/min, although RRs that are much higher have been reported with normal birth, such as > 40/min in puppies and >70/min in kittens [22, 28, 32]. If the RR is <15/min (including apnea or gasping), or if there is no clear vocalization, an overt increase in respiratory effort (i.e., labored breathing), or worsening cyanosis, then a specific set of resuscitative measures should be performed to support oxygenation.

5.5.1 | Bradypnea, Respiratory Distress, or Cyanosis in the Newborn With an HR >120/min

The first step in all newborns is to ensure the airway is patent; if excessive upper airway fluid is present, repeated, short, and gentle

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suctioning with a bulb syringe or DeLee suction catheter should be considered, remembering the caveats mentioned previously to avoid removing air from the lung.

Additionally, we believe administration of supplemental oxygen can be considered in the presence of clear signs of respiratory distress or bradypnea (e.g., RR < 15/min) in conjunction with cyanosis in spontaneously breathing newborns with an HR >120/min. As oxygen saturations are very low even in normal newborn infants (e.g., SaO_2 of 60%–65% is normal in the first minute after birth in newborn infants), low SpO_2 values and thus cyanosis alone in the first minute after birth are not by themselves a concern and can represent "healthy" values [63]. Free-flow oxygen can be administered, for example, by flow-by method, which will typically lead to an inspiratory oxygen concentration of <50% or via a face mask that can lead to an inspired oxygen concentration of >80% depending on fresh gas flow and distance between mask and muzzle [64, 65]. However, we could not find any evidence for or against short-term oxygen supplementation in spontaneously breathing newborns and only systematically reviewed scientific knowledge pertaining to oxygen supplementation in newborns undergoing PPV (see below, NB-03). In that population, there is ample evidence that ventilatory support with pure oxygen is either of no benefit or harmful when compared to room air [66–69]. In puppies and kittens receiving PPV, we therefore suggest the use of room air and to only increase to 100% oxygen if there is no response (e.g., no increase in HR) after 1–2 min of PPV alone (see NB-03).

Finally, we suggest administration of the appropriate reversal drug (i.e., naloxone, atipamezole, flumazenil) in bradypneic or cyanotic newborn puppies and kittens after a C-section if the bitch was premedicated with an opioid, α_2-adrenoceptor agonist, or benzodiazepine (Figure 3). While benzodiazepines are uncommonly used for premedication of bitches for C-sections, benzodiazepine use in the mother during the perinatal period can cause profound obtundation and respiratory depression in newborn infants, puppies, and kittens and often requires repeated administration or constant rate infusion (CRI) of flumazenil [70–72]. However, if newborn puppies and kittens are vigorous at birth, we found insufficient evidence to suggest for or against routine administration of reversal drugs, even if the dam was administered an opioid, α_2-adrenoceptor agonist, or benzodiazepine in the perinatal period (NB-20).

5.5.2 | Apnea, Gasping, or Severe Bradycardia in the Nonvigorous Newborn

In newborn puppies and kittens that are apneic or gasping, or are nonvigorous with a low HR (i.e., <120/min), we recommend active ventilatory support to aid in lung aeration by starting PPV once airway clearance (e.g., by oronasopharyngeal suctioning if required) has been accomplished (NB-01). Administration of positive pressure breaths is the most important step to support lung aeration in newborns that are nonvigorous and apneic/gasping, even though the majority of newborn infants receiving PPV only require it for at most a few minutes (median 129 s; interquartile range [IQR] 157) [73]. Nevertheless, every 30-s delay in starting PPV has been associated with an increase in mortality by 16% in newborn infants requiring PPV [74]. We therefore recommend starting PPV as early as possible and within the first minute of birth in nonvigorous puppies and kittens that are gasping or are apneic, regardless of the HR (NB-01, NB-05).

We suggest initiating PPV with a tight-fitting face mask at a rate of 20–30/min, with an inspiratory time of 1 s and a peak inspiratory pressure (PIP) of 20–25 cm H_2O (NB-06). A target tidal volume is approximately 10–15 mL/kg, so only around 5 mL for a 300-g puppy and an appropriately sized self-inflating resuscitator bag should be used to deliver small tidal volumes (Figure 4). However, data from newborn infants suggest that a PIP of 30 cm H_2O would produce a tidal volume of only 5 mL/kg initially due to the stiffness of the still fluid-filled lungs early after birth, which would increase to 10 mL/kg after 30 s of PPV [75]. In the veterinary setting, peak pressure and tidal volume generally cannot be measured in newborns. It is therefore reasonable to use chest excursion and auscultation for breath sounds, as well as changes in HR, to monitor the efficacy of PPV. To support the establishment of functional residual capacity, we further provide a weak recommendation for a PEEP of 4–8 cm H_2O, acknowledging that airway manometers and bag–mask systems with integrated PEEP valves are not widely available in the delivery areas of veterinary clinics (NB-06). While there is evidence supporting the application of PEEP in animal studies and preterm newborn infants needing PPV at birth, a randomized controlled trial in term newborn infants did not show an effect of PEEP on clinically relevant outcomes [76–78].

As in adult dogs and cats undergoing bag–mask ventilation, the snout, neck, and thoracic spine should be aligned to minimize upper airway resistance and reduce the risk for gastric insufflation. Cricoid pressure or, more recently, ultrasound-guided external compression of the esophagus has been used to prevent gastric gas distention during bag–mask ventilation in people [79]. Although untested, gentle digital pressure could be applied to the left side of the caudal third of the ventrolateral neck to occlude the esophagus and mitigate gastric insufflation during PPV.

In newborns that are nonvigorous, severely bradycardic, apneic, or gasping, we also recommend administering reversal drugs (i.e., naloxone, atipamezole, or flumazenil) if the dam received an opioid, α_2-adrenoceptor agonist, or benzodiazepine prepartum (NB-20) (Figure 3).

However, we suggest against routine atropine administration in this population (NB-23). Bradycardia can occur due to parasympathetic (i.e., "vagal") activation even in the fetus and the newborn [80, 81], and bradycardia due to severe hypoxemia is at least in part vagally mediated, in addition to direct hypoxic myocardial depression [56, 82, 83]. However, newborn bradycardia in response to hypoxemia is considered an adaptive response in newborns to preserve myocardial function; additionally, despite the fact that atropine can increase the HR, it was shown to have little effect on indices of oxygen delivery, which is the primary objective of treatment [84, 85]. Rather than helping, atropine can worsen myocardial ischemia in the face of severe hypoxemia and thereby aggravate myocardial injury and circulatory compromise. The main treatment for severe bradycardia in transitional newborns is reversal of hypoxemia through respiratory support, foremost in the form of PPV.

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Newborn Resuscitation Dosing Chart

		Weight (g)	50	100	200	300	400	500	600	700	800
DRUG	ROUTE	DOSE	ml	ml	ml	ml	ml	ml	ml	ml	ml
Epinephrine (1:10,000; 0.1mg/mL)	IV / IO	0.02 mg/kg (0.01-0.03 mg/kg)	0.01	0.02	0.04	0.06	0.08	0.1	0.12	0.14	0.16
	ET / IN	0.1 mg/kg	0.05	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8
Naloxone (0.4 mg/mL)	IV / IO / IM / SC	0.04 mg/kg	0.005	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08
	Topical SL	0.1 mg /newborn	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Atipamezole (5 mg/mL)	IV / IO / IM	0.05 mg/kg	0.0005	0.001	0.002	0.003	0.004	0.005	0.006	0.007	0.008
	Topical SL	0.1 mg/kg	0.001	0.002	0.004	0.006	0.008	0.01	0.012	0.014	0.016
Flumazenil (0.1 mg/mL)	IV / IO / IM / Topical SL	0.02 mg/kg	0.01	0.02	0.04	0.06	0.08	0.1	0.12	0.14	0.16
Dextrose (5%, 50 mg/mL)	IV / IO, slow	0.25 g/kg (5%)	0.25	0.5	1	1.5	2	2.5	3	3.5	4
Dextrose (50%, 500 mg/mL)	Topical SL	0.5 g/kg (50%)	0.05	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8
Doxapram (20 mg/mL)	IV / IO / IM	10 mg/kg	0.025	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4
	Topical SL / IN	15 mg/kg	0.04	0.07	0.15	0.22	0.3	0.37	0.45	0.52	0.6
		Weight (g)	50	100	200	300	400	500	600	700	800

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FIGURE 3 | Newborn resuscitation dosing chart. Drug volumes are provided by body weight in 100-g increments to reduce the risk of calculation errors. Depending on the drug route, different drug doses and thus drug volumes are recommended. ET, endotracheal; IM, intramuscular; IN, intranasal; IO, intraosseous; IP, intraperitoneal; SC, subcutaneous; SL, topical sublingual. Copyright: The RECOVER Initiative 2025. All rights reserved.

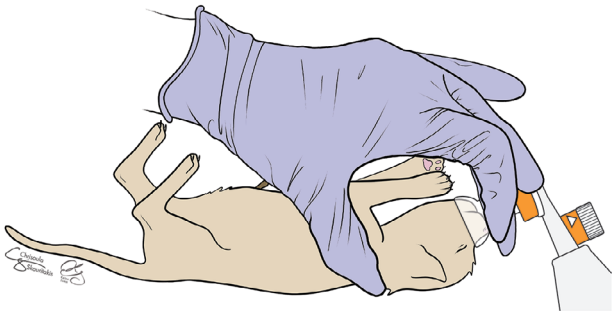


FIGURE 4 | Positive pressure ventilation is a critically important intervention in newborn resuscitation and requires early initiation. We suggest the use of a tight-fitting face mask and a suitable self-inflating resuscitator bag to deliver effective breaths. Snout, neck, and back should be aligned, and dorsal recumbency should be avoided for easier air passage into the lungs. Signs of effective ventilation are a visible chest rise and an increase in HR. PPV should be initiated with room air, and 100% oxygen should be considered if there is no response after 1–2 min (e.g., no increase in HR observed). Artwork by Chrisoula Toupadakis Skouritakis, Ph.D., MediaLab Services Director, and Kailee Suess, Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis. Copyright: The RECOVER Initiative 2025. All rights reserved.

If the newborn puppy or kitten is found to have no heartbeat, CPR should be initiated immediately. CPR involves initiating chest compressions in addition to PPV. CPR is discussed in detail later in the article.

6 | Respiratory Support Beyond the First Minute

Results from research in newborn infants and experimental animals suggest that even when effective, it typically takes ≥30 s for PPV to lead to an increase in HR [86–88]. We therefore believe it is reasonable to reassess the HR after 30–60 s of PPV and only then modify resuscitative measures as directed. If the HR increases to >120/min, RR and effort should be assessed, and de-escalation of respiratory support should be considered accordingly. However, if severe bradycardia persists (i.e., HR < 120/min) despite 1 min of PPV by bag–mask, the efficacy of this ventilation strategy should be questioned, and we suggest considering ET intubation when feasible (NB-05), ventilation with 100% oxygen (NB-03), and sustained inflation (SI) (NB-06).

ET intubation should be considered, particularly in cases in which bag–mask ventilation overtly fails to generate adequate chest expansions and thoracic auscultation reveals absent breath sounds. In newborn puppies and kittens, ET intubation is an advanced and technically challenging procedure due to the small patient size. In many cases, the newborn's voluminous, fleshy tongue obscures clear identification of laryngeal landmarks critical to ET intubation, such as epiglottis, arytenoids, and vocal folds. The risks of traumatic, prolonged intubation attempts precluding concurrent PPV should be balanced against the expected benefit of improved lung aeration after successful ET intubation. The resultant risk–benefit ratio varies from case to case based on experience and number of resuscitation personnel, available equipment, and size and number of newborns; since

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these variables are often known antepartum, teams can discuss an airway management strategy during prebriefing.

While outside of the scope of these guidelines, we hereafter provide a short overview of the technique of ET intubation in newborns. ET intubation can be accomplished with small, uncuffed ET tubes (i.e., internal diameter 2.0 mm) in larger puppies, or venous catheters of appropriate size (e.g., 20, 18, 16, or 14 gauge) commensurate with the size of the animal. Venous catheter hubs will accept an ET tube connector with a 3.5-mm internal diameter, which can thereby be connected to a resuscitator bag. A guidewire with a straight, blunt (atraumatic) end can be used to avoid exposure of delicate laryngeal tissue to the sharp end of the intravenous catheter. An otoscope speculum modified to form an open, illuminated track can assist ET intubation of very small newborns, while a human preterm laryngoscope blade (i.e., size-0 Miller laryngoscope blade) suffices for larger newborns. To avoid bronchial insertion of the ET tube, its tip should reach no further than 1–2 mm beyond the thoracic inlet. Once in place, the ET tube is secured, and PPV is initiated targeting the same ventilation parameters as for bag–mask ventilation (i.e., inspiratory time, 1 s; PIP, 20–25 cm H_2O; RR, 20–30/min). If available, a pressure safety ("pop-off") valve built into the manual resuscitator bag and limited to 25 cm H_2O will alleviate the risk for excessive PIPs. As long as the newborn is correctly intubated, gastric insufflation should not occur. Indicators of effective ventilation/lung aeration include the presence of chest movements after each breath, breath sounds on auscultation, and signs of improvement in hypoxemia (e.g., increase in HR, resolution of cyanosis, increase in SpO_2). Lack of chest movement and failure of the HR to increase warrant confirmation of correct intubation.

If the newborn puppy's or kitten's HR fails to increase to >120/min despite 1–2 min of PPV, we suggest switching the inspired gas from room air to 100% oxygen (NB-03). This might or might not precede the decision for ET intubation. The desirable and undesirable effects of supplemental oxygen (i.e., 100% oxygen) compared to the use of room air during PPV have been extensively studied in newborn infants and in experimental studies in piglets and lambs, but not in newborn puppies and kittens. The combined evidence shows that PPV with room air is as effective as with 100% oxygen and that high inspiratory oxygen concentration has several undesirable effects, including increased mortality in newborn infants and oxidative injury across several organ systems documented in multiple species [66–69, 89–92]. It is possible that a more tailored increase in inspiratory oxygen concentration (e.g., 40% oxygen) would improve hypoxemia while avoiding the risks of pure oxygen, but this has not been well studied and is clinically difficult to implement. Thus, we recommend initiating PPV with room air but suggest the use of 100% oxygen if the HR fails to increase after 1–2 min of PPV (NB-03). At this stage, especially if the HR continues to decrease, it is also reasonable to initiate monitoring of the HR several times a minute, such as by continuous ECG monitoring, to guide decision-making as the resuscitation effort evolves.

An additional measure we suggest undertaking if the newborn puppy's or kitten's HR fails to increase to >120/min despite 1–2 min of PPV is to administer a single SI (i.e., 30-s duration, 30–35 cm PIP) that is then followed by standard PPV (NB-06). While there are no clinical or experimental studies documenting the benefit or harm of this technique for the most critical outcomes of favorable neurologic outcome and survival to discharge, data from one experimental study in transitional, asphyxiated newborn lambs showed an improvement in oxygenation and a marked reduction in the time to achieve HR >120/min with a single SI (median 8 s, IQR 6), compared to standard PPV (median 64 s, IQR 75). We believe this to be a feasible intervention if the animal is intubated with a cuffed ET tube or is ventilated with a tight-fitting face mask. In the latter case, gentle digital pressure could be applied to the left side of the caudal third of the ventrolateral neck to occlude the esophagus and mitigate gastric insufflation during the maneuver.

7 | Cardiopulmonary Resuscitation

Eighty-five percent of term newborn infants start breathing within moments of birth, 10% will do so after drying and tactile stimulation, 5% will receive PPV, and only a small percentage (i.e., 0.1%–0.3%) undergo chest compressions, with even fewer receiving epinephrine [4, 93–95]. For newborn puppies and kittens, data on the prevalence of initial resuscitation measures are lacking, but we expect that, similar to people, CPR—the combined administration of chest compressions and PPV—will be required in a small subset of them.

7.1 | When to Start Chest Compressions

Like in adult dogs and cats, we recommend initiation of CPR immediately once the rescuer recognizes its indication [6].

7.1.1 | No Detectable Heartbeat

We suggest starting CPR (i.e., chest compressions in addition to PPV) in newborn puppies and kittens immediately if there is no heartbeat identified. As noted above, and in contrast to the recommendations for adult dogs and cats, the initial 30–60 s of nonresponsiveness and apnea in newborns should be treated with respiratory support maneuvers as long as the animal has a detectable heartbeat.

7.1.2 | Persistent, Severe Bradycardia

In contrast to the recommendations for adult dogs and cats, we also suggest starting CPR in newborn puppies and kittens in which a heartbeat can be identified but that are found to be very severely bradycardic (i.e., HR < 50/min) for longer than 30 s despite PPV with oxygen supplementation (NB-02). The rationale behind this recommendation is that the very poor cardiac output with extremely low HR can be augmented by external chest compressions. This specific HR cutoff, as well as the time interval of 30 s, has not been directly tested and is based on expert opinion, although findings in newborn lambs suggest that chest compressions in newborns with an HR <50/min improve blood flow [96, 97]. Due to the central importance of prioritizing lung aeration during newborn resuscitation and the fact that chest compressions may interfere with lung expansion, we suggest

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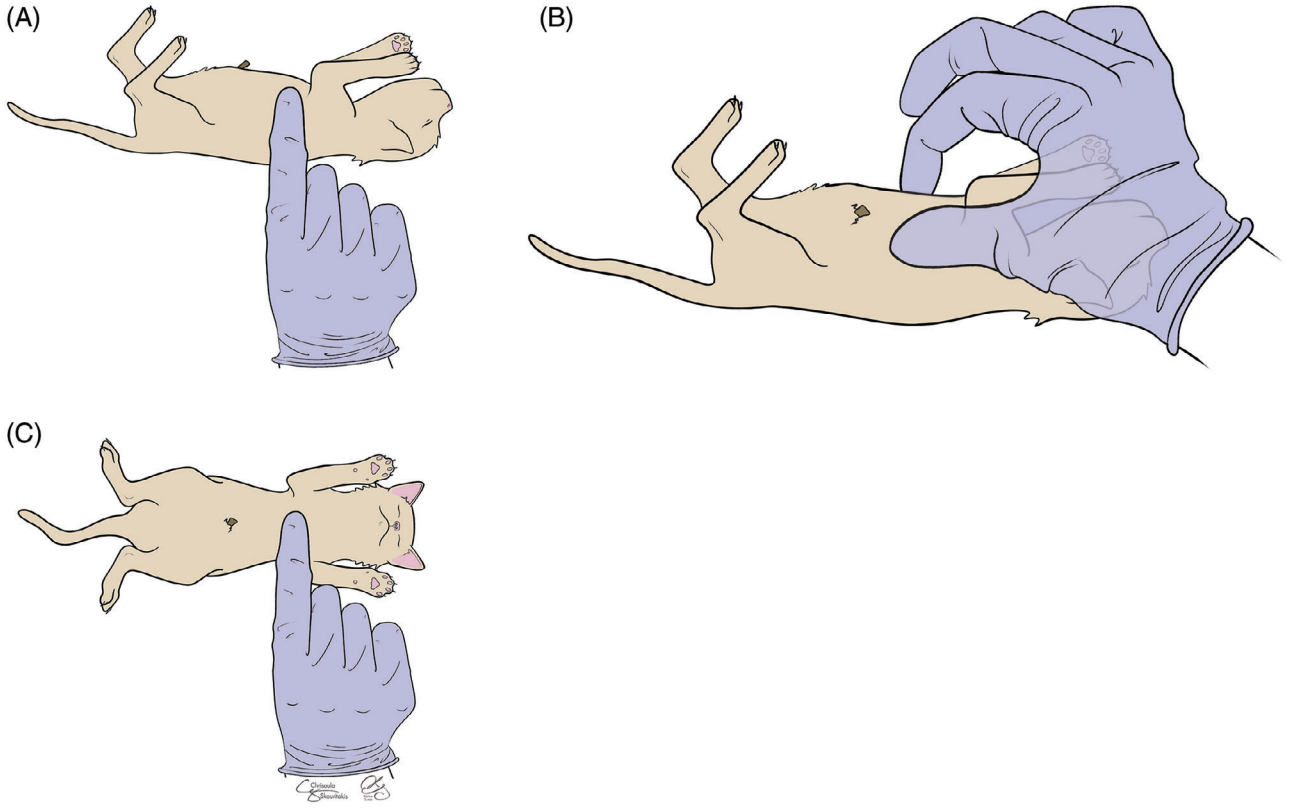


FIGURE 5 | Chest compression techniques for newborn puppies and kittens. Compressions should be applied directly over the ventricles regardless of technique and animal position. The preferred animal position is lateral recumbency, but sternal compressions might be preferable in some instances (see text). (A) Compress the chest over the ventricles with one or two fingers toward the table surface (rate, 120–150/min; depth, 1/3–1/2 of chest width). (B) Compress the chest wall over the ventricles between one or two fingers and the opposing thumb (rate, 120–150/min; depth, 1/3–1/2 of chest width). (C) Compress the sternum with the newborn in dorsal recumbency (rate, 120–150/min; depth, 1/3 anterior–posterior chest diameter). Artwork by Chrisoula Toupadakis Skouritakis, Ph.D., MediaLab Services Director, and Kailee Suess, Department of Surgical and Radiological Sciences, School of Veterinary Medicine, University of California, Davis. Copyright: The RECOVER Initiative 2025. All rights reserved.

providing PPV first in newborns with very severe bradycardia (i.e., HR <50/min), and only starting CPR if the HR fails to increase. Experimental evidence in a newborn piglet asphyxiation model suggests that an HR increase with PPV alone can be expected after 15–30 s in animals with the capacity to respond [87]. In addition, one study showed that very severe bradycardia at birth quickly resolved in the majority of newborn infants with PPV alone; in 78% and 90% of the infants with an initial HR <60/min at birth, the HR increased to >60/min after 30 and 60 s, respectively [98].

7.2 | Chest Compression Technique

While different chest compression techniques have not been studied in newborn puppies and kittens, the soft, malleable chest walls of newborns optimize the application of the cardiac pump mechanism for blood flow generation, where blood is expelled from the heart with pressure applied preferentially to the ventricles. We therefore suggest compressing the newborn chest in a laterolateral direction with the compression point located directly over the ventricles (NB-16). With the newborn puppy or kitten positioned in lateral recumbency, chest compressions can be applied by placing one or two fingers (index and middle finger) over the ventricles and compressing toward the table surface (Figure 5A). Alternatively, rescuers can oppose one or two fingers (index and middle finger) and thumb on the chest over the ventricles and compress the chest to the targeted compression depth (Figure 5B). During laterolateral compressions, we suggest a compression depth of one-third to one-half of the chest width (NB-17). Due to the very compliant chests, overcompression is easily possible in the newborn and must be avoided to prevent injury. Under specific circumstances (e.g., umbilical vein cannulation, pronounced wide-chested thoracic conformation), we suggest sternal compression and recommend doing so by compressing the sternum with one or two fingers (index and middle finger) toward the table surface to reach the target depth (NB-16) (Figure 4C). With sternal compression, a proportion of the external anterior–posterior chest diameter is internally occupied by the vertebral column, reducing the compressible portion of the chest cavity. We therefore suggest a compression depth of only one-third the anterior–posterior chest diameter during sternal compressions in newborns (NB-17). Considering the large fleshy tongues of newborn puppies and kittens, dorsal positioning carries the risk of significantly increasing upper airway resistance and thus may compromise PPV in nonintubated animals [99]. We therefore think it is reasonable to avoid routine dorsal positioning during newborn CPR in puppies and kittens.

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We suggest administering chest compressions in newborn puppies and kittens at a rate of 120–150/min, which is faster than what is recommended in adult dogs and cats (100–120/min) (NB-12) [6]. We did not identify any experimental or clinical studies that delineate the optimal compression rate in small mammals with a comparable size to newborn puppies or kittens (i.e., 100–800 g body weight), nor any studies in transitional newborns. However, indirect evidence suggests a compression rate of at least 120/min should be targeted. In post-transitional piglets (2 kg), compression rates of 150–180/min were associated with hemodynamic benefit over slower compression rates (i.e., 60/min to 120/min), with a compression rate of at least 120/min supported by other neonatal piglet studies [100–102]. Mathematical modeling furthermore suggests an optimal chest compression rate in animals <1 kg to be 150/min or more [103]. With very short compression distances of only 5–15 mm and the diminutive compression force required to achieve these distances, we consider a compression rate of 150/min feasible and of low probability to cause rescuer fatigue, unlike chest compressions in adult animals at higher rates [104].

7.3 | Compressions and Ventilation Are Coordinated in Newborn CPR

Given the critical importance of effective ventilation in newborn puppies and kittens requiring resuscitation, administering chest compressions and positive pressure breaths as recommended in adult dogs and cats could impair lung aeration.

In newborn puppies and kittens *without* a cuffed ET tube in place, we recommended pausing chest compressions for the delivery of a breath (NB-14). This applies to any newborns undergoing bag–mask ventilation. Chest compressions and ventilation are delivered in a coordinated or synchronized way where compressions alternate with ventilations at a predefined ratio (i.e., compression to ventilation ratio, or C:V ratio) of four chest compressions to one positive pressure breath (4:1) (NB-13). This approach prioritizes ventilation compared to CPR in nonintubated adult dogs and cats in which a C:V ratio of 30 compressions to two positive pressure breaths is recommended [6]. The recommended C:V of 4:1 also recognizes the higher chest compression rate target in newborn puppies and kittens compared to newborn infants, in whom a C:V ratio of 3:1 is recommended [105]. In practice, around 15 rounds of four compressions to one ventilation are delivered every 30 s, with one 4:1 round administered every 2 s. This will amount to 120 compressions and 30 breaths per minute. We suggest delivering breaths with 100% oxygen during CPR (NB-18). Patient response should be assessed every 30 s, and if the HR exceeds 50/min, chest compressions can be discontinued while continuing PPV and frequent/continuous HR monitoring.

In newborn puppies and kittens *with* a cuffed ET tube in place, we suggest delivering breaths concurrently to chest compressions (NB-14). Breaths do not need to be coordinated or synchronized with compressions. This is the equivalent approach to adult dogs and cats when intubated, except for higher compression (i.e., 120–150/min) and ventilation rates (i.e., 20–30/min) in newborns. As for nonintubated animals, we suggest the use of 100% oxygen during CPR in intubated newborns.

7.4 | Epinephrine and Vascular Access

If CPR lasting at least 1 min fails to lead to an increase in HR >50/min, we recommend parenteral administration of epinephrine (0.01–0.03 mg/kg) (NB-21; NB-22) (Figure 3). Multiple publications support the preferential use of IV or intraosseous (IO) routes over ET or intranasal (IN) routes [106–114]. Topical sublingual administration of epinephrine has not been tested, and it is plausible that it is not effective. If IV or IO access cannot be achieved in a timely manner, a single epinephrine dose by the ET route at a higher dose (0.05–0.1 mg/kg) was shown to have some effect, although with a delay [106]. However, ET administration also carries the same risk as for ET intubation, including prolonged interruption of PPV. ET drug administration, therefore, is most appropriate in newborns that are already intubated. As for the ET route, IN epinephrine at a higher dose showed lower plasma concentration and delayed but some effect when compared to IV administration [107, 115]. We suggest against the use of IM epinephrine, as data available from one small study did not identify an increase in epinephrine plasma concentrations until after return of spontaneous circulation (ROSC) [116]. We also advise against the practice of intralingual (IM) administration due to anecdotal reports of harm (i.e., tissue necrosis) associated with this practice. Although the effect of repeated administration of epinephrine has not been studied in newborn animals, we suggest administering IV/IO doses of epinephrine (0.01–0.03 mg/kg) every 3–5 min during ongoing CPR as recommended for adult dogs and cats [6].

In newborn puppies and kittens that require chest compressions, we suggest against the routine administration of atropine during CPR (NB-24), which is the same recommendation as for newborns with bradycardia (NB-23). We did not identify any evidence in newborn infants or experimental studies in newborn animals to support the use of atropine during CPR; instead, the primary goal of CPR is to reverse myocardial hypoxia by supporting lung aeration through PPV and coronary blood flow through high-quality chest compressions and epinephrine administration. This recommendation, however, should not preclude the use of atropine in specific situations in post-transitional neonatal puppies and kittens, such as severe bradycardia or CPA associated with ET intubation, gastrointestinal surgery, and other scenarios leading to vagal stimulation.

Vascular access (e.g., umbilical vein, jugular vein, IO cannula) should also be established to permit effective parenteral administration of other medications and IV fluids where the newborn is not responsive to prolonged resuscitation (see *adjunct interventions*). Which vascular access route to choose is contextually dependent on the size of the animal and the experience and preference of resuscitation team members [8].

7.5 | Discontinuation of Resuscitation

At present, there are no clinical studies reporting survival rates of newborn puppies and kittens undergoing CPR, let alone how these survival rates are impacted by the duration of CPR. Nevertheless, durations of 15–30 min were proposed in the veterinary literature based on expert opinion [8, 11]. The most direct evidence is therefore drawn from research in newborn

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infants. In full-term infants receiving CPR for a median duration of 6 min (IQR 13) in the delivery room ($n = 439$), 91% achieved ROSC and 83% survived to hospital discharge [117]. However, survival in newborn infants with a persistent Apgar score of 0 (i.e., absence of breathing, muscle tone, and consciousness), combined with an undetectable HR (indicating no detectable signs of life) despite 10 min of intensive resuscitation, is poor [118, 119]. On the other hand, multiple case series revealed that survival with a favorable neurologic outcome can occur even in infants with no signs of life after 10 min of CPR, that duration of CPR is only weakly associated with survival when adjusted for other risk factors, and that a definitive time point after which further resuscitation is considered futile has not been established [4, 117, 120–123]. For newborn puppies and kittens undergoing CPR, we suggest continuing resuscitation efforts for at least 15 min before considering discontinuation (NB-25). If there is no heartbeat identified after that duration of high-quality CPR, having exhausted all recommended measures including epinephrine, chances for a favorable outcome are likely very low. Beyond the individual animal, rescuers should ensure that prolonged resource allocation to one animal does not critically compromise the care of littermates needing resuscitation but having a more favorable prognosis. Next to the duration of CPR, pet owner goals, the presence of significant congenital malformations (e.g., anasarca, gastroschisis, anencephaly, atresia ani), clear signs of death, and the ability to provide post-cardiac arrest care will impact the decision whether to continue resuscitative efforts [29, 30].

8 | Adjunct Interventions

Several interventions can be considered in addition to the primary resuscitative measures. These are treatments that might be used during prolonged resuscitation but that we have assessed as noncritical, and therefore, we did not systematically review the evidence pertaining to them (e.g., bicarbonate, fluid administration). Adjunct interventions are also those that can be considered in nonvigorous newborn puppies and kittens that fail to adequately respond to prolonged resuscitation efforts (e.g., dextrose during resuscitation; doxapram) or need additional support in the post-resuscitative period (e.g., dextrose after resuscitation, temperature management). Finally, we also categorized GV 26 acupoint stimulation—an intervention that we did not reach consensus for or against its use—as an adjunctive measure until more evidence becomes available.

8.1 | Blood Glucose (BG) Management

Hepatic glycogen stores are low and rapidly depleted, and the capacity for gluconeogenesis is limited in newborn puppies and kittens, such that they depend on oral intake of energy-rich nutrients to maintain euglycemia after birth [124]. Nevertheless, hypoglycemia during the first few hours after birth, including during the initial resuscitation, is uncommon, and in newborn puppies, BG concentrations were similar if born by C-section (4.9 ± 0.2 mmol/L) or by vaginal eutocia (4.5 ± 0.2 mmol/L, $p = 0.31$) [32]. If newborns fail to nurse, hypoglycemia can occur and has been associated with death in puppies and in neonates of other species [125–128]. Indiscriminate glucose administration can be harmful, as not only hypoglycemia but also hyperglycemia has been shown to worsen neurologic outcome in newborns with hypoxic–ischemic brain injury [129–133]. We therefore suggest measuring BG concentration in newborn puppies and kittens that remain nonvigorous despite prolonged (i.e., >10 min) resuscitation (NB-19). A drop of blood sufficient for a glucometer can be obtained by puncture of a paw pad [124]. If hypoglycemia (i.e., BG < 3 mmol/L [BG < 54 mg/dL]) is present during prolonged resuscitation, we recommend dextrose supplementation with a slow bolus of 0.25 g/kg dextrose (e.g., 0.5 mL/100 g of 5% dextrose solution over 5 min), administered IV, IO, or, less preferably, by intraperitoneal (IP) injection (NB-19) (Figure 3). The intraperitoneal route is considered practical, effective, and safe if executed correctly, including maintenance of strict asepsis. Where parenteral dextrose administration cannot be accomplished, we suggest topical sublingual mucosal administration of dextrose (0.5 g/kg; 0.1 mL/100 of 50% dextrose solution) (NB-19). Should it be impractical to determine the BG concentration in a newborn puppy or kitten that fails to respond to prolonged (i.e., >10 min) standard resuscitation measures (e.g., rewarming, stimulation, PPV), we suggest empirical administration of dextrose by one of the above-cited routes (NB-19).

In newborn puppies and kittens *after* resuscitation (i.e., after CPR and ROSC) that are nonvigorous and not nursing, we recommend confirming hypoglycemia before supplementing, if possible. If an IV or IO catheter is present, we suggest administering dextrose by CRI (e.g., 2.5% dextrose in isotonic crystalloid fluids given at a physiologic rate IV or IO) rather than bolus injection to avoid large fluctuations in BG concentration that can be harmful (NB-26). After resuscitation, it may be more practical to establish IV or IO access and to initiate an infusion. A reasonable physiologic fluid rate is 80–120 mL/kg/day in neonatal puppies and 60–80 mL/kg/day in neonatal kittens. If an infusion is not feasible, we suggest proceeding as described above for dextrose supplementation in hypoglycemia during resuscitation (NB-26). In addition, dextrose administration by orogastric tube is another possibility after ROSC as long as it is performed by experienced staff to avoid injury to the newborn [124]. Oral administration of dextrose by syringe can be considered in alert newborns.

8.2 | Temperature Management

Targeted temperature management, a deliberate induction or maintenance of lower-than-normal body temperature within a certain range, is suggested in adult people, dogs, and cats that remain comatose after resuscitation from CPA, owing its benefits to multiple neuroprotective effects [7, 134, 135]. In term newborn infants with moderate to severe hypoxic–ischemic encephalopathy (HIE), therapeutic hypothermia (TH) (33°C–34°C for 72 h, started within 6 h of birth) has been recommended for over a decade [136]. However, TH or any temperature management has not previously been suggested in newborn puppies and kittens exposed to anoxic brain injury during birth. In fact, the clinical symptoms of HIE are not well delineated in this population, though they are well described in infants and foals [137, 138]. Clinical signs of HIE in these species include lethargy to stupor/coma, decreased to no activity, extensor rigidity to decerebrate posture, hypotonia to flaccidity, weak or absent sucking reflex, constricted or dilated pupils with absent pupillary light reflex, low HR, and intermittent breathing or apnea, depending on severity. Evidence

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suggests that the positive impacts of cooling on HIE outcomes in newborn animals depend on the severity of HIE, the time interval from injury to cooling, the degree of hypothermia, and the duration of TH [139]. Generally, a longer duration of TH is required for more severe injury [140, 141]; however, evidence from experimental animal studies suggests a neuroprotective effect can occur after cooling periods of only 24 h or less [142–144]. Given the restricted resources available in veterinary medicine, care of newborn puppies and kittens with moderate to severe HIE is generally out of reach. As only those newborns with milder signs of HIE have potential as viable animals, we considered a 24-h duration of permissive hypothermia to be a pragmatic approach to balance risk, benefit, and feasibility of TH until more clinical veterinary data are available. Specifically, we suggest permitting newborn puppies and kittens with signs of acute HIE to remain at a low normal temperature for newborn puppies and kittens (i.e., 35°C [95°F]) for 24 h after birth (NB-27). Since newborn puppies and kittens are relatively hypothermic at birth with rectal temperatures of 33.7 ± 1.4°C after C-section and 33.1 ± 3.1°C after eutocia, which then increase to 35.1 ± 1.8°C and 33.2 ± 4.7°C after 1 h, respectively, active cooling is probably not required, and avoidance of active rewarming should suffice.

The speed of rewarming is another topic of concern in animals with HIE. A number of experimental animal studies of HIE in populations other than newborns demonstrated harm with fast (i.e., >1°C/h) rewarming rates [145–150], and the RECOVER initiative therefore suggests to aim for slow rewarming (i.e., 0.25°C/h to 0.5°C/h) and recommends against rewarming rates that surpass 1°C/h in adult dogs and cats after ROSC [7, 151]. No clinical studies in newborn infants have been conducted, and in experimental animal studies including newborn transitional lambs and post-transitional piglet models, no benefit of slow versus fast rewarming was found despite a 10- to 20-fold difference in rewarming rates [152–156]. However, out of concern for rebound seizures, hypotension, and temperature overshoot (i.e., hyperthermia) with fast rewarming rates [157, 158], we suggest in newborns with clinical signs of HIE to rewarm at rates below 1°C/h to achieve normothermia (35.0°C–37.2°C [95°F–99°F]) while avoiding accidental hyperthermia (NB-28). The rewarming rate is less of a concern in animals that are hypothermic at birth, as most newborn puppies and kittens are, as long as they have no clinical signs of HIE and did not undergo CPR.

8.3 | Doxapram

The analeptic drug doxapram increases respiratory drive through effects on peripheral (i.e., carotid and aortic chemoreceptors) and central (i.e., brainstem respiratory control center) sites [159]. While doxapram was used for respiratory stimulation of newborn puppies and kittens with inadequate ventilatory function for more than 50 years, its routine use has been questioned more recently due to concerns about the drug's efficacy in severely hypoxic animals and the availability of other measures to support ventilation [9, 11, 160, 161]. In small animal medicine, it is effectively used as a respiratory stimulant to aid in the assessment of laryngeal dysfunction in dogs [162, 163]. There are currently no studies that support its use in newborn puppies and kittens with apnea/gasping or bradypnea. A recent randomized controlled trial studied the effect of intralingual injection of doxapram (approximately 10 mg/kg) versus saline injected within the first minute of birth in 171 puppies born by elective C-section, regardless of the presence of respiratory compromise [164]. The study did not identify an effect on the primary outcome of 7-day survival (92% with doxapram, 94% with saline, $P = 0.63$) or on Apgar scores over the first 20 min after birth. We therefore recommend against the routine administration of doxapram in newborn puppies and kittens undergoing resuscitation, such as after C-section (NB-07). Importantly, this study did not specifically evaluate the effect of doxapram in apneic/gasping newborns. Multiple clinical and experimental studies involving infants, calves, foals, and rats revealed a beneficial effect of doxapram on outcomes such as survival, oxygenation, and ventilation in neonates and newborns without apparent harm [165–170]. However, due to very serious indirectness (e.g., species, life stage, and/or condition treated) and methodological shortcomings, significant uncertainty regarding the benefit of doxapram in newborn puppies and kittens remains. Importantly, a focus on doxapram administration and its expected response carries the risk of distraction from other more effective interventions in apneic/gasping newborns, foremost PPV. Thus, we suggest the use of doxapram in transitional puppies and kittens with respiratory compromise (i.e., apnea/gasping or bradypnea) only if they fail to respond after a period of time (e.g., ≥10 min) to other appropriate measures of support (e.g., PPV) (NB-07). Doxapram is preferentially administered IV/IO, if this does not compromise other supportive measures, but intralingual IM, IN, or topical sublingual administration is also an acceptable route (Figure 3).

8.4 | GV 26 Acupoint Stimulation

Stimulation of the GV 26 (Jen Chung; Rhenzong) acupoint has been recommended in newborn puppies and kittens with low RR or apnea that have a heartbeat [8, 11, 161, 171]. The acupoint is located where the philtrum joins the lower edge of the nostril and is stimulated by the insertion and twisting of a 25-gauge needle at that point [172]. However, no controlled studies were conducted, and clinical reports are limited to case series, such that no conclusion regarding efficacy can be drawn [173, 174]. While these publications do not report overt harm due to GV 26 stimulation, the procedure may distract resuscitation team members from timely administration of interventions known to be effective, foremost PPV, particularly if the needle is applied for more than a few seconds. For these reasons, we initially formulated a recommendation against the use of GV 26, while a subset of subject matter experts strongly advocated for the use of GV 26 stimulation in nonvigorous, apneic newborn puppies and kittens. As no consensus could be achieved, we agreed to provide no recommendation for or against the use of GV 26 stimulation. We, however, also agreed that if resuscitation teams choose to use this technique in the absence of clear guidance, it should be brief (e.g., <2–3 seconds) and not interfere with initiation or quality of PPV.

8.5 | Fluid Administration and Bicarbonate

The RECOVER Initiative did not systematically review the literature regarding fluid therapy and the administration of parenteral sodium bicarbonate during the resuscitation, including CPR, of newborn puppies and kittens. On a cursory review of the litera-

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ture, we identified two experimental studies in post-transitional piglets that received volume infusion during resuscitation from asphyxial CPA [175, 176]. In one study, normovolemic piglets (age 8 ± 4 days) were asphyxiated to an MAP of <20 mm Hg and then resuscitated according to the newborn algorithm (i.e., PPV ± CPR ± epinephrine); two sequential boluses of either 0.9% NaCl (10 mL/kg IV), 5% albumin (10 mL/kg IV), or sham (no fluid administration) were given over 5 min. Fluid administration led to no hemodynamic benefit but resulted in worse pulmonary edema and lung compliance 2 h after resuscitation. These results suggest against volume administration in euvolemic newborns undergoing resuscitation at birth [175]. Notably, this harmful effect might be further accentuated in transitional newborns with increased lung water and hypoxia-related myocardial dysfunction [177]. A second study in neonatal piglets (age, 12–44 h), which combined asphyxiation with concurrent hemorrhagic arrest (blood loss, 30–34 mL/kg), tested the effect of standard resuscitation measures (i.e., PPV, chest compressions, and epinephrine) in combination with bolus administration of 0.9% saline or autologous whole blood on time to ROSC [176]. Volume expansion consisted of boluses of 10 mL/kg every 2 min until ROSC occurred. Time to ROSC was not different between animals receiving saline versus blood, although only a small volume of 3–4 mL/kg of either fluid needed to be administered until animals achieved ROSC. Based on the scarce evidence available, it is reasonable—just as during CPR in adult dogs and cats [6]—to reserve volume therapy for newborns with strong evidence of hypovolemia, such as overt blood loss (e.g., from umbilical cord hemorrhage, placental laceration), but to advise against its use in normovolemic newborns. Bolus administration of a balanced isotonic crystalloid at 1 mL/100 g over 5 min IV/IO is a reasonable starting point in newborn puppies and kittens with hypovolemia. It is often difficult to determine the volume status of newborn puppies and kittens and thus to ascertain ahead of time which animal will benefit from or be harmed by intravenous volume resuscitation. We therefore suggest a trial bolus of a balanced isotonic crystalloid (e.g., 1 mL/100 g IV or IO) if there is a suspicion of hypovolemia and the newborn has failed to respond to standard resuscitative measures.

Some degree of acidemia is always present at birth in both newborn puppies, kittens, and infants, and its severity has been associated with unfavorable outcomes, such as HIE, and might be of prognostic value [24, 32, 178–180]. However, the benefit of remediation of severe acidemia with buffer therapy, specifically the benefit of sodium bicarbonate administration, is uncertain. A single small randomized, controlled clinical trial, in which newborn infants requiring PPV for at least 5 min at birth received either sodium bicarbonate (1.8 mEq/kg IV) or an equivalent volume of 5% dextrose (4 mL/kg IV), showed no effect on the composite outcome of death or survival with abnormal neurological function at discharge ($p = 0.88$) [181]. We therefore consider it reasonable to follow the current recommendation for newborn infants when treating newborn puppies and kittens. We suggest against the administration of sodium bicarbonate to newborn puppies and kittens undergoing CPR unless all four of the following are true: resuscitation is prolonged (≥10 min), the animal fails to respond to standard measures (i.e., PPV, chest compressions, and epinephrine), effective ventilation is in place to avoid worsening of respiratory acidosis, and IV access is present [4].

9 | Discussion

The 59 treatment recommendations (Table 1), prose explanations, dosage chart, images, and algorithm contained in this paper constitute the RECOVER Newborn Resuscitation Guidelines, a consensus guidelines paper synthesized from exhaustive evaluation and analysis of evidence relating to resuscitation of newborns across many species and honed through an iterative modified Delphi process considering input from subject matter experts and the international veterinary community. An international group of veterinary experts in small animal theriogenology and small animal emergency and critical care collaborated to tailor these recommendations to puppies and kittens based on a combination of this evidence evaluation and analysis, and expert opinion where inadequate evidence was available.

The primary goal of the RECOVER Newborn Resuscitation Guidelines is that they serve as foundational step-by-step instructions for the support ("resuscitation") of puppies and kittens in the first minutes following birth in the clinical setting. All puppies and kittens delivered by C-section, and many following medical dystocia, will require newborn resuscitation as presented here. Most will be delivered alive but in need of support, while some may be markedly distressed, and others may be "stillborn". These guidelines contain treatment recommendations and an algorithm for prebriefing and use as a cognitive aid to optimize patient assessment and resultant treatments for these litters.

There are many differences between these Newborn Resuscitation Guidelines and the RECOVER CPR Guidelines for Dogs and Cats. The two main differences are the life stage addressed (newborn vs adult) and, notably, the fact that newborn resuscitation includes vital, life-preserving treatments of animals that have not experienced CPA. The RECOVER CPR Guidelines focus almost entirely on dogs and cats that require CPR, whereas only a fraction of puppies and kittens for which these Newborn Resuscitation Guidelines are relevant will require CPR; in fact, while the majority will not require CPR, every puppy and kitten delivered by C-section requires some resuscitative measures addressed in these guidelines to optimize their outcome. Additionally, while the focus of resuscitation in adult dogs and cats currently lies in delivering high-quality chest compressions along with PPV, support of the newborn in transition focuses almost entirely on respiratory support in an effort to aerate the newborn lung. In addition to PPV, chest compressions are performed in newborns that have very severe bradycardia (i.e., HR < 50/min), and atropine is not recommended for such cases. These differences in treatment recommendations underscore the dissimilarity between newborn and adult physiology and, thus, the cause of instability: hypoxemia is nearly always the culprit in newborn distress, and thus, respiratory support is nearly always the answer.

Scarce evidence was available in newborn puppies and none in newborn kittens, and therefore, most of the evidence we used to develop these guidelines was highly indirect in species and setting. Much information was gleaned from studies out of human delivery rooms and from experimental studies in near-term fetal lambs and other species. While modern veterinary medicine provides many advantages for animal health, our

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hospitals generally lack the material and personnel resources of human delivery rooms and bear little resemblance to the tightly controlled laboratory environments in which near-term lamb fetuses are studied. Therefore, the recommendations contained herein are the best we could develop with the evidence available in combination with the expert opinions of a group of small animal theriogenologists, a group of small animal emergency and critical care specialists, and the international veterinary community. There are many knowledge gaps. We have outlined many of these knowledge gaps in the accompanying paper [19] and hope research will address these knowledge gaps so that future iterations of these guidelines will be built on species- and setting-specific evidence.

While these RECOVER Newborn Resuscitation Guidelines are a first attempt at consensus guidelines for resuscitation of newborn puppies and kittens, we anticipate that the recommendations and algorithm contained here will enable practitioners to address C-section and dystocia deliveries in a systematic way to enhance patient outcomes. We urge practitioners to prebrief the algorithm and dosage chart prior to deliveries and then to follow the recommendations. The RECOVER Initiative welcomes input regarding outcomes and future directions of inquiry, and we encourage clinical researchers in the small animal theriogenology and emergency spaces to perform clinical studies to address critical knowledge gaps regarding newborn resuscitation.

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Conflicts of Interest

Dr. Burkitt-Creedon is the Editor of the Journal but only participated in the peer review process as an author. The authors declare no other conflicts of interest.

Endnotes

[a] Boller, Manuel; Burkitt-Creedon, Jamie M; and Fletcher, Daniel J. 2025. "RECOVER Newborn Guidelines 2025." OSF. June 14. https://osf.io/wxzqa/ [accessed on June 14, 2025].

[b] Covidence, Melbourne, VIC, Australia.

[c] NowComment, www.nowcomment.com (accessed on June 8, 2025).

References

1. A. Katheria and N. N. Finer, "Newborn Resuscitation," in *Avery's Diseases of the Newborn*, 10th ed., ed. C. A. Gleason and S. E. Juul (Elsevier, 2018), 273–288.

2. S. B. Hooper, M. J. Kitchen, G. R. Polglase, et al., "The Physiology of Neonatal Resuscitation," *Current Opinion in Pediatrics* 30, no. 2 (2018): 187–191.

3. A. Finnemore and A. Groves, "Physiology of the Fetal and Transitional Circulation," *Seminars in Fetal & Neonatal Medicine* 20, no. 4 (2015): 210–216.

4. M. H. Wyckoff, J. Wyllie, K. Aziz, et al., "Neonatal Life Support: 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations," *Circulation* 142, no. 16_suppl_1 (2020): S185–S221.

5. N. K. Yamada, E. Szyld, M. L. Strand, et al., "2023 American Heart Association and American Academy of Pediatrics Focused Update on Neonatal Resuscitation: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care," *Circulation* 149, no. 1 (2024): e157–e166.

6. J. M. Burkitt-Creedon, M. Boller, D. J. Fletcher, et al., "2024 RECOVER Guidelines: Updated Treatment Recommendations for CPR in Dogs and Cats," *Journal of Veterinary Emergency and Critical Care* 34, no. Suppl 1 (2024): 104–123.

7. D. J. Fletcher, M. Boller, B. M. Brainard, et al., "RECOVER Evidence and Knowledge Gap Analysis on Veterinary CPR. Part 7: Clinical Guidelines," *Journal of Veterinary Emergency and Critical Care* 22, no. Suppl 1 (2012): S102–S131.

8. A. M. Traas, "Resuscitation of Canine and Feline Neonates," *Theriogenology* 70, no. 3 (2008): 343–348.

9. P. F. Moon, B. J. Massat, and P. J. Pascoe, "Neonatal Critical Care," *Veterinary Clinics of North America: Small Animal Practice* 31, no. 2 (2001): 343–367.

10. A. A. Cavanagh, "Neonatal Resuscitation," *Veterinary Team Brief* 5, no. 5 (2017): 27–28.

11. A. P. Davidson, "Neonatal Resuscitation: Improving the Outcome," *Veterinary Clinics of North America: Small Animal Practice* 44, no. 2 (2014): 191–204.

12. M. Bruckner and G. M. Schmölzer, "Physiologic Changes During Neonatal Transition and the Influence of Respiratory Support," *Clinics in Perinatology* 48, no. 4 (2021): 697–709.

13. S. B. Hooper, A. B. te Pas, J. Lang, et al., "Cardiovascular Transition at Birth: A Physiological Sequence," *Pediatric Research* 77, no. 5 (2015): 608–614.

14. P. M. Barker and R. E. Olver, "Invited Review: Clearance of Lung Liquid During the Perinatal Period," *Journal of Applied Physiology* 93, no. 4 (2002): 1542–1548.

15. S. B. Hooper, M. J. Kitchen, M. J. Wallace, et al., "Imaging Lung Aeration and Lung Liquid Clearance at Birth," *The FASEB Journal* 21, no. 12 (2007): 3329–3337.

16. A. B. te Pas, P. G. Davis, S. B. Hooper, and C. J. Morley, "From Liquid to Air: Breathing After Birth," *Journal of Pediatrics* 152, no. 5 (2008): 607–611.

17. D. J. Fletcher, M. Boller, J. M. Burkitt-Creedon, et al., "2024 RECOVER Guidelines: Methods, Evidence Identification, Evaluation, and Consensus Process for Development of Treatment Recommendations," *Journal of Veterinary Emergency and Critical Care* 34, no. S1 (2024): 3–15.

18. G. H. Guyatt, A. D. Oxman, R. Kunz, et al., "GRADE: Going From Evidence to Recommendations," *BMJ* 336, no. 7652 (2008): 1049–1051.

19. M. B. J. Boller, "RECOVER Newborn Resuscitation Treatment Recommendations: Place Holder," *Journal of Veterinary Emergency and Critical Care* (2025).

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70013, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

20. R. Boulkedid, H. Abdoul, M. Loustau, et al., "Using and Reporting the Delphi Method for Selecting Healthcare Quality Indicators: A Systematic Review," *PLoS ONE* 6, no. 6 (2011): e20476.

21. P. R. Greig, D. Zolger, D. N. Onwochei, et al., "Cognitive Aids in the Management of Clinical Emergencies: A Systematic Review," *Anaesthesia* 78, no. 3 (2023): 343–355.

22. M. C. Veronesi, "Assessment of Canine Neonatal Viability—The Apgar Score," *Reproduction in Domestic Animals = Zuchthygiene* 51 (2016): 46–50.

23. N. R. Santos, A. Beck, and A. Fontbonne, "A Review of Maternal Behaviour in Dogs and Potential Areas for Further Research," *Journal of Small Animal Practice* 61, no. 2 (2020): 85–92.

24. F. G. Vassalo, C. R. B. Simões, M. J. Sudano, et al., "Topics in the Routine Assessment of Newborn Puppy Viability," *Topics in Companion Animal Medicine* 30, no. 1 (2015): 16–21.

25. R. Titkova, M. Fialkovicova, M. Karasova, and J. Hajurka, "Puppy Apgar Scores After Vaginal Delivery and Caesarean Section," *Veterinarni Medicina* 62, no. 9 (2017): 488–492.

26. M. C. Veronesi, S. Panzani, M. Faustini, and A. Rota, "An Apgar Scoring System for Routine Assessment of Newborn Puppy Viability and Short-Term Survival Prognosis," *Theriogenology* 72, no. 3 (2009): 401–407.

27. V. Apgar, "A Proposal for a New Method of Evaluation of the Newborn Infant," *Current Researches in Anesthesia and Analgesia* 32, no. 4 (1953): 260–267.

28. V. Y. Hibaru, K. Pereira, K. D. M. Fuchs, et al., "Topics in the Routine Assessment of Newborn Kitten Vitality: Apgar Score, Reflexes and Complementary Assessments," *Journal of Feline Medicine and Surgery* 24, no. 6 (2022): e34–e42.

29. M. V. Estevam, G. H. Toniollo, and M. Apparicio, "The Most Common Congenital Malformations in Dogs: Literature Review and Practical Guide," *Research in Veterinary Science* 171 (2024): 105230.

30. J. D. Hoskins, "Congenital Defects of Cats," *Compendium: Continuing Education for the Practicing Veterinarian* 17, no. 3 (1995): 385–405.

31. L. C. G. Silva, C. F. Lúcio, G. A. L. Veiga, et al., "Neonatal Clinical Evaluation, Blood Gas and Radiographic Assessment After Normal Birth, Vaginal Dystocia or Caesarean Section in Dogs," *Reproduction in Domestic Animals = Zuchthygiene* 44, no. s2 (2009): 160–163.

32. R. A. Abreu, L. L. Almeida, R. R. D. Rosa Filho, et al., "Canine Pulmonary Clearance During Feto-Neonatal Transition According to the Type of Delivery," *Theriogenology* 224 (2024): 156–162.

33. D. J. Adams, R. E. Ellerbrock, M. L. Wallace, et al., "Risk Factors for Neonatal Mortality Prior to Hospital Discharge in Brachycephalic and Nonbrachycephalic Dogs Undergoing Cesarean Section," *Veterinary Surgery* 51, no. 7 (2022): 1052–1060.

34. S. A. Abd-El Hamid, M. M. Badr-El Din, N. I. Dabous, and K. M. Saad, "Effect of the Use of a Polyethylene Wrap on the Morbidity and Mortality of Very Low Birth Weight Infants in Alexandria University Children's Hospital," *Journal of the Egyptian Public Health Association* 87, no. 5-6 (2012): 104–108.

35. R. Lenclen, M. Mazraani, M. Jugie, et al., "[Use of a Polyethylene Bag: A Way to Improve the Thermal Environment of the Premature Newborn at the Delivery Room]," *Archives De Pediatrie* 9, no. 3 (2002): 238–244.

36. M. P. Meyer, M. J. Payton, A. Salmon, et al., "A Clinical Comparison of Radiant Warmer and Incubator Care for Preterm Infants From Birth to 1800 Grams," *Pediatrics* 108, no. 2 (2001): 395–401.

37. A. R. Laptook, W. Salhab, and B. Bhaskar, "Admission Temperature of Low Birth Weight Infants: Predictors and Associated Morbidities," *Pediatrics* 119, no. 3 (2007): e643–e649.

38. L. C. Mullany, J. Katz, S. K. Khatry, et al., "Risk of Mortality Associated With Neonatal Hypothermia in Southern Nepal," *Archives of Pediatrics & Adolescent Medicine* 164, no. 7 (2010): 650–656.

39. B. W. Christensen and H. N. Erb, "An Investigation of the Discrepancy Between Set and Actual Temperature of Neonatal Incubators: Concern for Hypothermia and Hyperthermia," *Journal of the American Veterinary Medical Association* 262, no. 1 (2024): 68–71.

40. Rech Morassutti F, F. Cavallin, P. Zaramella, et al., "Association of Rewarming Rate on Neonatal Outcomes in Extremely Low Birth Weight Infants With Hypothermia," *Journal of Pediatrics* 167, no. 3 (2015): 557.e2–561.e2.

41. A. Feldman, B. De Benedictis, G. Alpan, et al., "Morbidity and Mortality Associated With Rewarming Hypothermic Very Low Birth Weight Infants," *Journal of Neonatal-Perinatal Medicine* 9, no. 3 (2016): 295–302.

42. P. Jain, J. S. Dalal, and G. Gathwala, "Rapid vs. Slow Rewarming for Management of Moderate to Severe Hypothermia in Low-Birth-Weight Pre-Term Neonates—An Open Label Randomized Controlled Trial," *Journal of Tropical Pediatrics* 67, no. 1 (2021): fmaa098.

43. E. Rossi, D. M. Maziku, D. E. Leluko, et al., "Rewarming Rate of Hypothermic Neonates in a Low-Resource Setting: A Retrospective Single-Center Study," *Frontiers in Pediatrics* 11 (2023): 1113897.

44. K. J. Motil, M. G. Blackburn, and J. R. Pleasure, "The Effects of Four Different Radiant Warmer Temperature Set-Points Used for Rewarming Neonates," *Journal of Pediatrics* 85, no. 4 (1974): 546–550.

45. E. M. Scarpelli, S. Condorelli, and E. V. Cosmi, "Cutaneous Stimulation and Generation of Breathing in the Fetus," *Pediatric Research* 11, no. 1 Pt 1 (1977): 24–28.

46. E. E. Faridy, "Instinctive Resuscitation of the Newborn Rat," *Respiration Physiology* 51, no. 1 (1983): 1–19.

47. M. Kaufmann, L. Mense, L. Springer, and J. Dekker, "Tactile Stimulation in the Delivery Room: Past, Present, Future. A Systematic Review," *Pediatric Research* 96, no. 3 (2024): 616–624.

48. J. Dekker, T. Martherus, S. J. E. Cramer, et al., "Tactile Stimulation to Stimulate Spontaneous Breathing During Stabilization of Preterm Infants at Birth: A Retrospective Analysis," *Frontiers in Pediatrics* 5 (2017): 61.

49. S. Chettri, B. Adhisivam, and B. V. Bhat, "Endotracheal Suction for Nonvigorous Neonates Born Through Meconium Stained Amniotic Fluid: A Randomized Controlled Trial," *Journal of Pediatrics* 166, no. 5 (2015): 1208.e1–1213.e1.

50. S. Nangia, S. Sunder, R. Biswas, and A. Saili, "Endotracheal Suction in Term Non Vigorous Meconium Stained Neonates—A Pilot Study," *Resuscitation* 105 (2016): 79–84.

51. A. Kumar, P. Kumar, and S. Basu, "Endotracheal Suctioning for Prevention of Meconium Aspiration Syndrome: A Randomized Controlled Trial," *European Journal of Pediatrics* 178, no. 12 (2019): 1825–1832.

52. V. R. Viraraghavan, S. Nangia, B. H. Prathik, et al., "Yield of Meconium in Non-Vigorous Neonates Undergoing Endotracheal Suctioning and Profile of all Neonates Born Through Meconium-Stained Amniotic Fluid: A Prospective Observational Study," *Paediatrics and International Child Health* 38, no. 4 (2018): 266–270.

53. S. Lakshminrusimha, B. Mathew, J. Nair, et al., "Tracheal Suctioning Improves Gas Exchange but Not Hemodynamics in Asphyxiated Lambs With Meconium Aspiration," *Pediatric Research* 77, no. 2 (2015): 347–355.

54. T. F. Baskett and F. Nagele, "Bernhard Schultze and the Swinging Neonate," *Resuscitation* 51, no. 1 (2001): 3–6.

55. S. A. Grundy, S. M. Liu, and A. P. Davidson, "Intracranial Trauma in a Dog due to Being "Swung"," *Topics in Companion Animal Medicine* 24, no. 2 (2009): 100–103.

56. D. A. Giussani, J. A. Spencer, P. J. Moore, et al., "Afferent and Efferent Components of the Cardiovascular Reflex Responses to Acute Hypoxia in Term Fetal Sheep," *The Journal of Physiology* 461, no. 1 (1993): 431–449.

57. L. K. McCarthy, C. J. Morley, P. G. Davis, et al., "Timing of Interventions in the Delivery Room: Does Reality Compare With Neonatal

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70013, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

Resuscitation Guidelines?," *Journal of Pediatrics* 163, no. 6 (2013): 1553.e1–1557.e1.

58. J. P. Verstegen, L. D. Silva, K. Onclin, and I. Donnay, "Echocardiographic Study of Heart Rate in Dog and Cat Fetuses in Utero," *Journal of Reproduction and Fertility Supplement* 47 (1993): 175–180.

59. L. M. Walter, B. Ahmed, A. Odoi, et al., "Bradycardias Are Associated With More Severe Effects on Cerebral Oxygenation in Very Preterm Infants Than in Late Preterm Infants," *Early Human Development* 127 (2018): 33–41.

60. B. Iglesias, M. A. J. Rodri Guez, E. Aleo, et al., "3-Lead Electrocardiogram Is More Reliable Than Pulse Oximetry to Detect Bradycardia During Stabilisation at Birth of Very Preterm Infants," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 103, no. 3 (2018): F233–F237.

61. A. Katheria, W. Rich, and N. Finer, "Electrocardiogram Provides a Continuous Heart Rate Faster Than Oximetry During Neonatal Resuscitation," *Pediatrics* 130, no. 5 (2012): e1177–e1181.

62. M. C. Murphy, L. De Angelis, L. K. McCarthy, and C. P. F. O'Donnell, "Comparison of Infant Heart Rate Assessment by Auscultation, ECG and Oximetry in the Delivery Room," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 103, no. 5 (2018): F490–F492.

63. O. D. Saugstad, "Oxygen Saturations Immediately After Birth," *Journal of Pediatrics* 148, no. 5 (2006): 569–570.

64. P. Davies, D. Cheng, A. Fox, and L. Lee, "The Efficacy of Noncontact Oxygen Delivery Methods," *Pediatrics* 110, no. 5 (2002): 964–967.

65. J. A. Dawson, P. G. Davis, C. P. O'Donnell, et al., "Free-Flow Oxygen Delivery to Newly Born Infants," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 92, no. 2 (2007): F132–F134.

66. O. D. Saugstad, T. Rootwelt, and O. Aalen, "Resuscitation of Asphyxiated Newborn Infants With Room Air or Oxygen: An International Controlled Trial: The Resair 2 Study," *Pediatrics* 102, no. 1 (1998): e1.

67. S. Ramji, S. Ahuja, S. Thirupuram, et al., "Resuscitation of Asphyxie Newborn Infants With Room Air or 100% Oxygen," *Pediatric Research* 34, no. 6 (1993): 809–812.

68. S. Ramji, R. Rasaily, P. K. Mishra, et al., "Resuscitation of Asphyxiated Newborns With Room Air or 100% Oxygen at Birth: A Multicentric Clinical Trial," *Indian Pediatrics* 40, no. 6 (2003): 510–517.

69. N. Bajaj, R. H. Udani, and R. N. Nanavati, "Room Air vs. 100 Per Cent Oxygen for Neonatal Resuscitation: A Controlled Clinical Trial," *Journal of Tropical Pediatrics* 51, no. 4 (2005): 206–211.

70. A. M. Cone, S. Nadel, and B. Sweeney, "Flumazenil Reverses Diazepam-Induced Neonatal Apnoea and Hypotonia," *European Journal of Pediatrics* 152, no. 5 (1993): 458–459.

71. P. Richard, E. Autret, J. Bardol, et al., "The Use of Flumazenil in a Neonate," *Journal of Toxicology Clinical Toxicology* 29, no. 1 (1991): 137–140.

72. J. C. Dixon, B. D. Speidel, and J. J. Dixon, "Neonatal Flumazenil Therapy Reverses Maternal Diazepam," *Acta Paediatrica* 87, no. 2 (1998): 225–226.

73. H. Pike, V. Kolstad, J. Eilevstjønn, et al., "Newborn Resuscitation Timelines: Accurately Capturing Treatment in the Delivery Room," *Resuscitation* 197 (2024): 110156.

74. H. L. Ersdal, E. Mduma, E. Svensen, and J. M. Perlman, "Early Initiation of Basic Resuscitation Interventions Including Face Mask Ventilation May Reduce Birth Asphyxia Related Mortality in Low-Income Countries: A Prospective Descriptive Observational Study," *Resuscitation* 83, no. 7 (2012): 869–873.

75. A. W. Boon, A. D. Milner, and I. E. Hopkin, "Lung Expansion, Tidal Exchange, and Formation of the Functional Residual Capacity During Resuscitation of Asphyxiated Neonates," *Journal of Pediatrics* 95, no. 6 (1979): 1031–1036.

76. K. Holte, H. Ersdal, J. Eilevstjønn, et al., "Positive End-Expiratory Pressure in Newborn Resuscitation Around Term: A Randomized Controlled Trial," *Pediatrics* 146, no. 4 (2020): e20200494.

77. M. E. Probyn, S. B. Hooper, P. A. Dargaville, et al., "Positive End Expiratory Pressure During Resuscitation of Premature Lambs Rapidly Improves Blood Gases Without Adversely Affecting Arterial Pressure," *Pediatric Research* 56, no. 2 (2004): 198–204.

78. S. B. Hooper, M. L. Siew, M. J. Kitchen, and A. B. te Pas, "Establishing Functional Residual Capacity in the Non-Breathing Infant," *Seminars in Fetal & Neonatal Medicine* 18, no. 6 (2013): 336–343.

79. E. H. Kim, S. A. Cho, P. Kang, et al., "Ultrasound-Guided Esophageal Compression During Mask Ventilation in Small Children: A Prospective Observational Study," *BMC Anesthesiology* 22, no. 1 (2022): 257.

80. P. Danilo Jr., M. R. Rosen, and A. J. Hordof, "Effects of Acetylcholine on the Ventricular Specialized Conducting System of Neonatal and Adult Dogs," *Circulation Research* 43, no. 5 (1978): 777–784.

81. R. C. Goodlin and H. C. Haesslein, "Fetal Reacting Bradycardia," *American Journal of Obstetrics and Gynecology* 129, no. 8 (1977): 845–856.

82. A. M. Walker, J. P. Cannata, M. H. Dowling, et al., "Age-Dependent Pattern of Autonomic Heart Rate Control During Hypoxia in Fetal and Newborn Lambs," *Biology of the Neonate* 35, no. 3/4 (1979): 198–208.

83. C. A. Lear, M. J. Beacom, S. K. Dhillon, et al., "Dissecting the Contributions of the Peripheral Chemoreflex and Myocardial Hypoxia to Fetal Heart Rate Decelerations in Near-Term Fetal Sheep," *The Journal of Physiology* 601, no. 10 (2023): 2017–2041.

84. J. T. Parer, "The Effect of Atropine on Heart Rate and Oxygen Consumption of the Hypoxic Fetus," *American Journal of Obstetrics and Gynecology* 148, no. 8 (1984): 1118–1122.

85. W. Joyce and T. Wang, "Regulation of Heart Rate in Vertebrates During Hypoxia: A Comparative Overview," *Acta Physiologica* 234, no. 3 (2022): e13779.

86. C. H. Yam, J. A. Dawson, G. M. Schmolzer, et al., "Heart Rate Changes During Resuscitation of Newly Born Infants <30 Weeks Gestation: An Observational Study," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 96, no. 2 (2011): F102–F107.

87. M. L. Espinoza, P.-Y. Cheung, T.-F. Lee, et al., "Heart Rate Changes During Positive Pressure Ventilation After Asphyxia-Induced Bradycardia in a Porcine Model of Neonatal Resuscitation," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 104, no. 1 (2019): F98–F101.

88. A. Kibsgaard, H. Ersdal, J. T. Kvaløy, et al., "Newborns Requiring Resuscitation: Two Thirds Have Heart Rate ≥100 Beats/Minute in the First Minute After Birth," *Acta Paediatrica* 112, no. 4 (2023): 697–705.

89. M. Vento, M. Asensi, J. Sastre, et al., "Six Years of Experience With the Use of Room Air for the Resuscitation of Asphyxiated Newly Born Term Infants," *Biology of the Neonate* 79, no. 3-4 (2001): 261–267.

90. M. Vento, M. Asensi, J. Sastre, et al., "Oxidative Stress in Asphyxiated Term Infants Resuscitated With 100% Oxygen," *Journal of Pediatrics* 142, no. 3 (2003): 240–246.

91. M. Vento, J. Sastre, M. A. Asensi, and J. Viña, "Room-Air Resuscitation Causes Less Damage to Heart and Kidney Than 100% Oxygen," *American Journal of Respiratory and Critical Care Medicine* 172, no. 11 (2005): 1393–1398.

92. S. Lakshminrusimha, R. H. Steinhorn, S. Wedgwood, et al., "Pulmonary Hemodynamics and Vascular Reactivity in Asphyxiated Term Lambs Resuscitated With 21 and 100% Oxygen," *Journal of Applied Physiology* 111, no. 5 (2011): 1441–1447.

93. P. A. Bjorland, K. Oymar, H. L. Ersdal, and S. I. Rettedal, "Incidence of Newborn Resuscitative Interventions at Birth and Short-Term Outcomes: A Regional Population-Based Study," *BMJ Paediatrics Open* 3, no. 1 (2019): e000592.

94. E. E. Foglia, B. A. Shah, and E. Szyld, "Positive Pressure Ventilation at Birth," *Seminars in Perinatology* 46, no. 6 (2022): 151623.

95. P. Kapadia, C. Hurst, D. Harley, et al., "Trends in Neonatal Resuscitation Patterns in Queensland, Australia — A 10-Year Retrospective Cohort Study," *Resuscitation* 157 (2020): 126–132.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70013, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

96. Z. Alhassen, P. Vali, A. Lesneski, et al., "What Is the Optimal Heart Rate Cut-Off for Initiating Chest Compressions in Neonatal Bradycardia?," *Pediatrics* 147 (2021): 753.

97. P. Chandrasekharan, S. Gugino, C. Koenigsknecht, et al., "Chest Compressions During Neonatal Bradycardia Do Not Enhance Flow to Vital Organs but Reduce Inherent Cardiac Activity," *Pediatrics* 149 (2022): 654.

98. S. Rettedal, A. Kibsgaard, J. T. Kvaløy, et al., "Prevalence of Bradycardia in 4876 Newborns in the First Minute After Birth and Association With Positive Pressure Ventilation: A Population-Based Cross-Sectional Study," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 109, no. 4 (2024): 371–377.

99. J. P. Mortola and J. T. Fisher, "Mouth and Nose Resistance in Newborn Kittens and Puppies," *Journal of Applied Physiology: Respiratory, Environmental and Exercise Physiology* 51, no. 3 (1981): 641–645.

100. M. Bruckner, M. Neset, M. O'Reilly, et al., "Haemodynamic Changes With Varying Chest Compression Rates in Asphyxiated Piglets," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 108, no. 2 (2023): 200–203.

101. S. Patel, P.-Y. Cheung, T.-F. Lee, et al., "Asynchronous Ventilation at 120 Compared With 90 or 100 Compressions per Minute Improves Haemodynamic Recovery in Asphyxiated Newborn Piglets," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 105, no. 4 (2020): 357–363.

102. J. T. Hamrick, J. L. Hamrick, U. Bhalala, et al., "End-Tidal CO2-Guided Chest Compression Delivery Improves Survival in a Neonatal Asphyxial Cardiac Arrest Model," *Pediatric Critical Care Medicine* 18, no. 11 (2017): e575–e584.

103. C. F. Babbs, A. Meyer, and V. Nadkarni, "Neonatal CPR: Room at the Top—A Mathematical Study of Optimal Chest Compression Frequency Versus Body Size," *Resuscitation* 80, no. 11 (2009): 1280–1284.

104. M. Reyes-Martínez and V. J. Herrería-Bustillo, "Evaluation of Compressor Fatigue at 150 Compressions per Minute During Cardiopulmonary Resuscitation Using a Large Dog Manikin," *Journal of Veterinary Emergency and Critical Care* 33, no. 5 (2023): 495–500.

105. J. Madar, C. C. Roehr, S. Ainsworth, et al., "European Resuscitation Council Guidelines," *Resuscitation* 161 (2021): 291–326.

106. G. R. Polglase, Y. Brian, D. Tantanis, et al., "Endotracheal Epinephrine at Standard Versus High Dose for Resuscitation of Asystolic Newborn Lambs," *Resuscitation* 198 (2024): 110191.

107. J. de Jager, R. Pothof, K. J. Crossley, et al., "Evaluating the Efficacy of Endotracheal and Intranasal Epinephrine Administration in Severely Asphyxic Bradycardic Newborn Lambs: A Randomised Preclinical Study," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 110, no. 2 (2025): 207–212.

108. P. Vali, P. Chandrasekharan, M. Rawat, et al., "Evaluation of Timing and Route of Epinephrine in a Neonatal Model of Asphyxial Arrest," *Journal of the American Heart Association* 6, no. 2 (2017): e004402.

109. C. A. Barber and M. H. Wyckoff, "Use and Efficacy of Endotracheal Versus Intravenous Epinephrine During Neonatal Cardiopulmonary Resuscitation in the Delivery Room," *Pediatrics* 118, no. 3 (2006): 1028–1034.

110. C. Halling, J. E. Sparks, L. Christie, and M. H. Wyckoff, "Efficacy of Intravenous and Endotracheal Epinephrine During Neonatal Cardiopulmonary Resuscitation in the Delivery Room," *Journal of Pediatrics* 185 (2017): 232–236.

111. J. Nair, P. Vali, S. F. Gugino, et al., "Bioavailability of Endotracheal Epinephrine in an Ovine Model of Neonatal Resuscitation," *Early Human Development* 130 (2019): 27–32.

112. J. R. Roberts, M. I. Greenberg, M. A. Knaub, et al., "Blood Levels Following Intravenous and Endotracheal Epinephrine Administration," *Journal of the American College of Emergency Physicians* 8, no. 2 (1979): 53–56.

113. C. T. Roberts, S. Klink, G. M. Schmölzer, et al., "Comparison of Intraosseous and Intravenous Epinephrine Administration During Resuscitation of Asphyxiated Newborn Lambs," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 107, no. 3 (2022): 311–316.

114. A. M. Steele and J. L. Oram, "Catheterization of the Venous Compartment," in *Advanced Monitoring and Procedures for Small Animal Emergency and Critical Care*, 2nd ed., ed. J. M. Burkitt Creedon and H. Davis (Wiley Blackwell, 2023), 81–101.

115. N. T. Songstad, C. Klingenberg, E. V. McGillick, et al., "Efficacy of Intravenous, Endotracheal, or Nasal Adrenaline Administration During Resuscitation of Near-Term Asphyxiated Lambs," *Frontiers in Pediatrics* 8 (2020): 262.

116. S. K. Berkelhamer, P. Vali, J. Nair, et al., "Inadequate Bioavailability of Intramuscular Epinephrine in a Neonatal Asphyxia Model," *Frontiers in Pediatrics* 10 (2022): 828130.

117. E. E. Foglia, E. A. Jensen, M. H. Wyckoff, et al., "Survival After Delivery Room Cardiopulmonary Resuscitation: A National Registry Study," *Resuscitation* 152 (2020): 177–183.

118. H. Patel and P. J. Beeby, "Resuscitation Beyond 10 Minutes of Term Babies Born Without Signs of Life," *Journal of Paediatrics and Child Health* 40, no. 3 (2004): 136–138.

119. D. J. Harrington, C. W. Redman, M. Moulden, and C. E. Greenwood, "The Long-Term Outcome in Surviving Infants With Apgar Zero at 10 Minutes: A Systematic Review of the Literature and Hospital-Based Cohort," *American Journal of Obstetrics and Gynecology* 196, no. 5 (2007): 463.e1–463.e5.

120. H. Steiner and G. Neligan, "Perinatal Cardiac Arrest. Quality of the Survivors," *Archives of Disease in Childhood* 50, no. 9 (1975): 696–702.

121. E. Kasdorf, A. Laptook, D. Azzopardi, et al., "Improving Infant Outcome With a 10 Min Apgar of 0," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 100, no. 2 (2015): F102–F105.

122. T. Sproat, R. Hearn, and S. Harigopal, "Outcome of Babies With no Detectable Heart Rate Before 10 Minutes of Age, and the Effect of Gestation," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 102, no. 3 (2017): F262–F265.

123. J. Shibasaki, T. Mukai, K. Tsuda, et al., "Outcomes Related to 10-min Apgar Scores of Zero in Japan," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 105, no. 1 (2020): 64–68.

124. K. da Mata Fuchs, K. Pereira, G. M. Xavier, et al., "Neonatal Hypoglycemia in Dogs—Pathophysiology, Risk Factors, Diagnosis and Treatment," *Frontiers in Veterinary Science* 11 (2024): 1345933.

125. S. A. Grundy, "Clinically Relevant Physiology of the Neonate," *Veterinary Clinics of North America: Small Animal Practice* 36, no. 3 (2006): 443–459.

126. H. Mila, A. Grellet, M. Delebarre, et al., "Monitoring of the Newborn Dog and Prediction of Neonatal Mortality," *Preventive Veterinary Medicine* 143 (2017): 11–20.

127. A. R. Hollis, M. O. Furr, K. G. Magdesian, et al., "Blood Glucose Concentrations in Critically Ill Neonatal Foals," *Journal of Veterinary Internal Medicine* 22, no. 5 (2008): 1223–1227.

128. A. Panzardi, M. L. Bernardi, A. P. Mellagi, et al., "Newborn Piglet Traits Associated With Survival and Growth Performance Until Weaning," *Preventive Veterinary Medicine* 110, no. 2 (2013): 206–213.

129. R. A. Sheldon, J. C. Partridge, and D. M. Ferriero, "Postischemic Hyperglycemia Is Not Protective to the Neonatal Rat Brain," *Pediatric Research* 32, no. 4 (1992): 489–493.

130. R. C. Vannucci, A. Rossini, and J. Towfighi, "Effect of Hyperglycemia on Ischemic Brain Damage During Hypothermic Circulatory Arrest in Newborn Dogs," *Pediatric Research* 40, no. 2 (1996): 177–184.

131. W. A. Salhab, M. H. Wyckoff, A. R. Laptook, and J. M. Perlman, "Initial Hypoglycemia and Neonatal Brain Injury in Term Infants With Severe Fetal Acidemia," *Pediatrics* 114, no. 2 (2004): 361–366.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70013, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

132. M. Nadeem, D. M. Murray, G. B. Boylan, et al., "Early Blood Glucose Profile and Neurodevelopmental Outcome at Two Years in Neonatal Hypoxic-Ischaemic Encephalopathy," *BMC Pediatrics* 11 (2011): 10.

133. S. K. Basu, J. R. Kaiser, D. Guffey, et al., "Hypoglycaemia and Hyperglycaemia Are Associated With Unfavourable Outcome in Infants With Hypoxic Ischaemic Encephalopathy: A Post Hoc Analysis of the CoolCap Study," *Archives of Disease in Childhood: Fetal and Neonatal Edition* 101, no. 2 (2016): F149–F155.

134. R. Greif, J. E. Bray, T. Djärv, et al., "2024 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations: Summary From the Basic Life Support; Advanced Life Support; Pediatric Life Support; Neonatal Life Support; Education, Implementation, and Teams; and First Aid Task Forces," *Circulation* 150, no. 24 (2024): e580–e687.

135. K. H. Polderman, "Mechanisms of Action, Physiological Effects, and Complications of Hypothermia," *Critical Care Medicine* 37, no. 7 (2009): S186–S202.

136. J. M. Perlman, J. Wyllie, J. Kattwinkel, et al., "Part 11: Neonatal Resuscitation: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations," *Circulation* 122, no. 16 SUPPL. 2 (2010): S516–S538.

137. B. Lemyre and V. Chau, "Hypothermia for Newborns With Hypoxic-Ischemic Encephalopathy," *Paediatrics & Child Health* 23, no. 4 (2018): 285–291.

138. R. E. Toribio, "Equine Neonatal Encephalopathy: Facts, Evidence, and Opinions," *Veterinary Clinics of North America: Small Animal Practice* 35, no. 2 (2019): 363–378.

139. J. O. Davidson, G. Wassink, L. G. van den Heuij, et al., "Therapeutic Hypothermia for Neonatal Hypoxic-Ischemic Encephalopathy—Where to From Here?," *Frontiers in Neurology* 6 (2015): 198.

140. F. Colbourne and D. Corbett, "Delayed and Prolonged Post-Ischemic Hypothermia Is Neuroprotective in the Gerbil," *Brain Research* 654, no. 2 (1994): 265–272.

141. D. L. Clark, M. Penner, I. M. Orellana-Jordan, and F. Colbourne, "Comparison of 12, 24 and 48 h of Systemic Hypothermia on Outcome After Permanent Focal Ischemia in Rat," *Experimental Neurology* 212, no. 2 (2008): 386–392.

142. D. M. Agnew, R. C. Koehler, A.-M. Guerguerian, et al., "Hypothermia for 24 Hours After Asphyxic Cardiac Arrest in Piglets Provides Striatal Neuroprotection That Is Sustained 10 Days After Rewarming," *Pediatric Research* 54, no. 2 (2003): 253–262.

143. A. R. Laptook, R. J. T. Corbett, R. Sterett, et al., "Modest Hypothermia Provides Partial Neuroprotection When Used for Immediate Resuscitation After Brain Ischemia," *Pediatric Research* 42, no. 1 (1997): 17–23.

144. M. Thoresen, S. Satas, E. M. Løberg, et al., "Twenty-Four Hours of Mild Hypothermia in Unsedated Newborn Pigs Starting After a Severe Global Hypoxic-Ischemic Insult Is Not Neuroprotective," *Pediatric Research* 50, no. 3 (2001): 405–411.

145. X. Lu, L. Ma, S. Sun, et al., "The Effects of the Rate of Postresuscitation Rewarming Following Hypothermia on Outcomes of Cardiopulmonary Resuscitation in a Rat Model," *Critical Care Medicine* 42, no. 2 (2014): e106–e113.

146. C. Berger, F. Xia, M. Köhrmann, and S. Schwab, "Hypothermia in Acute Stroke-Slow Versus Fast Rewarming. An Experimental Study in Rats," *Experimental Neurology* 204, no. 1 (2007): 131–137.

147. E. Suehiro, Y. Ueda, E. P. Wei, et al., "Posttraumatic Hypothermia Followed by Slow Rewarming Protects the Cerebral Microcirculation," *Journal of Neurotrauma* 20, no. 4 (2003): 381–390.

148. E. Suehiro and J. T. Povlishock, "Exacerbation of Traumatically Induced Axonal Injury by Rapid Posthypothermic Rewarming and Attenuation of Axonal Change by Cyclosporin A," *Journal of Neurosurgery* 94, no. 3 (2001): 493–498.

149. L. L. A. Bisschops, C. W. E. Hoedemaekers, T. E. Mollnes, and J. G. van der Hoeven, "Rewarming After Hypothermia After Cardiac Arrest Shifts the Inflammatory Balance," *Critical Care Medicine* 40, no. 4 (2012): 1136–1142.

150. S.-Z. Zhu, Y. Gu, Z. Wu, et al., "Hypothermia Followed by Rapid Rewarming Exacerbates Ischemia-Induced Brain Injury and Augments Inflammatory Response in Rats," *Biochemical and Biophysical Research Communications* 474, no. 1 (2016): 175–181.

151. S. D. Smarick, S. C. Haskins, M. Boller, et al., "RECOVER Evidence and Knowledge Gap Analysis on Veterinary CPR. Part 6: Post-Cardiac Arrest Care," *Journal of Veterinary Emergency and Critical Care* 22, no. Suppl 1 (2012): S85–S101.

152. J. O. Davidson, G. Wassink, V. Draghi, et al., "Limited Benefit of Slow Rewarming After Cerebral Hypothermia for Global Cerebral Ischemia in Near-Term Fetal Sheep," *Journal of Cerebral Blood Flow and Metabolism* 39, no. 11 (2019): 2246–2257.

153. B. Wang, J. S. Armstrong, J.-H. Lee, et al., "Rewarming From Therapeutic Hypothermia Induces Cortical Neuron Apoptosis in a Swine Model of Neonatal Hypoxic-Ischemic Encephalopathy," *Journal of Cerebral Blood Flow and Metabolism* 35, no. 5 (2015): 781–793.

154. B. Wang, J. S. Armstrong, M. Reyes, et al., "White Matter Apoptosis Is Increased by Delayed Hypothermia and Rewarming in a Neonatal Piglet Model of Hypoxic Ischemic Encephalopathy," *Neuroscience* 316 (2016): 296–310.

155. V. Draghi, G. Wassink, K. Q. Zhou, et al., "Differential Effects of Slow Rewarming After Cerebral Hypothermia on White Matter Recovery After Global Cerebral Ischemia in Near-Term Fetal Sheep," *Scientific Reports* 9, no. 1 (2019): 10142.

156. A. McDouall, K. Q. Zhou, A. Davies, et al., "Slow Rewarming After Hypothermia Does Not Ameliorate White Matter Injury After Hypoxia-Ischemia in Near-Term Fetal Sheep," *Pediatric Research* 97, no. 3 (2025): 1209–1219.

157. M. Thoresen and A. Whitelaw, "Cardiovascular Changes During Mild Therapeutic Hypothermia and Rewarming in Infants With Hypoxic-Ischemic Encephalopathy," *Pediatrics* 106, no. 1 Pt 1 (2000): 92–99.

158. M. Battin, L. Bennet, and A. J. Gunn, "Rebound Seizures During Rewarming," *Pediatrics* 114, no. 5 (2004): 1369–1369.

159. C. S. Yost, "A New Look at the Respiratory Stimulant Doxapram," *CNS Drug Reviews* 12, no. 3-4 (2006): 236–249.

160. J. R. Holladay, "Routine Use of Doxapram Hydrochloride in Neonatal Pups Delivered by Cesarean Section," *Veterinary Medicine, Small Animal Clinician* 66, no. 1 (1971): 28.

161. R. R. Wilborn, "Small Animal Neonatal Health," *Veterinary Clinics of North America: Small Animal Practice* 48, no. 4 (2018): 683–699.

162. C. J. Miller, B. C. McKiernan, J. Pace, and M. J. Fettman, "The Effects of Doxapram Hydrochloride (Dopram-V) on Laryngeal Function in Healthy Dogs," *Journal of Veterinary Internal Medicine* 16, no. 5 (2002): 524–528.

163. K. M. Tobias, A. M. Jackson, and R. C. Harvey, "Effects of Doxapram HCl on Laryngeal Function of Normal Dogs and Dogs With Naturally Occurring Laryngeal Paralysis," *Veterinary Anaesthesia and Analgesia* 31, no. 4 (2004): 258–263.

164. T. H. Hyndman, S. Fretwell, R. S. Bowden, et al., "The Effect of Doxapram on Survival and APGAR Score in Newborn Puppies Delivered by Elective Caesarean: A Randomized Controlled Trial," *Journal of Veterinary Pharmacology and Therapeutics* 46, no. 6 (2023): 353–364.

165. E. Balıkcı and A. Yıldız, "Effects on Arterial Blood Gases and Some Clinical Parameters of Caffeine, Atropine Sulphate or Doxapram Hydrochloride in Calves With Neonatal Asphyxia," *Revue de Medecine Veterinaire* 160, no. 6 (2009): 282–287.

166. T. Yamazaki, M. Kajiwara, K. Itahashi, and M. Fujimura, "Low-Dose Doxapram Therapy for Idiopathic Apnea of Prematurity," *Pediatrics International* 43, no. 2 (2001): 124–127.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70013, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

167. H. Uehara, H. Yoshioka, H. Nagai, et al., "Doxapram Accentuates White Matter Injury in Neonatal Rats Following Bilateral Carotid Artery Occlusion," *Neuroscience Letters* 281, no. 2-3 (2000): 191–194.

168. U. Bleul and T. Bylang, "Effects of Doxapram, Prethcamide and Lobeline on Spirometric, Blood Gas and Acid-Base Variables in Healthy New-Born Calves," *Veterinary Journal* 194, no. 2 (2012): 240–246.

169. R. Flint, N. Halbmeijer, N. Meesters, et al., "Retrospective Study Shows That Doxapram Therapy Avoided the Need for Endotracheal Intubation in Most Premature Neonates," *Acta Paediatrica* 106, no. 5 (2017): 733–739.

170. S. Giguere, L. C. Sanchez, A. Shih, et al., "Comparison of the Effects of Caffeine and Doxapram on Respiratory and Cardiovascular Function in Foals With Induced Respiratory Acidosis," *American Journal of Veterinary Research* 68, no. 12 (2007): 1407–1416.

171. S. Allweiler, "Anesthesia for Small Animal Cesarean Surgery and Neonatal Resuscitation," *Clinical Theriogenology* 14, no. 3 (2022): 170–173.

172. W.-W. Chan, K.-Y. Chen, H. Liu, et al., "Acupuncture for General Veterinary Practice," *Journal of Veterinary Medical Science* 63, no. 10 (2001): 1057–1062.

173. L. Janssens, S. Altman, and P. A. Rogers, "Respiratory and Cardiac Arrest Under General Anaesthesia: Treatment by Acupuncture of the Nasal Philtrum," *The Veterinary Record* 105, no. 12 (1979): 273–276.

174. R. T. Skarda, "Anesthesia Case of the Month," *Journal of the American Veterinary Medical Association* 214, no. 1 (1999): 37–39.

175. M. Wyckoff, D. Garcia, L. Margraf, et al., "Randomized Trial of Volume Infusion During Resuscitation of Asphyxiated Neonatal Piglets," *Pediatric Research* 61, no. 4 (2007): 415–420.

176. M. R. Mendler, S. Schwarz, L. Hechenrieder, et al., "Successful Resuscitation in a Model of Asphyxia and Hemorrhage to Test Different Volume Resuscitation Strategies. A Study in Newborn Piglets After Transition," *Frontiers in Pediatrics* 6 (2018): 192.

177. D. Sankaran, E. C. A. Lane, R. Valdez, et al., "Role of Volume Replacement During Neonatal Resuscitation in the Delivery Room," *Children* 9, no. 10 (2022): 1484.

178. A. Antończyk, M. Ochota, and W. Niżański, "Umbilical Cord Blood Gas Parameters and Apgar Scoring in Assessment of New-Born Dogs Delivered by Cesarean Section," *Animals* 11, no. 3 (2021): 685.

179. P. Yeh, K. Emary, and L. Impey, "The Relationship Between Umbilical Cord Arterial pH and Serious Adverse Neonatal Outcome: Analysis of 51,519 Consecutive Validated Samples," *BJOG: An International Journal of Obstetrics & Gynaecology* 119, no. 7 (2012): 824–831.

180. P. Lorain, A. Bower, E. Gottardi, et al., "Risk Factors for Hypoxic-Ischemic Encephalopathy in Cases of Severe Acidosis: A Case-Control Study," *Acta Obstetricia et Gynecologica Scandinavica* 101, no. 4 (2022): 471–478.

181. L. Lokesh, P. Kumar, S. Murki, and A. Narang, "A Randomized Controlled Trial of Sodium Bicarbonate in Neonatal Resuscitation—Effect on Immediate Outcome," *Resuscitation* 60, no. 2 (2004): 219–223.

14764431, 2025, S1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/vec.70013, Wiley Online Library on [04/10/2025]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License