Evaluating Quality Improvement Initiatives for Respiratory Distress

Insights for Adopting an Early Rescue Strategy

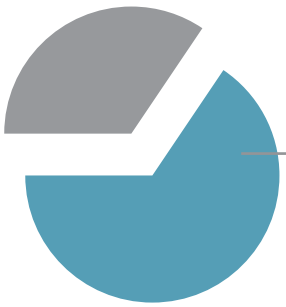
Please see Important Safety Information on back cover

Chiesi

RESPIRATORY DISTRESS SYNDROME AND SURFACTANT ADMINISTRATION

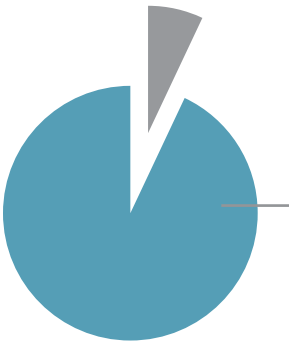
Premature birth: A significant concern

In 2020, 10% of infants born in the United States were premature (<37 weeks gestational age [GA]).[1] Premature infants are at a higher risk for developing complications.[2,3] (For additional information, see Stoll and Pravia, 2020.[3,4]) In the United States, 66% of all infant deaths in 2019 occurred in premature infants.[5]



66%
OF ALL INFANT DEATHS IN 2019 OCCURRED IN PREMATURE INFANTS[5]

In a study of infants born extremely preterm (22-28 weeks GA), 93% developed respiratory distress syndrome (RDS).[3] Therefore, it is important to have an effective protocol in place for the management of RDS in the neonatal intensive care unit (NICU).



93%
OF EXTREMELY PRETERM INFANTS (22-28 weeks GA) DEVELOPED RDS[3]

Surfactant replacement therapy

Primary surfactant deficiency in premature infants can result in atelectasis and poor lung compliance, contributing to RDS. Surfactant replacement therapy is intended to replace the endogenous surfactant the infant is not producing in sufficient quantities, and plays an important role in treating RDS.[6] In a study evaluating premature infants born between 2000 and 2009 at Vermont Oxford Network (VON) hospitals, a majority (66%) of those weighing 501 to 1500 g were treated with surfactant.[7]

ALIGNING NICU PROTOCOLS TO INDIVIDUALIZE CARE

Individualizing care

Clinicians today have many choices regarding ventilation modes (eg, mechanical ventilation [MV], nasal continuous positive airway pressure [nCPAP], noninvasive positive-pressure ventilation [NIPPV], high-frequency ventilation [HFV], neurally adjusted ventilatory assist [NAVA]) and must not only select the mode that is right for each neonate, but also determine if and when to incorporate surfactant. Because premature infants with RDS can differ in disease severity, GA, and comorbidities, treatment protocols should account for individualization of care.[8,9] For example, in the most premature infants, rapid extubation after surfactant administration may not be achievable or desirable. Ultimately, it is up to the clinician to decide when each infant is stable enough to be extubated or transitioned to noninvasive ventilation.[10]

Recent recommendations support less-invasive RDS treatment protocols

Improvements in prenatal care, such as increased use of antenatal corticosteroids, have reduced the need for routine intubation and subsequent MV for many infants.[11-14] Postdelivery treatment protocols have also evolved: Less-invasive ventilation, such as CPAP, is a viable option for initial stabilization in many infants. Due to long-term complications of MV, such as bronchopulmonary dysplasia (BPD), invasive ventilation is typically recommended as a lifesaving measure only for infants who fail noninvasive support.[15,16]

In line with these respiratory support advances, the use of surfactant has also evolved. In 2014, the American Academy of Pediatrics (AAP) published specific recommendations regarding the management of infants in need of respiratory support.[10,11]

2014 American Academy of Pediatrics Recommendations[10,11]	
STRONG RECOMMENDATION	CPAP immediately after birth with subsequent selective surfactant administration may be considered as an alternative to routine intubation
STRONG RECOMMENDATION	If respiratory support with a ventilator is likely needed, early administration of surfactant followed by rapid extubation is preferable to prolonged ventilation

There have been additional changes in other guidelines globally since 2014:

- In 2019, the European Consensus Guidelines revised its optimal threshold, recommending that when an infant with RDS on CPAP has fraction of inspired oxygen (FiO_2) >0.3, exogenous surfactant should be administered[17*]
- In 2021, the Canadian Paediatric Society updated its guidelines for surfactant replacement therapy. The updated guidelines recommended CPAP use in preterm infants with RDS at birth and early surfactant administration to infants with severe RDS and/or increased oxygen requirements of FiO_2 0.3 to 0.5[18*]

Teamwork and communication among the stakeholders

Management of RDS is complex, and the care delivered in the first few hours of life can affect outcomes. For this reason, teamwork and communication are critical in optimizing neonatal care.[19] This teamwork begins as early as the planning phase during protocol development and should be maintained throughout each infant's care. Close partnerships among neonatologists, nurse practitioners (NPs), registered nurses (RNs), respiratory therapists (RTs), pharmacists, physical therapists (PTs), and physician assistants (PAs) are essential to ensure that the best RDS protocols are chosen and followed throughout each premature infant's stay.

Stakeholders to consult

Consultation and collaboration with all stakeholders can help to identify and weigh how different protocol considerations may impact patient treatment goals. Gathering information from these stakeholders creates potential partnerships with leadership across the institution. Some individuals to consider consulting include:

- NICU medical director
- Staff neonatologists
- NICU nurse manager
- Director of respiratory services
- NICU clinical pharmacist
- Hospital director of pharmacy

Open communication, early and often, can help keep everyone on the same page, minimize delays in care, and ensure buy-in to the final consensus protocol for your institution.

*The European Consensus and Canadian Paediatric Society guidelines on the managing of RDS reflect the clinical practice standards and medications approved for use in European Union (EU) and Canadian hospitals, respectively; as such, certain recommendations may not be relevant to US clinical practice. US, EU, and Canadian patient populations and clinical practice standards are widely accepted to be distinct; therefore, there may be significant limitations to the extrapolation of certain data from EU and/or Canadian studies to the US patient population.

Delivery room and NICU decisions

Collaboration among all stakeholders can help identify and balance unique concerns that may impact patient treatment goals.

- Delivery room teams are present both before and after the birth of the premature infant and are responsible for all initial treatments, including resuscitation and stabilization immediately after birth. Infants in need of long-term care will subsequently be passed to the NICU teams[20]
- NICU teams receive the stabilized infant and are responsible for continuing care after stabilization, including continuous evaluation of treatments initiated by the delivery room team to determine any necessary changes as the infant's condition changes[20]

It is critical to have separate protocols defined for the delivery room and for the NICU. Protocols that define each stakeholder's role ensure that everyone understands what to do in specific environments. This ensures all members of the care team are prepared to act immediately during the first few critical hours of an infant's life.[21]

CONSIDERATIONS FOR EARLY SURFACTANT ADMINISTRATION

Golden Hour Initiative

The Golden Hour Initiative describes the first few hours after birth, during which the focus is on initial stabilization and continued monitoring of the premature infant to improve infant outcomes. Efficient evidence-based care during this time includes thermoregulatory aid, respiratory support, cardiovascular stability, and fluid management.[22,23]

Optimal golden hour stabilization may improve important outcomes for preterm infants[24]

Early rescue strategy

Early rescue can be defined as the administration of surfactant within the first 2 hours of life for infants with RDS or CPAP failure. Early rescue with surfactant therapy fits within the Golden Hour Initiative, both in the timing—occurring <2 hours after birth—and the decision to treat RDS.[11] An early rescue strategy identifies infants at high risk for developing RDS, seeks the earliest possible detection of RDS, and aims both to treat RDS and prevent complications from developing.[11,24]

Predicting CPAP failure to increase the odds of successful outcomes

Noninvasive respiratory therapy is recommended for initial treatment of premature infants in need of respiratory support.[18,25,26] CPAP is one such assistive ventilation tool widely and successfully used both in the United States and worldwide.[17,25,26] However, not all infants thrive on CPAP. In one study of 66 infants born between 25 and 28 weeks gestation, 30 infants failed CPAP (defined as the need for mechanical ventilation within 72 hours after birth).[26] Investigation into the health of infants who experienced CPAP failure revealed a significantly higher risk for major morbidity or death compared with infants who responded to CPAP therapy.[27]

Prompt recognition of CPAP nonresponders is key to successful early rescue with surfactant replacement.[28] Using stringent and outdated definitions of CPAP failure may delay surfactant therapy beyond the Golden Hour Initiative and lead to potentially preventable lung damage.[26,28,29]

Incorporate multiple factors to evaluate an infant's risk for CPAP failure

Multiple studies have investigated a variety of factors to consider when looking for early signs of respiratory distress and predicting CPAP failure.[26,28,30,31] These risk factors encompass objective measurements of respiratory function and infant characteristics, as well as clinical observation of subjective signs and symptoms, both with respect to the infant and mother.

Infant factors that may contribute to an increased risk for RDS, CPAP failure, and the need for early surfactant administration[8,30]:

- <32 weeks GA
- Cesarean delivery
- Hypothermia
- Low birth weight/GA
- APGAR score ≤3 at 1 minute
- Silverman score >2 at 2 hours
- Objective RDS symptoms (high oxygen requirements eg, FiO_2 >0.30, apnea, rapid breathing, cyanosis)
- Subjective RDS symptoms (nasal flaring, working hard to breathe, grunting, and rib retractions)

Maternal factors that may contribute to an infant's increased risk for RDS, CPAP failure, and the need for early surfactant administration[17,31-36]:

- No antenatal steroid use
- Premature rupture of membranes
- Comorbidities (eg, hypertension, overweight/obesity, diabetes)
- Nutritional status
- Smoking
- Exposure to air pollution
- Social disadvantages

FiO_2 strongly predicts CPAP failure

One final factor that may strongly predict CPAP failure is FiO_2. Multiple studies have investigated potential thresholds for the optimal criteria to begin exogenous surfactant to provide the best care of premature infants. In a retrospective study of infants from 23 to 29 weeks gestation, changing the FiO_2 threshold from ≥0.60 to ≥0.35-0.45 would reduce the time to recognize CPAP failure and administer surfactant therapy.[28] Multiple studies investigated the FiO_2 threshold that could predict a greater percentage of CPAP failures. These studies found that an FiO_2 threshold of ≥0.3 could predict 70% to 83% of infants at risk for CPAP failure during the first 2 hours of life.[26,37,38]

FiO_2 ≥0.3 in first 2 HOURS of life predict[26,37,38]

>70% OF INFANTS at risk for CPAP failure[26,37,38]

These data support early rescue with exogenous surfactant, defining the level of FiO_2 at which it is advantageous for the infant to be treated with surfactant replacement therapy.

Lower FiO_2 thresholds and earlier administration of surfactant after birth are also supported by clinical guidelines released by the 2014 AAP Committee on Fetus and Newborn and the 2019 European Consensus Guidelines on the Management of RDS.[11,17]

In patients with multiple risk factors for CPAP failure, an individualized approach with early CPAP, lower FiO_2 threshold, and early surfactant replacement therapy may improve premature infant outcomes [26,28,37,38]

QUALITY IMPROVEMENT INITIATIVES DRIVE ENHANCED QUALITY CARE

Developing QI initiatives

Having reviewed the considerations for early rescue treatment of RDS with surfactant administration and multiple risk factors for CPAP failure, it is clear that providers have many factors to integrate into their care plan to optimize RDS treatment for a premature infant. Admittedly, although the guidelines leave room for individualization of care, that also leaves room for unclear interpretation of the recommendations, which may introduce inconsistent care from one provider to the next. Developing quality improvement (QI) initiatives are an efficient and productive way for the care team to align protocols and optimize care.

Every delivery room and NICU provider makes multifactorial risk assessments when caring for a preterm infant, monitoring a variety of clinical measures during the Golden Hour Initiative and beyond. It has been shown repeatedly that patient outcomes improve when employing continuous QI initiatives to ensure adherence to best care practices.[25,29]

To begin any QI initiative, the burden is on providers and hospitals to collect and review data, arrive at a consensus, and make clear recommendations to bring consistency and quality to neonatal care. Additionally, implementing standardized QI initiatives may mitigate the risk for unequal management for care based on individual biases.

Sample/Potential QI initiatives

QI initiatives allow for the measurement of outcomes across pre-established goals set by the providers and hospitals. Some suggested goals of QI initiatives that incorporate early rescue strategy include:

- Reducing the number of days on MV
- Decreasing reintubations
- Reducing CPAP failures
- Reducing the number of patients requiring MV in first 72 hours
- Reducing the rates of severe complications (ie, BPD and pneumothorax)

In addition to promptly recognizing risk factors of the infant and mother (described on page 5), the following are approaches to consider when aiming to achieve QI goals:

- Extubate early and continue noninvasive ventilation
- Administer surfactant at the first signs of RDS (early rescue)
- Identify infants at risk for CPAP failure and treat accordingly
- Begin respiratory management in the delivery room and maintain that management in the NICU

By taking the initiative to implement early rescue QI protocols, providers and hospitals may bring even greater consistency and quality to neonatal care.

Driving change in practice

Once a QI initiative is developed and agreed upon, all stakeholders must implement the change consistently throughout the institution. The following are multiple ways in which to approach this transformation and drive change in your practice:

- Showcase evidence to guide practice by aggregating, synthesizing, and disseminating the data
- Track metrics when participating in QI initiatives (eg, VON Collaborative)
- Develop multimodal training to increase confidence in the data and maintain a high level of competency with procedures, even as they change over time
- Establish new protocols for standardization within and among practice settings (eg, collect and share data with leadership before proposing practice changes)
- Create methods for real-time review of evidence-based practices (eg, establish a respiratory director role responsible for weekly rounds)
- Engage critical stakeholders such as neonatologists, NPs/RNs, RTs, pharmacists, PTs, and PAs

See Resources and Additional Information on pages 8-9

RESOURCES AND ADDITIONAL INFORMATION

Predicting CPAP failure

Multifactorial risk assessment is integral to delivery room and NICU management of a preterm infant. The following articles detail infant and maternal factors that may influence the risk for CPAP failure.

INFANT

- Fuchs H, Lindner W, Leiprecht A, Mendler MR, Hummler HD. Predictors of early nasal CPAP failure and effects of various intubation criteria on the rate of mechanical ventilation in preterm infants of <29 weeks gestational age. *Arch Dis Child Fetal Neonatal Ed.* 2011;96:F343-F347.
- Dargaville PA, Gerber A, Johansson S, et al. Incidence and outcome of CPAP failure in preterm infants. *Pediatrics.* 2016;138(1):e20153985.
- Kakkilaya V, Wagner S, Mangona KLM, et al. Early predictors of continuous positive airway pressure failure in preterm neonates. *J Perinatol.* 2019; 39:1081-1088.
- Gulczyńska E, Szczapa T, Hożejowski R, Borszewska-Kornacka MK, Rutkowska M. Fraction of inspired oxygen as a predictor of CPAP failure in preterm infants with respiratory distress syndrome: a prospective multicenter study. *Neonatology.* 2019;116(2):171-178.

MOTHER

- Ovesen P, Rasmussen S, Kesmodel U. Effect of prepregnancy maternal overweight and obesity on pregnancy outcome. *Obstet Gynecol.* 2011;118:305-312.
- Tian T, Wang L, Ye R, Liu J, Ren A. Maternal hypertension, preeclampsia, and risk of neonatal respiratory disorders in a large-prospective cohort study. *Pregnancy Hypertens.* 2020;19:131-137.
- Barfield W. Social disadvantage and its effect on maternal and newborn health. *Semin Perinatol.* 2021;45:151407.
- Terfa ZG, Nantanda R, Lesosky M, et al. Household food insecurity, maternal nutrition, environmental risks and infants' health outcomes: protocol of the IMPALA birth cohort study in Uganda. *BMJ Open.* 2022;12:e050729.

Delivery room and NICU QI

Establishing a hospital protocol based on evidence-based practices and standardizing its implementation across your team can improve quality and consistency of care in premature infants. The following studies demonstrate how other institutions successfully initiated NICU QI initiatives.

- DeMauro SB, Douglas E, Karp K, et al. Improving delivery room management for vey preterm infants. *Pediatric.* 2013;132(4):e1018-1025.
  - Implementing evidence-based guidelines, DeMauro et al. significantly reduced hypothermia and supplemental oxygen exposure and increased the use of noninvasive respiratory support in the delivery room for very preterm infants.
- Croop SEW, Thoyre SM, Aliaga S, McCaffrey MJ, Peter-Wohl S. The golden hour: a quality improvement initiative for extremely premature infants in the neonatal intensive care unit. *J Perinatol.* 2020;40(3):530-539.
  - Using a golden hour QI initiative, Croop et al. successfully reduced hypothermia and hypoglycemia in infants <27 weeks gestation.
- Ratliff-Crain D, Wallingford B, Jorgenson L. Using a bundle approach to prevent bronchopulmonary dysplasia in very premature infants. *Adv Neonatal Care.* 2022;22(4):300-308.
  - Using a multidisciplinary bundle approach guided by plan-do-study-act (PDSA) cycles, Ratliff-Crain et al. decreased use of MV and use of oxygen at discharge, and decreased the severity of BPD.
- Travers CP, Gentle S, Freeman AE, et al. A quality improvement bundle to improve outcomes in extremely preterm infants in the first week. *Pediatrics.* 2022;149(2):e2020037341.
  - By ensuring adherence to a bundle of evidence-based practices, Travers et al. reduced the rate of intracranial hemorrhage or death in the first week of life in infants <27 weeks gestation.

Framework to begin a QI initiative

Once the multidisciplinary team is established, the next step includes investigation of various frameworks and tools to help structure the QI intervention and decide on a NICU smart aim. The following articles illustrate several strategies and useful diagrams of previous QI initiatives to help you and your institution frame your own NICU QI initiative.

- Read B, Lee DSC, Fraser D. Evaluation of a practice guideline for the management of respiratory distress syndrome in preterm infants: a quality improvement initiative. *Paediatr Child Health.* 2016;21(1):e4-e9.
  - Read et al. used a QI initiative to minimize the use of MV and evaluated the effect that implementing the new practice guideline had on respiratory outcomes of premature infants. Additionally, they describe the use of an audit tool that allowed them to monitor compliance with the new guideline and include the tool itself.
- Picarillo AP, Carlo W. Using quality improvement tools to reduce chronic lung disease. *Clin Perinatol.* 2017;44:701-712.
  - Picarillo and Carlo describe several QI strategies that may lead to the goal of reducing chronic lung disease: the proposed changes in protocol, identifying existing barriers within the team, and evaluating output measurements. They include a key driver diagram that details the aim, primary and secondary drivers, and the interventions needed for an example QI project.
- Kim JE, Brewer M, Spinazzola R, et al. A quality improvement project to standardize surfactant delivery in the era of noninvasive ventilation. *Pediatr Qual Saf.* 2020;5(4):e311.
  - Kim et al. aimed to standardize RDS diagnosis and reduce the time to intubation and surfactant administration, with a long-term effect of reducing BPD and other respiratory difficulties. They describe their process of developing the QI initiative in detail, including specific PDSA cycles that focused on incremental ways to achieve their QI goal.

In addition to the preceding articles, the following links to QI initiative tools may be helpful:

- Institute for healthcare Improvement: http://www.ihi.org/resources/Pages/Tools/Quality-Improvement-Essentials-Toolkit.aspx
- Vermont Oxford Network: https://portal.vtoxford.org/

Please see References on pages 10-11

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INDICATION

CUROSURF® (poractant alfa) Intratracheal Suspension is indicated for the rescue treatment of Respiratory Distress Syndrome (RDS) in premature infants. CUROSURF reduces mortality and pneumothoraces associated with RDS.

IMPORTANT SAFETY INFORMATION

CUROSURF® (poractant alfa) is intended for intratracheal use only. The administration of exogenous surfactants, including CUROSURF, can rapidly affect oxygenation and lung compliance. Therefore, infants receiving CUROSURF should receive frequent clinical and laboratory assessments so that oxygen and ventilatory support can be modified to respond to respiratory changes.

CUROSURF should only be administered by those trained and experienced in the care, resuscitation, and stabilization of preterm infants.

Transient adverse reactions associated with administration of CUROSURF include bradycardia, hypotension, endotracheal tube blockage, and oxygen desaturation. These events require stopping CUROSURF administration and taking appropriate measures to alleviate the condition. After the patient is stable, dosing may proceed with appropriate monitoring.

Pulmonary hemorrhage, a known complication of premature birth and very low birth-weight, has been reported with CUROSURF. The rates of common complications of prematurity observed in a multicenter single-dose study that enrolled infants 700–2000 g birth weight with RDS requiring mechanical ventilation and $FiO_2 \geq 0.60$ are as follows for CUROSURF 2.5 mL/kg (200 mg/kg) (n=78) and control (n=66; no surfactant) respectively: acquired pneumonia (17% vs. 21%), acquired septicemia (14% vs. 18%), bronchopulmonary dysplasia (18% vs. 22%), intracranial hemorrhage (51% vs. 64%), patent ductus arteriosus (60% vs. 48%), pneumothorax (21% vs. 36%) and pulmonary interstitial emphysema (21% vs. 38%).

Please see accompanying full Prescribing Information.

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