# Week 1: Clinical Trials and General Neonatology

## Neonatal/Infant Resuscitation

**Tuesday, June 9 2:30-4:00 pm EDT**

*AAP Neonatal Resuscitation Program Steering Committee (NRPSC) Highlighted Program*

**Moderators:**
Satyan Lakshminrusimha  
Tetsuya Isayama

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Note: Schedule subject to change based on presenter availability.
CONTROL ID: 3378957

TITLE: Randomized Controlled Trial of Oxygen Saturation Targets During Resuscitation of Preterm Neonates in the Delivery Room: The START Study

PRESENTER: Vishal Kapadia

AUTHORS (LAST NAME, FIRST NAME): Kapadia, Vishal\(^1\); Mir, Imran N.\(^1\); Ramachandran, Shalini\(^1\); Weydig, Heather M.\(^1\); Caraig, Maria\(^1\); Pavageau, Lara\(^1\); Lal, Charitharth V.\(^2\); Chalak, Lina F.\(^1\); Savani, Rashmin C.\(^1\); Wyckoff, Myra\(^1\)

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CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal/Infant Resuscitation

KEYWORDS: Oxygen Saturation, Preterm, Oxygen.

SESSION TITLE: Neonatal/Infant Resuscitation | Neonatal/Infant Resuscitation

SESSION TYPE: Webinar|Platform

ABSTRACT BODY:

Background: Hyperoxic resuscitation results in oxidative stress and is associated with bronchopulmonary dysplasia, cardiac and renal damage and even childhood leukemia. Hypoxic resuscitation results in higher pulmonary vascular resistance, lower respiratory drive and a higher need for positive pressure ventilation. An optimal O\(\text{2}\) strategy in the delivery room (DR) that avoids both hypoxia and hyperoxia and improves survival without adverse outcomes remains a critical knowledge gap. The current goal oxygen saturations (SpO\(\text{2}\)) for preterm resuscitation are extrapolated by approximating 50\(^{th}\) percentile SpO\(\text{2}\) (Ox50) of healthy term infants.

Objective: To determine the efficacy of goal SpO\(\text{2}\) Ox25 (25th percentile) and Ox75 (75th percentile) with the current neonatal resuscitation program recommended Ox50 (50th percentile) to prevent oxidative stress in premature newborns ≤ 30 weeks’ gestation.

Design/Methods: A randomized controlled trial of preterm infants ≤ 30 weeks was conducted where DR resuscitation was started with 30% O\(\text{2}\) and O\(\text{2}\) was titrated by 10-20% every 30 seconds to meet the goal SpO\(\text{2}\) based on their randomized arm (Figure 1). Cerebral O\(\text{2}\) saturation (CrSO\(\text{2}\)) was measured in the DR. Total hydroperoxide (TH), biological antioxidant potential (BAP), and the oxidative balance ratio (BAP/TH) were analyzed in cord blood and in blood samples obtained within one hour of admission to the NICU. Secondary outcomes included delivery room interventions, respiratory support in the NICU and short-term morbidities.

Results: Ox25, Ox50 and Ox75 infants had similar demographics (Table). FiO\(\text{2}\) at 4 and 5 minutes and SpO\(\text{2}\) at 3, 4 and 5 minutes in Ox75 infants were higher (Figure 2). Ox75 infants had earlier spontaneous breathing in the DR, spent less time in the DR with <10th percentile CrSO\(\text{2}\) and fewer Ox75 infants had SpO2 <80% at 5 minutes of life. Although O\(\text{2}\) load during the first 15 minutes was similar, Ox75 infants had less TH, higher BAP and higher Ox balance ratio (Figure 3). Ox75 infants also had a lower respiratory severity score for the first 4 hours. The incidence of persistent pulmonary hypertension (PPHN) was higher in Ox25 and Ox50 infants.

Conclusion(s): Targeting 75th percentile SpO\(\text{2}\) for preterm resuscitation resulted in earlier spontaneous breathing and less cerebral hypoxia in the DR, less oxidative stress on admission to NICU and less PPHN. A randomized controlled trial powered for long-term critical outcomes is warranted to inform optimal SpO\(\text{2}\) targets in the DR.
Flow Diagram showing screening of eligible infants, enrollment and randomization. Table shows goal oxygen saturation per randomized arm.

A. Median SpO\textsubscript{2} per minute of life in the DR for Ox25, Ox50 and Ox75. *p<0.05.

B. Median FiO\textsubscript{2} per minute of life in the DR for Ox25, Ox50 and Ox75. *p<0.05
A. Total Hydroperoxide B. Biological Antioxidant Potential C. Redox Oxidative Balance ratio in cord blood and on admission to NICU in Ox25, Ox50 and Ox75 preterm infants. * p<0.05

**IMAGE CAPTION:**

Flow Diagram showing screening of eligible infants, enrollment and randomization. Table shows goal oxygen saturation per randomized arm.

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A. Total Hydroperoxide B. Biological Antioxidant Potential C. Redox Oxidative Balance ratio in cord blood and on admission to NICU in Ox25, Ox50 and Ox75 preterm infants. * p<0.05
Background: Majority of 1 million deaths from perinatal asphyxia in the world occur in low-resource settings. During asphyxial arrest, chest compressions (CC) and epinephrine increase cerebral and coronary perfusion by increasing BP resulting in return of spontaneous circulation (ROSC). Bilateral femoral occlusion in a neonate (including flexing of lower limbs) can increase afterload and promote carotid/coronary flow similar to administration of epinephrine and/or volume through the umbilical venous catheter (UVC) (Figure 1). Femoral occlusion can be performed rapidly (within a few seconds of initiation of CC) and requires less skill and resources than UVC epinephrine/volume.

Objective: To determine the impact of bilateral femoral occlusion during CC on incidence and timing of ROSC, systemic and pulmonary hemodynamics and gas exchange.

Design/Methods: In this prospective randomized study, 15 term fetal lambs were asphyxiated by umbilical cord occlusion resulting in asphyxia leading to cardiac arrest. Lambs were resuscitated based on NRP guidelines and randomized to 2 groups: Femoral Occlusion during CC or Controls. Bilateral femoral arteries were occluded by applying pressure using two fingers during chest compression. Blood gases and hemodynamic parameters were obtained. Lambs were resuscitated for 20 minutes or till the ROSC was achieved, whichever was earlier.

Results: 6 out of 9 lambs in femoral occlusion group achieved ROSC in 5.3±1.7 min as compared to 2 out of 6 in controls in 13.2±5 min (Table). Achievement of ROSC was significantly earlier in femoral occlusion group. Three lambs achieved ROSC without epinephrine in the femoral occlusion group and all control lambs received epinephrine. Lambs with femoral occlusion had higher peak carotid, pulmonary, and coronary flows during CC. Femoral occlusion resulted in higher systolic and diastolic blood pressures. (Figure 2) Although ventilatory parameters were similar among the two groups, femoral occlusion group had lower PaCO₂ and lactate levels.

Conclusion(s): Femoral occlusion during CC resulted in faster and higher incidence of ROSC with lower need for epinephrine most likely secondary to higher carotid and coronary perfusion. Femoral occlusion is a low-tech approach that can be easily adapted during CPR in resource-limited settings to enhance survival and neurodevelopmental outcomes of over 75,000 births worldwide that require extensive resuscitation in the delivery room.
Figure 2: Hemodynamic parameters - coronary artery flow, carotid artery flow and diastolic pressures were significantly higher in femoral occlusion group.

**IMAGE CAPTION:**
Figure 1: BIOPAC snapshot showing changes in aortic pressure, carotid artery flow and coronary artery flow with femoral occlusion.

Figure 2: Hemodynamic parameters - coronary artery flow, carotid artery flow and diastolic pressures were significantly higher in femoral occlusion group.

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**CONTROL ID:** 3375623

**TITLE:** Resuscitation with an intact cord enhances pulmonary vasodilation and ventilation but reduces systemic oxygen toxicity and oxygen load in a preterm ovine model

**PRESENTER:** Praveen Chandrasekharan

**AUTHORS (LAST NAME, FIRST NAME):** Chandrasekharan, Praveen\(^1\); Gugino, Sylvia F.\(^1\); Koenigsknecht, Carmon\(^1\); Helman, Justin\(^1\); Nielsen, Lori\(^1\); Rawat, Munmun\(^1\); Nair, Jayasree\(^1\); Sankaran, Deepika\(^2\); Agrawal, Vikash\(^1\); Lakshminrusimha, Satyan\(^2\)

**AUTHORS/INSTITUTIONS:** P. Chandrasekharan, S.F. Gugino, C. Koenigsknecht, J. Helman, L. Nielsen, M. Rawat, J. Nair, V. Agrawal, Pediatrics, University at Buffalo, Buffalo, New York, UNITED STATES; D. Sankaran, S. Lakshminrusimha, Pediatrics, UC Davis, Sacramento, California, UNITED STATES;

**CURRENT CATEGORY:** Neonatology

**CURRENT SUBCATEGORY:** Neonatal/Infant Resuscitation

**KEYWORDS:** Preterm, delayed cord clamping, oxygen.

**SESSION TITLE:** Neonatal/Infant Resuscitation | Neonatal/Infant Resuscitation

**SESSION TYPE:** Webinar|Platform

**ABSTRACT BODY:**

**Background:** Resuscitation with an intact cord in depressed term infants has shown to improve saturation (SpO\(_2\)) and Apgar scores (NEPCORD III trial). Initiating resuscitation with 21% oxygen has been associated with increased death from respiratory failure in extremely preterm infants (Oei et al Pediatrics 2017). We hypothesized that resuscitation with 30-60% oxygen with an intact cord would promote pulmonary vasodilation, enhance gas exchange but would reduce oxygen load (O\(_2\)L) and systemic oxygen toxicity due to continued contribution from umbilical venous flow to left ventricular preload.

**Objective:** To study the effect of delayed cord clamping with ventilation (DCCV) and early cord clamping with ventilation (ECCV) on oxygen (O\(_2\)) exposure, gas exchange and hemodynamics in an asphyxiated preterm ovine model with RDS.
**Design/Methods:** Preterm lambs (127-128d) were randomly assigned to DCCV or ECCV. Asphyxia was induced by cord occlusion until the heart rate (HR) was <90 bpm. In DCCV, positive pressure ventilation (PPV) was initiated with an intact cord for 5 min, followed by clamping. In ECCV, the cord was clamped once target HR<90 bpm was achieved and PPV was initiated. Oxygen load per breath was calculated as [VT*FiO$_2$]/kg, where VT is tidal volume and the total O$_2$L calculated as the summation of breaths for 5 min.

**Results:** Fifteen asphyxiated preterm lambs were randomized to DCCV (N=7) or ECCV (N=8) (fig 1). The FiO$_2$ (0.4 (IQR 0.3-0.4) vs. 0.6 (IQR 0.4-0.8), p<0.01) and O$_2$L (520 (IQR 414-530) vs. 775(IQR 623-868), p<0.01) in the DCCV group were significantly lower than ECCV to maintain target SpO$_2$ (fig 2). Arterial PaO$_2$ and PaCO$_2$ were significantly lower (fig 3) and systolic pulmonary blood flow was higher with DCCV (fig 4).

**Conclusion(s):** In an asphyxiated preterm lambs, resuscitation with an intact cord decreased FiO$_2$ required to achieve NRP recommended target SpO$_2$. Ventilation was significantly better in DCCV suggesting an active contribution of placenta for gas exchange. Lower arterial oxygenation and O$_2$L in the DCCV group along with higher pulmonary blood flow suggests that resuscitation with an intact cord may minimize oxidative injury while facilitating pulmonary vascular transition in asphyxiated preterm infants with RDS.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DCCV (n=7)</th>
<th>ECCV (n=8)</th>
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<tbody>
<tr>
<td>Infant heart rate (bpm)</td>
<td>109 (98-122)</td>
<td>127 (120-130)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>5</td>
<td>4</td>
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<tr>
<td>Birth weight (kg)</td>
<td>1.16 (1.1-1.3)</td>
<td>1.33 (1.2-1.4)</td>
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<tr>
<td>Birth weight (g)</td>
<td>1169 (1020-1340)</td>
<td>1239 (1190-1390)</td>
</tr>
<tr>
<td>Apgar score at 1 minute</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Apgar score at 5 minutes</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Mean blood pressure at asphyxia (mmHg)</td>
<td>24 (12-36)</td>
<td>20 (12-30)</td>
</tr>
<tr>
<td>Mean blood pressure at asphyxia (mmHg)</td>
<td>7.04 (6.0-8.0)</td>
<td>7.29 (6.0-8.0)</td>
</tr>
<tr>
<td>Mean blood pressure at asphyxia (mmHg)</td>
<td>109 (90-119)</td>
<td>86 (70-100)</td>
</tr>
<tr>
<td>Mean blood pressure at asphyxia (mmHg)</td>
<td>151 (111)</td>
<td>136 (113)</td>
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</tbody>
</table>

Data presented as numbers or as average and standard deviation.

**Table 1: Characteristics of preterm lambs**

![Figure 2: Saturations (SpO$_2$) and fraction of inspired oxygen (FiO$_2$) are shown during the first 5 min between DCCV and ECCV. * p<0.05 statistical significance by ANOVA. The grey interrupted line represents NRP recommended SpO$_2$ ranges.]
Figure 3: Gas exchange – Arterial carbon dioxide (PaCO₂) and arterial Oxygenation (PaO₂) are shown during the first 5 min between DCCV and ECCV. * p<0.05 statistical significance by ANOVA.

Figure 4: Hemodynamics – Pulmonary, Carotid and Ductal flow are shown during the first 5 min between DCCV and ECCV. * p<0.05 statistical significance by ANOVA. A positive ductal value indicated right to left ductal shunting.
Continuous Chest Compressions with Asynchronous Ventilations Increase Cerebral Blood Flow and Oxygen Delivery in the Perinatal Asphyxiated Cardiac Arrest Lamb Model

Payam Vali

Vali, Payam; Hardie, Morgan; Lesneski, Amy; Chen, Peggy; Alhassen, Ziad; Ferrier, William; Underwood, Mark A.; Sankaran, Deepika; Joudi, Houssam; Lakshminrusimha, Satyan

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Neonatology

Neonatal/Infant Resuscitation

chest compression, epinephrine.

Neonatal/Infant Resuscitation

Webinar/Platform

Background: In newborns with persistent bradycardia (heart rate <60/min) despite effective ventilation, interrupted chest compressions (CC) 3:1 compression-to-ventilation – C:V ratio with a pause during ventilation; 90 CC/min and 30 breaths/min) are recommended. In neonates, heart rate is the primary determinant of cardiac output and achieving a higher rate of CC (e.g. continuous CC at 120 CC/min and asynchronous ventilations at 30/min) may increase blood flow to essential organs.

Objective: Continuous CC with asynchronous ventilations (CCCaV) leads to quicker ROSC and better hemodynamics compared to the current recommended interrupted 3:1 C:V resuscitation.

Design/Methods: Twenty-two near-term fetal lambs (~140/147d) were partially exteriorized, intubated and instrumented. Lambs were randomized to interrupted 3:1 C:V or CCCaV. Asphyxiation to cardiac arrest (asystole) was induced by cord occlusion. After five min of asystole, positive pressure ventilation (PPV) was provided by a T-piece resuscitator. CC was started after 30s with PPV with 100%O₂. The first dose of epinephrine (EPI) was given at 6 min if return of spontaneous circulation (ROSC) was not achieved and repeated q3 min until ROSC (or max of 4 doses). Invasive arterial blood pressure (BP) and left carotid blood flow were continuously measured. Arterial blood gases were collected at defined time-points during the study period.

Results: There were no differences in baseline characteristics between groups (Table 1). Rate of ROSC was similar in both groups at 91%, as was time to ROSC (5.5 ±2.3 vs. 5.7 ±1.5 min in the 3:1 C:V compared to the CCCaV group, respectively). Lambs that received CCCaV had significantly greater left carotid blood flow compared to 3:1 C:V (7.5 ±3.1 vs. 4.3 ±2.6 ml/kg/min, p <0.01; Fig). During CC, PaO₂ and left carotid oxygen delivery were significantly greater with CCCaV compared to 3:1 C:V (0.4 ±0.15 vs. 0.13 ±0.07 mL O₂/kg/min, p <0.01; Table 2). There was no difference in systolic, diastolic and mean BP between the groups.

Conclusion(s): In a perinatal asphyxiated cardiac arrest lamb model, CCCaV showed greater carotid blood flow and oxygen delivery to the brain compared to the conventional 3:1 C:V resuscitation. No difference between groups was observed in the time to ROSC, the rate of ROSC or the number of EPI doses administered. Clinical studies assessing the survival and neurodevelopmental outcomes comparing CCCaV to 3:1 C:V during newborn resuscitation are warranted.
Background: Acute perinatal asphyxia remains a significant cause of morbidity and mortality. Early return of spontaneous circulation (ROSC) in asphyxial arrest is associated with better outcomes. In severe bradycardia/asystole, NRP recommends administering epinephrine (EPI) by a low umbilical venous catheter (UVC) followed by a saline flush. Umbilical access with a low UVC is time-consuming and requires advanced skills and specialized equipment. Direct umbilical vein (UV) injection offers the potential for quick administration of IV EPI and milking of the cut umbilical cord serves as a flush to propel EPI into the circulation (Figure 1).

Objective: To show feasibility and effectiveness of direct injection of EPI into the UV followed by cord milking as a quick method of IV EPI administration.

Design/Methods: Ten near-term fetal lambs were exteriorized, intubated, and instrumented. The umbilical cord was
occluded to induce asphyxia, then tied and cut at the placental end to leave a long 15-20 cm segment. After a five minutes (min) of asystole, resuscitation following current NRP guidelines was initiated. Upon initiation of chest compressions, preparation to administer EPI began. IV EPI of 0.03 mg/kg/dose was administered into the UV at the base of the umbilicus with a syringe attached to a 23G needle, followed by 3 quick successive cord milkings to flush EPI. If ROSC was not achieved, a UVC was placed and UVC EPI was given and repeated every 3 min until ROSC with a max of 4 doses or 15 min of CPR. Plasma samples were collected to analyze pharmacokinetics.

Results: The average weight of the lambs was 3.65 ± 0.71 kg. The male:female ratio was 6:4. 90% of lambs achieved ROSC; 70% following direct UV EPI injection alone. Average time of UV EPI administration was 2.28 ± 2.13 min and average time to ROSC was 5.82 ± 2.81 min. Plasma EPI assay concentration for two lambs showed an average concentration of 562 ± 471 ng/mL, similar to historical values following UVC injection of 0.03 mg/kg EPI (450 ± 190 ng/ml, Vali et al. JAHA 2017).

Conclusion(s): In an asphyxia cardiac arrest lamb model, direct UV EPI administration followed by cord milking is quick and efficacious with a good success rate of ROSC. Preliminary data suggest adequate epinephrine plasma concentration following direct UV EPI administration. Experiments are underway to compare success and time to ROSC between direct UV and UVC EPI administration. Further evaluation of direct UV EPI followed by cord milking may have high relevance in resource-limited settings.

Figure 1. Direct injection of EPI with a 23G needle into the base of the umbilical vein followed by milking of the cut umbilical cord to flush EPI into the circulation.

Table 1. Compiled resuscitation data by individual lamb experiment.

IMAGE CAPTION:
Figure 1. Direct injection of EPI with a 23G needle into the base of the umbilical vein followed by milking of the cut umbilical cord to flush EPI into the circulation.

Table 1. Compiled resuscitation data by individual lamb experiment.

CONTROL ID: 3380291
TITLE: Return of Spontaneous Circulation is Associated with Excess Oxygen Delivery in Near-term Asphyxiated Lambs
PRESENTER: Shiraz Badurdeen
AUTHORS (LAST NAME, FIRST NAME): Badurdeen, Shiraz1; Gill, Andrew W.2; Kluckow, Martin3; Roberts,
Background: Tailoring delivery room management of infants with hypoxic-ischemia to reduce early secondary brain injury may improve short and long-term outcomes.

Objective: We aimed to describe cerebral oxygen kinetics and hemodynamics following return of spontaneous circulation (ROSC) and identify physiological correlates for non-invasive bedside monitoring.

Design/Methods: Near-term sheep fetuses (139±2 (SD) days gestation, n=16) were instrumented to measure carotid artery flow, pressure, right brachial arterial and jugular venous saturation (SaO₂ and SvO₂, respectively). Cerebral oxygenation (crSO₂) was measured using near-infrared spectroscopy (NIRS). Fetal asphyxia was induced by umbilical cord clamping or internal iliac artery occlusion. All ventilated newborn lambs received cardiopulmonary resuscitation in 100% oxygen until ROSC, with oxygen subsequently weaned according to saturation nomograms.

Results: Oxygen delivery (DO₂) was markedly elevated until 15 minutes after ROSC. Cerebral fractional oxygen extraction (cFOE) was low during this period before returning to fetal levels, indicating excessive DO₂ in relation to oxygen consumption. The surge in DO₂ was mediated by a pressure-passive increase in carotid artery flow (Figure 1). Changes in heart rate and crSO₂ between adjacent timepoints correlated strongly with fluctuations in both DO₂ and mean carotid artery blood pressure (CAp). An increase in heart rate by 80 beats per minute or crSO₂ by 15% between timepoints corresponded in all instances with a rise in DO₂ by 150ml/kg/min and/or an increase in CAp by 20mmHg. In contrast, SaO₂ levels showed little change when DO₂ varied between -100 to +100 ml/kg/min (Figure 2). Following ROSC, SaO₂ remained >90% and was less useful for identifying trends in DO₂ or cFOE. CrSO₂ correlated inversely with cFOE, allowing monitoring of oxygen delivery-consumption matching.

Conclusion(s): ROSC from perinatal asphyxia is characterized by excess oxygen delivery that is driven by rapid increases in cerebrovascular pressure, flow, and oxygen saturation. Fluctuations in DO₂, cFOE and carotid artery pressure may be monitored using NIRS and heart rate. However, SpO₂ levels are less useful, remaining normal or high once ROSC is achieved. The current standard of SpO₂ targeting during resuscitation following perinatal hypoxic-ischemia should be re-evaluated.
Figure 1. Changes in oxygenation and hemodynamic parameters following return of spontaneous circulation (ROSC). (A) Spontaneous respiration in the first 120 min. (B) Changes in airway pressure (CPP) and mean arterial pressure (MAP) over time. (C) Changes in heart rate (HR) and mean arterial pressure (MAP) over time. (D) Changes in inspired oxygen saturation (Sätt) and central venous oxygen saturation (Scvo2) over time. 
**AUTHORS/INSTITUTIONS:** M. Bruschettini, Cochrane Sweden, Lund University Hospital, Lund, SWEDEN; C.P. O'Donnell, Neonatal Unit, National Maternity Hospital, Dublin, IRELAND; P.G. Davis, Neonatal Research, Royal Women's Hospital, Melbourne, Victoria, AUSTRALIA; C.J. Morley, Dept Obstetrics and Gynecology, University of Cambridge, Cambridge, UNITED KINGDOM; L. Moja, Dept Biomedical Sciences for Health, University of Milan Clinical Epidemiology Unit, IRCCS Galeazzi Orthopaedic Institute, Milan, ITALY; M. Calevo, Epidemiology, Biostatistics and Committees Unit, Istituto Giannina Gaslini, Genoa, ITALY;

**CURRENT CATEGORY:** Neonatology
**CURRENT SUBCATEGORY:** Neonatal/Infant Resuscitation
**KEYWORDS:** metanalysis, sustained inflation, resuscitation.

**SESSION TITLE:** Neonatal/Infant Resuscitation
**SESSION TYPE:** Webinar/Platform

**ABSTRACT BODY:**

**Background:** At birth, infants' lungs are fluid-filled; this fluid must be replaced by air to allow for effective breathing. Some infants are judged to have inadequate breathing at birth and are resuscitated with positive pressure ventilation (PPV). Giving sustained lung inflations (SLI) may help clear lung fluid and more rapidly establish lung aeration.

**Objective:** We assessed the efficacy of an initial SLI (> one second duration) compared to standard inflations (≤ one second) in newly born infants receiving resuscitation with intermittent PPV.

**Design/Methods:** We searched the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL, clinical trials databases, conference proceedings, and the reference lists of retrieved articles for randomized controlled trials (RCTs) and quasi-RCTs. We included trials comparing giving SLI versus standard inflations to infants receiving resuscitation with PPV at birth. We assessed methodological quality of the included trials using Cochrane Effective Practice and Organisation of Care Group (EPOC) criteria.

**Results:** Ten RCTs enrolling 1467 infants met our inclusion criteria. Investigators in 9 RCTs (1458 infants) administered SLI with no chest compressions. Use of SLI had no impact on the primary outcomes of this review - mortality in the delivery room (typical RR 2.66, 95% confidence interval (CI) 0.11 to 63.40 (I² not applicable); typical RD 0.00, 95% CI -0.02 to 0.02 (I² 0%); participants = 479; studies = 5) and mortality during hospitalisation (typical RR 1.09, 95% CI 0.83, 1.43 (I² 42%); typical RD 0.01, 95% CI -0.02 to 0.04 (I² 24%); participants = 1458; studies = 9). The quality of the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) was low for death in the delivery room because of limitations in study design and imprecision of estimates (only one death was recorded across studies). For death before discharge the quality was moderate: with longer follow-up there were more deaths (n=143) but limitations in study design remained.

**Conclusion(s):** Our meta-analysis shows that SLI was not better than intermittent ventilation for reducing mortality in the delivery room (low-quality evidence) or during hospitalization (moderate-quality evidence); the primary outcomes of this review. However, the most recent RCT, which was well-conducted and had the largest sample size, was stopped early for higher mortality rate at 48 hours in the SLI group. There is no evidence to support the use of sustained inflation based on evidence from our review.

**PRISMA flow diagram**
Risk of bias summary

Forest plot for death

**IMAGE CAPTION:**
PRISMA flow diagram

Risk of bias summary

Forest plot for death