Tennessee's Tiniest Babies: Chronic Lung Disease (CLD)

Tennessee Initiative for Perinatal Quality Care

Inter-Institutional Quality Improvement Project

Funded under a grant from the Tennessee Department of Health (TDH)

Project Development Leaders
Scott Guthrie, MD
State Project Leader & TIPQC Infant Medical Director

Malinda Harris, MD
East Tennessee Children's Hospital

Vineet Lamba, MD
Regional One Medical Center

Marla Kirk, MBA, RRT
Methodist LeBonheur Germantown Hospital

Patricia A. Scott, DNP, APRN, NNP-BC, C-NPT
TIPQC Infant Quality Improvement Specialist

Brenda Barker, MEd, MBA
TIPQC Executive Director

Sharon Wadley, BSN, RN, CLS, CCRP
TIPQC Data Manager

Michael Devoe, MD

DISCLAIMER: The authors of this toolkit used reasonable efforts to provide accurate information. The information and resources included in this toolkit are provided for informational purposes only. Nothing contained herein constitutes medical, legal, or other professional advice nor does it represent an endorsement of any treatment or particular product. Referral to specific programs, resources, or websites does not imply endorsement by the toolkit's authors or the authors' organizations or their sponsors, contents, expressed views, programs or activities. Further, the authors do not endorse any commercial products that may be referred to in this toolkit or that may be advertised or available from these programs, resources, or websites. This toolkit is not meant to be comprehensive; the exclusion of a program, resource or website does not reflect the quality of that program, resource, or website. Please note that websites and URLs are subject to change without advance notice.

The Tennessee Initiative for Perinatal Quality Care (TIPQC) would like to thank other PQCs who have done this project. We have learned from their efforts and initiatives and have adapted portions from this work. Together, we can make a difference!

Project Pilot Teams

Jackson-Madison County General Hospital, East Tennessee Children's Hospital, Regional One Health, and Niswonger Children's Hospital

Tennessee Tiniest Babies Review Committee:

Kirk Bass, MD
Mike Devoe, MD
Amy Hall, NP
Dupree Hatch, MD
Kristi Ramirez, RRT
Darshan Shah, MD
Ajay Talati, MD
Amy Whittlesey, NP

Specific Acknowledgments

Thanks to those who served on the Tennessee Tiniest Babies Committee to help draft and formulate the ongoing quality improvement initiatives for the Level III and IV NICUs in the state, and especially thanks to the project leaders who met weekly to develop and finalize this project. Your tireless effort and dedication to our state's smallest citizens is inspiring—and will result in improved care, outcomes, and better quality of life for these infants and their families.

Table of Contents

Introduction: *What are we trying to accomplish?*

Problem

Tennessee's preterm birth rate is amongst the highest in the nation as approximately 11% of all births in Tennessee are preterm.[1] Deaths secondary to prematurity are one of the leading contributors to Tennessee's high infant mortality rate (IMR).[2] This has historically been approximately 7 deaths per 1,000 live births.[3] While the IMR has decreased for both Black and White infants, the rate of infant mortality is still 50% higher for Black infants in Tennessee compared to White infants. A stated national priority in the "2030 Healthy People" objectives is the reduction of the US infant mortality rate to 5 deaths per 1,000 live births.[4] For Tennessee to meet this goal, there will need to be a reduction of approximately 25% of the current infant mortality rate.

Preterm birth is a multi-factorial problem, despite national and state efforts, that remains relatively unchanged.[5] [6] Specifically, an increase in the number of the earliest preterm births (infants with birth weights of <750 grams (g) and gestational age of <28 weeks) has been implicated as the primary contributor to infant mortality rates.[7] Very preterm births, defined as <32 weeks and birth weight <1500g, represented 33% of all infant deaths in one report. In this study, more than two thirds of deaths attributable to preterm birth occurred during the first day of life and 27% of deaths occurred within the next 27 days. [8]

Variation in outcomes among NICUs have also been reported.[9] [10] [11] Practice variation, even amongst providers in the same group, can be a contributing factor to these varied outcomes.[12] [13] We have fortunately witnessed significant progress in the care of preterm infants over the past few decades. These advances have gradually moved from new technologies and medicines to how we care for these infants. This has led to improved survival rates and outcomes by the centers who have focused on improving the delivery of care.[14]

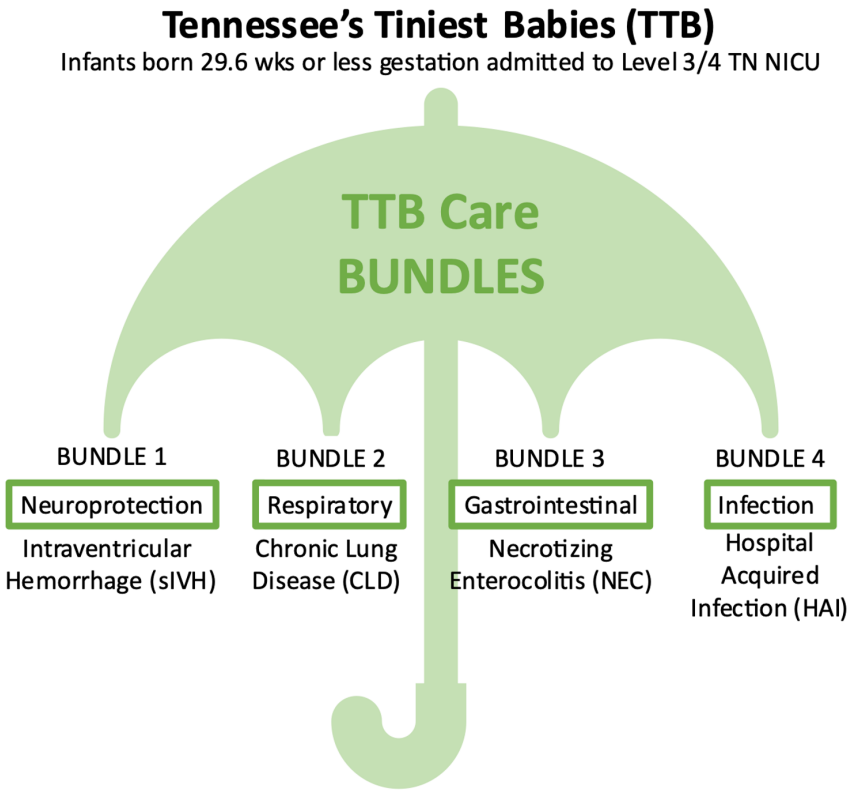
Tennessee has twelve level 3 and 4 NICUs across the state who care for infants <32 weeks and a birth weight <1500g. In 2020, 1,352 babies, or 1.7% of live births, were born very preterm (<32 weeks and birth weight <1500g) in Tennessee and cared for at these facilities. [3] Statistically, this group of infants represents approximately one-third of our state's infant deaths. To lower Tennessee's infant mortality rate, meet the goal as put forth in the "2030 Healthy People" objectives, and improve outcomes by reducing differences in care, a collaborative approach to the care along with the implementation of effective care strategies for Tennessee's Tiniest Babies should be undertaken.

Project Description (*what*)

We are seeking to lower Tennessee's infant mortality rate to 5 deaths per 1,000 live births by focusing on the implementation of potentially better practices which can improve the survival rates and the outcomes of preterm infants born at less than 29.6 or less weeks gestation.

The development and implementation of the "Tennessee's Tiniest Babies'' (TTB) project will occur from Q3 2022 to Q3 2027. The project has been developed and will be launched in phases determined by specific care *bundles* – see Figure 1. The intent is to have participating hospitals implement the care bundles *cumulatively* – incorporating the potentially better practices from each bundle into their unit. *This toolkit is focused on the reduction of chronic lung disease (CLD) care bundle.* The project is proposed to end in Q3 2025.

Figure 1: Tennessee's Tiniest Babies (TTB) Care Bundles



TIPQC agrees to the following:

- Provide a toolkit (see attachments) and other resources to participating teams.
- Offer monthly huddles, quarterly learning sessions, and annual statewide meetings.
- Facilitate the sharing between participating teams, allowing them to learn from each other.
- Facilitate capture of data metrics and provide reports to participating teams to show their progress towards improvement.
- Provide guidance and feedback to participating teams, facilitating their achievement of the project aim.

Participating teams will agree to the following:

- Hold regular, at least monthly, team meetings.
- Regularly review and revise your goals, current system, opportunities for improvement, and barriers.
- Plan and conduct tests of the recommended changes detailed in this toolkit.
- After successful testing and adaptation, implement the changes in your facility.
- Attend and actively participate in the monthly huddles, quarterly learning session, and annual statewide meetings.
- Capture and submit the defined project data as required (with minimal to no data lag).
- Submit a monthly report that includes data as well as information on changes being tested and/or implemented.
- Strive to achieve the project aim and the project's process and structure measure goals:
    - At least 90% compliance on all defined process measures.
    - Have all structures (defined by the structure measures) in place by the end of the project.

A dedicated extremely low birth weight (ELBW) team of staff (physicians, NNPs, nurses, respiratory therapists, speech/physical/occupational therapists, and lactation consultants) that have received special training in care of these babies can have a big impact on overall care delivered. Many units across the country have developed small baby units dedicated to providing care for the ELBW infants and have seen a significant reduction in mortality and morbidity in this

population. Providing detailed guidelines to develop small baby units are out of scope for this project, but each unit should assess its own capability /resources to develop specialized protocols/guidelines to care for their smallest babies.

Rationale (*why*)

Despite early improvements with concerted efforts to improve the care of expectant mothers and infants, Tennessee's preterm birth rate and infant mortality rate have shown no significant, nor maintained, drop over the past decade. Twelve NICU's across the state care for infants which comprise approximately one-third of the state's infant mortality rate. No project has addressed the optimization of care in this population to improve the infant mortality rate despite this population's statistical importance.

There is a significant variation of care in the very preterm infant (29.6 weeks or less). Some NICUs in Tennessee have individually developed and implemented potentially better practices for the care of this population. Resources at many of the other centers have made this difficult.

The California Perinatal Quality Care Collaborative (CPQCC) has previously demonstrated the impact a state's PQC can have on the mortality and morbidity in the very preterm infant population. CPQCC led a Delivery Room QI Collaborative which resulted in a reduction in mortality, severe intraventricular hemorrhage (sIVH), chronic lung disease (CLD), and retinopathy of prematurity (ROP) in infants 29.6 weeks or less[15]. As the state's perinatal care collaborative, TIPQC is poised to guide participating level 3 and 4 NICUs in the sharing of information and resources so that potentially better practices for this population can be developed and implemented across the network. Several of the participating hospitals already submit their data to the Vermont Oxford Network.

Expected Outcomes and Benefits

Participating in this project will help participating centers improve the care of the very preterm infant (29.6 weeks or less) at their site. If successful, this project will (in turn) result in an improved survival rate with decreased morbidities in very preterm infants born in Tennessee. This will lead to meeting the "2030 Healthy People" objective. Ultimately, improving outcomes in Tennessee's Tiniest Babies should lead to decreased long term costs to the healthcare system.

Aim Statement

The aim of the overarching TBB quality improvement (QI) project is:

- To reduce the mortality in infants less than or equal to 29.6 weeks gestational age by 25% of the Tennessee state baseline. There should be a dose response effect seen with the implementation of bundles which address broader global aims.

<u>The aim of this CLD care bundle is:</u>

- 25% relative reduction (over last 3 years institutional baseline) in chronic lung disease in infants less than or equal to 29.6 weeks gestational age in participating TN NICUs by June 2025.
- Secondary aim: 10% relative reduction in Grade 3 bronchopulmonary dysplasia (BPD).

The proposed aims of the past and forthcoming care bundles are:

- 25% relative reduction (over last 3 years institutional baseline) in <u>*severe intraventricular hemorrhage*</u> in infants less than or equal to 29.6 weeks gestational age in participating TN NICUs by June 2024.
- 25% relative reduction (over last 3 years institutional baseline) in <u>*necrotizing enterocolitis*</u> in infants less than or equal to 29.6 weeks gestational age in participating TN NICUs by June 2026.

- 25% relative reduction (over last 3 years institutional baseline) in ***hospital acquired infections*** in infants less than or equal to 29.6 weeks gestational age in participating TN NICUs by June 2027.

Summary of Evidence: *Prevention of Chronic Lung Disease (CLD)*

Chronic Lung Disease (CLD) or Bronchopulmonary Dysplasia (BPD) is defined as the need for oxygen or respiratory support at 36-weeks postmenstrual age. It remains the most common complication of prematurity. Infants who develop CLD have a higher incidence of mortality. Morbidities are also higher in infants that develop CLD and include long-term neurodevelopmental delays and late onset sepsis. Infants that develop CLD also have increased utilization of medical resources and are more likely to be readmitted to the hospital during the first year of life.

CLD incidence is inversely correlated with gestational age at delivery and is the highest among extremely low birthweight infants (<1000 g). While advances in neonatal care have significantly improved ELBW survival, BPD rates have not improved. Multiple factors contribute to CLD including mechanical ventilation, oxygen toxicity, infection, inflammation, and secondary lung injury. Collectively, improvements in these areas can reduce morbidity and mortality in preterm infants. Quality improvement (QI) projects focused on the implementation of potentially better practices have demonstrated that single institutions and even collaborative efforts can decrease the incidence of CLD.[1]

Bapat et al. noted an incidence of CLD at Nationwide Children's Hospital of 73% prior to the initiation of an CLD reduction project.[2] Through a focus on oxygen management in the first month of life and development of a guideline for ventilation strategies, they were able to decrease their "any BPD" rate to 41% and their "severe BPD" rate to 21%. Both decreases represent approximately a halving of the rates at the start of the project. Part of the success of this project focused on the consistency in care that each infant received based on guidelines developed by the care team and implementation of respiratory-therapist-driven protocols. A detailed discussion with Dr. Bapat is available on the Healthy Mom, Healthy Baby Tennessee Podcast, Episode 75.[3]

Recognizing the importance of care in the delivery room and in the first few days of life, Dylag et al. focused on the "Golden Hour" and the events beyond which may influence CLD development.[4] As part of a QI project, they reported an initial incidence of CLD in their unit of 33.5%. Their stated goal was to decrease the incidence of CLD to the Vermont Oxford Network (VON) average of 24% for comparable level ≥ 3 NICUs. Following several interventions, the incidence of CLD decreased to 16.5% and was sustained for >18 months. This represents a 51% reduction in the incidence of CLD in this single institution report. This was accomplished through a focus on the "Golden Hour" and included a protocolization of mechanical ventilation, surfactant administration, CPAP usage, medications, and nutrition/fluid management.

Four exclusively collaborative QI projects focusing on CLD have been reported.[1] These include projects by the Canadian Neonatal Network, the VON, the National Institute of Child Health and Human Development (NICHD), and the California Perinatal Quality Care Collaborative (CPQCC). These collaboratives included a median of 12 (range 9–20) NICUs. Of note, there are 12 Level 3 & 4 NICUs in Tennessee. These collaborative QI projects implemented a median of 9 (6–40) PBPs at the participating sites. The collaborative approach was shown to be effective for impacting CLD in this limited number of reports. For TIPQC's project to be successful, PBPs need to be easily implemented, sustained, and become part of a culture of change within the participating NICU.

Evaluation of the existing literature indicates the development and implementation of PBPs can effectively decrease CLD and reduce mortality and morbidity in the population TIPQC is targeting for this project. Review of the 2021 data

reported to the VON database by 1044 hospitals revealed a median hospital rate of CLD to be 31.3% (IQR: 15.4%-45.9%), for infants 22-29 weeks' gestational age. Ten centers from TIPQC report data to the VON database and an analysis of these hospitals found median hospital rates of CLD in 2020 to be 41.7% (IQR: 33.8%-50.6%). A concerted and collaborative approach amongst Tennessee's level 3 and 4 NICUs to improve care and prevent CLD and the resulting morbidity and mortality in "Tennessee's Tiniest Babies'' is clearly warranted.

References:

[1]Healy, H., Croonen, L.E.E., Onland, W., van Kaam, A.H., Gupta, M. A systematic review of reports of quality improvement for bronchopulmonary dysplasia. *Semin Fetal Neonatal Med*. 2021;26(1):101201. doi:10.1016/j.siny.2021.101201

[2]Bapat, R., Nelin, L., Shepherd, E. *et al.* A multidisciplinary quality improvement effort to reduce bronchopulmonary dysplasia incidence. *J Perinatol* 40, 681–687 (2020). https://doi.org/10.1038/s41372-019-0574-8

[3]https://healthy-mom-healthy-baby.captivate.fm/episode/eo-75-chronic-lung-disease-bpd-qi-project-at-nationwide-childrens-hospital-with-dr-roopali-bapat

[4]Dylag, A.M., Tulloch, J., Paul, K.E., Meyers, J.M. A Quality Improvement Initiative to Reduce Bronchopulmonary Dysplasia in a Level 4 NICU—Golden Hour Management of Respiratory Distress Syndrome in Preterm Newborns. *Children*. 2021; 8(4):301. https://doi.org/10.3390/children8040301

Potentially Better Practices for the Prevention of CLD

All improvement requires change. And while there are many kinds of changes that will lead to improvement, the specific changes are developed from a limited number of *change concepts*. As described in the Model for Improvement, "A change concept is a general notion or approach to change that has been found to be useful in developing specific ideas for changes that lead to improvement." These change concepts are used to design and run tests of change (i.e., Plan-Do-Study-Act (PDSA) cycles) to see if they result in improvement.

A similar idea to change concepts are *Potentially Better Practices* (PBPs), which are a set of clinical practices that have the potential to improve the outcomes of care. They are labeled 'potentially better' rather than 'better' or 'best' because until the practices are evaluated, customized, and tested in individual institutions, a hospital will not know whether the practices are truly 'better' or 'best' (or 'worse'). Depending on the circumstances, a facility may need to implement other practices or modify existing ones to successfully improve outcomes. The PBPs in this collection are not necessarily the only ones required to achieve the improved outcomes targeted. Thus, this list of PBPs is not exhaustive, exclusive, or all inclusive. Changes in practice, guided by these PBPs, will require testing and adaptation to individual hospital circumstances and context to achieve measured improvements in outcomes.

In designing this project and reviewing the evidence for practices that can reduce CLD, TIPQC's experts have recommended that all participating NICUs implement all PBPs at a minimum. The relative decrease of CLD when a bundle of PBPs has been adopted has been reported to be 24.5–91%.[16–23] It is vitally important that each NICU forms a multi-disciplinary team to effectively implement these PBPs and possibly identify others to join their QI team. It is also vitally important that teams understand that babies at different gestational ages require different approaches to their management and implementation of these PBPs. To that end, we highlight different approaches for infants 22 0/7 - 25 6/7 and 26 0/7 to 29 6/7 weeks birth GA.

Antenatal Practices

Prolonging the pregnancy and preventing or delaying preterm birth is the most important thing that can be done to prevent the mortality and morbidity associated with CLD. Because of this, TIPQC recommends that neonatal and obstetrical care providers work together to ensure:

- ***All eligible mothers with pregnancies at 22 weeks and above who present with preterm labor should be given betamethasone and magnesium.***
    - **Antenatal steroids:** TIPQC has identified this as a PBP since current evidence shows corticosteroid administration before anticipated preterm birth is one of the most important antenatal therapies available to improve newborn outcomes.[1–5] Furthermore, the American College of Obstetricians and Gynecologists (ACOG) has stated that a single course of corticosteroids is recommended for pregnant women between 22 0/7 weeks and 33 6/7 weeks of gestation who are at risk of preterm delivery within 7 days.[6] The optimal therapeutic window for delivery is 2-7 days after administration of antenatal corticosteroids.[6] Infants expected to deliver at 22 0/7 weeks may benefit from antenatal steroid administration at 21 5/7 based on expert opinion.
    - A **single repeat course** should be considered in women who are less than 34 0/7 weeks of gestation at risk of preterm delivery within 7 days, and whose prior course of antenatal corticosteroids was given more than 14 days previously.[6]
        - A multicenter observational cohort in 2018 and a systematic review and meta-analysis in 2021 found that antenatal corticosteroids improved survival among the 22 0/7 and 22 6/7 weeks gestation infants that received antenatal steroids.[7,8] Because of this, if resuscitation is expected or requested at 22 0/7, antenatal steroids should be administered at 21 5/7, if possible.
        - Numerous studies have shown no long-term evidence of harm, particularly for the single course of corticosteroids given to the less than 34 0/7 weeks gestation. [9,10]

References:

[1]Periviable birth. Obstetric Care Consensus No.4. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016;127:e157–69.

[2]Carlo, W. A., McDonald, S. A., Fanaroff, A. A., Vohr, B. R., Stoll, B. J., Ehrenkranz, R. A., & et al. (2011). Association of antenatal cortico- steroids with mortality and neurodevelopmental outcomes among infants born at 22 to 25 weeks' gestation. Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. *JAMA*, 306, 2348–58.

[3]Mori, R., Kusuda, S., & Fujimura, M. (2011). Antenatal corticosteroids promote survival of extremely preterm infants born at 22 to 23 weeks of gestation. Neonatal Research Network Japan. *J Pediatr*, 159, 110–114.e1.

[4]Chawla, S., Natarajan, G., Rane, .S, Thomas, R., Cortez, J., & Lua, J. (2010). Outcomes of extremely low birth weight infants with varying doses and intervals of antenatal steroid exposure. *J Perinat Med*, 38, 419–23.

[5]Chawla, S., Bapat, R., Pappas, A., Bara, R., Zidan, M., & Natarajan, G. (2013). Neurodevelopmental outcome of extremely premature infants exposed to incomplete, no or complete antenatal steroids. *J Matern Fetal Neonatal Med*, 26, 1542–7.

[6]American College of Obstetricians and Gynecologists' Committee on Obstetric Practice (October 2016, reaffirmed 2020). *Antenatal corticosteroid therapy for fetal maturation* (Committee Opinion # 713). American Academy of Obstetricians and Gynecologists.

[7]Backes, C. H., Rivera, B. K., Pavlek, L., Beer, L. J., Ball, M. .K, Zettler, E. T. &,et al. (2021). Proactive neonatal treatment at 22 weeks of gestation: a systematic review and meta-analysis. *Am J Obstet Gynecol,* 224, 158–74. doi: 10.1016/j.ajog.2020.07.051

[8]Ehret, D. E., Edwards, E. M., Greenberg, L. T., Bernstein, I. M., Buzas, J. S., Soll, R. F., & et al. (2018). Association of antenatal steroid exposure with survival among infants receiving postnatal life support at 22 to 25 weeks' gestation. *JAMA Netw,*1:e183235. doi: 10.1001/jamanetworkopen.2018.3235

[9]Roberts, D., & Dalziel, S. R. (2006). Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database of Systematic Reviews,* 3. Art. No.: CD004454. DOI: 10.1002/14651858.CD004454

[10]Sotiriadis, A., et al. (2015). Neurodevelopmental outcome after a single course of antenatal steroids in children born preterm: A systematic review and meta-analysis. *Obstet Gynecol.,* 125(6), 1385-1396.

- **Magnesium**: While not directly impacting the incidence of chronic lung disease, prenatal magnesium has been recognized as a neuroprotective agent and may reduce the risk of cerebral palsy.[1-4] As this was included in the IVH prevention bundle and since these two interventions are done on the obstetrical side, participating NICUs are advised to discuss antenatal steroids and antenatal magnesium administration with their obstetrical team.

References:
[1]American College of Obstetricians and Gynecologists' Committee on Obstetric Practice (Reaffirmed 2020). *Magnesium sulfate before anticipated preterm birth for neuroprotection* (Committee Opinion #455). American Academy of Obstetricians and Gynecologists.
[2]Doyle, L. W., Crowther, C. A., Middleton, P., Marret, S., & Rouse, D. (2009). Magnesium sulfate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database of Systematic Reviews, 1. Art. No.: CD004661 . DOI: 10.1002/14651858.CD004661.pub3.
[3]Conde-Agudelo, & A., Romero, R. (2009). Antenatal magnesium sulfate for the prevention of cerebral palsy in preterm infants less than 34 weeks' gestation: A systematic review and meta- analysis. Am J Obstet Gynecol, 200, 595–609.
[4]Costantine, M. M., & Weiner, S. J. (2009). Effects of antenatal exposure to magnesium sulfate on neuro- protection and mortality in preterm infants: a meta-analysis. Eunice Kennedy Shriver Na- tional Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Obstet Gynecol., 114, 354–64.

- ***Obstetrical care providers should ensure that care of the extremely preterm pregnancy that is threatening to deliver is transferred to a facility that has a Level 3 or 4 NICU or neonatal care providers who cover that hospital who are familiar with these PBPs and can implement them.***
  - Delivery at advanced facilities is vital to the initial management of the targeted population and can reduce associated mortalities and morbidities. If this is not possible due to the imminent nature of delivery, consultation with obstetrical and neonatal care providers at Level 3 and 4 facilities is necessary. To ensure this is done, participating NICUs should make sure their referral base has contact information for both obstetrical and neonatal teams at their facility and consults are welcomed.[1,2]

References
[1]Wyckoff, M.H. Initial resuscitation and stabilization of the periviable neonate: the Golden-Hour approach. *Semin Perinatol*. 2014;38(1):12-16. doi:10.1053/j.semperi.2013.07.003
[2]McNamara, P.J., Mak, W., Whyte, H.E. Dedicated neonatal retrieval teams improve delivery room resuscitation of outborn premature infants. *J Perinatol*. 2005;25(5):309-314. doi:10.1038/sj.jp.7211263

Delivery Room Practices

- **Immediate use of continuous positive airway pressure (CPAP) at +5 to +6 cm of H2O pressure in the delivery room.**
  - To facilitate lung recruitment and the formation of functional residual capacity (FRC).[1]
  - Minimize interruption in the delivery of positive end expiratory pressure - during transfer from delivery room to the NICU and during routine NICU care.
  - Routine use of early CPAP is associated with less need for intubation/mechanical ventilation and significantly decreased the combined outcome of chronic lung disease or death.[2, 3.]
- **Use of T-piece resuscitator**
  - Consistent end expiratory pressure while precisely delivering the desired peak inspiratory pressure.
- **Facility and gestational age specific intubation criteria** [2, 4]

References:

[1]Foglia, E. E., Jensen, E. A., Kirpalani, H. (2017). *State of the art review: Delivery room interventions to prevent bronchopulmonary dysplasia in extremely preterm infants.* Journal of Perinatology, 37(11), 1171-1179.
[2]Lapcharoensap, W., & Lee, H. C. (2017). Tackling quality improvement in the delivery room. Clinics in Perinatology, 44, 663-581.
[3]Wright, C. J., Sherlock, L. G., Sahni, R., & Polin, R. A. (2018). *Preventing Continuous Positive Airway Pressure Failure: Evidence-based and physiologically sound practices from delivery room to the neonatal intensive care unit.* Clinics in Perinatology, 45, 257-271.
[4]Picarillo, A. P., & Carlo, W. (2017). *Using quality improvement tools to reduce chronic lung disease.* Clinics in Perinatology, 44, 701-712.

- **Early and timely surfactant administration is essential to the treatment of Respiratory Distress Syndrome (RDS) and can mitigate CLD.**
    - If a preterm baby < 30 weeks of gestation requires intubation for stabilization, they should be given surfactant.[1]
    - Rescue surfactant should be given early in the course of the disease. A suggested protocol would be to treat worsening babies with RDS immediately when Fi02 > 0.30 on CPAP pressure ≥ 6 cm H_2O. When the clinical decision has been made to administer surfactant, preterm infants with RDS should receive surfactant early (≤2 hours of life), preferably within 1 hour of life (HOL).[2]
    - A second, and occasionally a third dose, of surfactant should be given if there is ongoing evidence of RDS such as persistently high oxygen requirement and other problems that have been excluded.
    - INSURE is the most widely used method of surfactant administration across Tennessee. It is important that this is practiced correctly. INSURE as ideally practiced should target surfactant administration with subsequent removal of the endotracheal tube removal within 10 minutes.[3] After removal of the endotracheal tube, non-invasive ventilation is optimized. Hospital protocols should focus on shortening the duration of intubation for INSURE if this is the primary method used to deliver surfactant. Infants 22 0/7 to 25 6/7 may benefit from routine methods of surfactant administration.
    - Minimally invasive methods of surfactant administration such as LISA or SALSA (in neonates > 1000 grams) may be considered in spontaneously breathing neonates.[1] These methods may optimize non-invasive ventilation and may decrease the risk of CLD. The choice of delivery method should be made with careful consideration of the environment, resources available, operator experience, and patient characteristics, including gestational age and degree of illness.

References:

[1]Sweet DG, Carnielli VP, Greisen G, et al. European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update. *Neonatology*. 2023;120(1):3-23. doi:10.1159/000528914
[2]Bhandari, V., Black, R., Gandhi, B. *et al.* RDS-NExT workshop: consensus statements for the use of surfactant in preterm neonates with RDS. *J Perinatol* 43, 982–990 (2023). https://doi.org/10.1038/s41372-023-01690-9
[3]Fortas, F., Loi, B., Centorrino, R. *et al.* Enhanced INSURE (ENSURE): an updated and standardised reference for surfactant administration. *Eur J Pediatr* 181, 1269–1275 (2022). https://doi.org/10.1007/s00431-021-04301-x

Early Management Practices (DOL 0-7)

- **Gentle Ventilation Strategies:** TIPQC recommends each unit should have guidelines in place to limit ventilator related lung injury. An example of unit specific guidelines can be found in Appendix 1 (Vanderbilt's Respiratory Pathway - not all aspects of the pathway apply to this project). It is important that unit guidelines take gestational ages into account. Cochrane review has shown that volume-targeted ventilation has potential to reduce the rate of death or BPD as well as pneumothoraxes , severe IVH and duration of mechanical ventilation.[1,2] The following PBP should be incorporated in unit-specific guidelines:
    - Use of volume targeted ventilation where available. Limiting exposure to tidal volumes >6 mL/kg when using pressure-controlled ventilation.
    - Optimizing PEEP to avoid overdistention of the lung.

  - Use of high respiratory rates and lower tidal volumes in the range of 4-6 mL/kg initially.[3]
  - First Intention high frequency ventilation may be beneficial for neonates 22 0/7 to 25 6/7 weeks GA. Strategies for the best management practices in this population are available in the toolkit. [4]
- **Age appropriate pCO2 targeting:** Permissive hypercapnia is a ventilatory strategy that permits relatively high levels of CO2 in ventilated neonates, thereby allowing lower tidal volumes to be used in patients who are mechanically ventilated. A randomized controlled trial among 220 extremely low birth weight infants found that permissive hypercapnia (PaCO2 > 52.0 mmHg) did not significantly decrease mortality or incidence of BPD ($p = 0.43$). However, the use of mechanical ventilation at 36 weeks is significantly lesser in the minimally ventilated group as compared to the routine ventilation group ($p < 0.01$). This indicates that permissive hypercapnia might lower the severity of lung injury but not the incidence.[5]
  - Based on this evidence, TIPQC recommends targeting pCO2 levels of 45mmHg - 55mmHg and pH ≥7.25 during the first week of life in mechanically ventilated infants to facilitate weaning. Transcutaneous CO2 monitors are useful for maintaining this range.
- **Early prophylactic caffeine and high dose maintenance:** The Caffeine for Apnea of Prematurity (CAP) trial showed that caffeine administration resulted in a reduction in time on positive pressure ventilation by one week, as well as lowering the incidence of BPD.[6] Subsequent data has demonstrated that earlier initiation of caffeine shows reduced incidence of BPD and a shorter duration of mechanical ventilation, and a higher dose of caffeine may enhance its beneficial effect on BPD.[7-11]
  - Based on this evidence, TIPQC recommends that all infants <30 weeks GA should be started on caffeine within 24 hours of birth with a loading dose equivalent to 20mg/kg/day caffeine citrate and maintained on a dose equivalent to 10 mg/kg/day caffeine citrate with regular adjustment of dose till 33–34-week PMA or longer based on provider discretion. Infants admitted on NCPAP/NIPPV may benefit from very early caffeine administration (<2 hours of life).[12, 13]
- **Guidelines for reduction of extubation failure:** Extubation failure has been independently associated with increased mortality rates, longer length of hospital stay, and more days on oxygen and ventilator support.[14] Reintubation after elective extubation is also independently associated with increased likelihood of death/BPD in extremely preterm infants. Infants who remain extubated >7 days after planned extubation show the lowest risk of BPD or death.[15] TIPQC recommends that every unit should aim to reduce extubation failure in infants <30-week GA, failure defined as need for reintubation within 7 days of elective extubation, some PBPs to achieve this are:
  - Use of NIPPV or NIV-NAVA as initial post extubation support. Evidence: Meta-analysis of 19 trials shows that compared to NCPAP, NIPPV reduced the risk of extubation failure.[16]
  - Use of higher post-extubate PEEP/MAP Evidence: RCT of 139 infants <28 weeks gestation showed significantly lower rates of extubation failure at 7 days in infants randomized to high NCPAP pressures, no difference in pneumothorax or mortality.[17]
  - Administration of caffeine in peri-extubation period. Administration of caffeine prior to extubation is effective in reducing risk of extubation failure.[18]
  - Units should develop extubation criteria and consider using externally validated extubation success calculators such as the Wayne State Extubation Success Calculator.[19,20] http://extubation.net/
  - Special caution should be taken in very early extubation of infants 22 0/6 and 25 6/7 weeks GA.
- **Early fluid management and nutrition:** Water balance changes during the early postnatal period are a critical variable for respiratory function and survival among preterm infants. [21-23] Evidence suggests that excessive fluid balance (reflected by daily weight) during the first 10-14 days of life may be associated with severe BPD or death.[24,25] Mother's own milk feedings are shown to reduce the risk of BPD and in one study, a 9.5% reduction in the odds of BPD is noted for every 10% increase in mother's own milk.[26]

- Based on this evidence, TIPQC recommends that excessively positive fluid balance (>10% change from birth weight) should be avoided till 10-14 days of life and all efforts should be made to provide mother's own milk to reduce risk of BPD.

References:

[1]Klingenberg, C., K.I., McCallion, N., Morley, C.J., & Davis, P.G. (2017). Volume-targeted versus pressure-limited ventilation in neonates. *Cochrane Database Syst Rev.*, 10(10):CD003666.

[2]Cuevas Guaman, M., Hagan, J., Sabic, D., Tillman, D.M., & Fernandes, C.J. (2022). Volume-guarantee vs. pressure-limited ventilation in evolving bronchopulmonary dysplasia. *Front Pediatr*, 10:952376.

[3]Keszler, M., Nassabeh-Montazami, S., & Abubakar, K. Evolution of tidal volume requirement during the first 3 weeks of life in infants <800 g ventilated with Volume Guarantee. (2009). *Arch Dis Child Fetal Neonatal Ed.*,94(4):F279-282.

[4]Sindelar R, Nakanishi H, Stanford AH, Colaizy TT, Klein JM. Respiratory management for extremely premature infants born at 22 to 23 weeks of gestation in proactive centers in Sweden, Japan, and USA. Semin Perinatol. 2022;46(1):151540. doi:10.1016/j.semperi.2021.151540

[5]Carlo, W.A., Stark, A.R., Wright, L.L., & et al. (2002). Minimal ventilation to prevent bronchopulmonary dysplasia in extremely-low-birth-weight infants. *J Pediatr.*, 141(3):370-374.

[6]Schmid, B., Roberts, R.S., Davis, L., & et al. (2006). Caffeine therapy for apnea of prematurity. *N Engl J Med.*, 354(20):2112-2121.

[7]Davis, P.G., Schmidt, B., Roberts, R.S., & et al. (2010). Caffeine for Apnea of Prematurity trial: benefits may vary in subgroups. *J Pediatr.*, 156(3):382-387.

[8]Dobson, N.R., Patel, R.M., Smith, P.B., et al. (2014). Trends in caffeine use and association between clinical outcomes and timing of therapy in very low birth weight infants. *J Pediatr.,*164(5):992-998.e3.

[9]Lodha, A., Seshia, M., , McMillan, D.D., & et al. (2015). Association of early caffeine administration and neonatal outcomes in very preterm neonates. *JAMA Pediatr*, 169(1):33-38.

[10]Vliegenthart, .R, Miedema, M,. Hutten, G.J.,, van Kaam, A.H., & Onland, W. (2018). High versus standard dose caffeine for apnoea: a systematic review. *Arch Dis Child Fetal Neonatal Ed*, 103(6):F523-F529.

[11]Lamba, V., Winners, O., & Fort, P. (2021). Early high-dose caffeine improves respiratory outcomes in preterm infants. *Children (Basel)*,8(6):501.

[12]Dekker J, Hooper SB, van Vonderen JJ, Witlox RSGM, Lopriore E, Te Pas AB. Caffeine to improve breathing effort of preterm infants at birth: a randomized controlled trial. Pediatr Res. 2017;82(2):290-296.

[13]Katheria AC, Sauberan JB, Akotia D, Rich W, Durham J, Finer NN. A pilot randomized controlled trial of early versus routine caffeine in extremely premature infants. Am J Perinatol. 2015;32(9):879-886.

[14]Epstein, S.K., Ciubotaru, R.L., & Wong, J.B. (1997). Effect of failed extubation on the outcome of mechanical ventilation. *Chest*, 112(1):186-192.

[15]Shalish, W., Kanbar, L., Kovacs, L., & et al. (2019). The impact of time interval between extubation and reintubation on death or bronchopulmonary dysplasia in extremely preterm infants. *J Pediatr.*, 205:70-76.e2.

[16]Lemyre, B., Deguise, M.O., Benson, P, Kirpalani, H., De Paoli, A.G., & Davis, P.G. (2023). Nasal intermittent positive pressure ventilation (Nippv) versus nasal continuous positive airway pressure (Ncpap) for preterm neonates after extubation. *Cochrane Database Syst Rev.*, 7(7):CD003212.

[17]Kidman, A.M., Manley, B.J., Boland, R.A., Malhotra, A., Donath, S.,M., Beker, F., Davis, P.G., & Bhatia, R. (2023). Higher versus lower nasal continuous positive airway pressure for extubation of extremely preterm infants in Australia (ÉCLAT): a multicentre, randomized, superiority trial. *The Lancet Child & Adolescent Health*, 2023.

[18]Henderson-Smart, D.J., & Davis, P.G. (2010). Prophylactic methylxanthines for endotracheal extubation in preterm infants. *Cochrane Database Syst Rev.,* (12:CD00013, 9.

[19]Gupta,D., Greenberg, R.G., Sharma, A., & et al. (2019). A predictive model for extubation readiness in extremely preterm infants. *J Perinatot.*, 39(12):1663-1666.

[20]Dryer, R.A., Salem, A., Saroha, V., & et al. (2022). Evaluation and validation of a prediction model for extubation success in very preterm infants. *J Perinatol.*, 42(12):1674-1679.

[21]Oh, W., Poindexter, B.B., Perritt, R., & et al. (2005). Association between fluid intake and weight loss during the first ten days of life and risk of bronchopulmonary dysplasia in extremely low birth weight infants. *J Pediatr.*, 147(6):786-790.

[22]Matsushita, F.Y., Krebs, V.L.J., Ferraro, A.A.,& de Carvalho, W.B. (2020). Early fluid overload is associated with mortality and prolonged mechanical ventilation in extremely low birth weight infants. *Eur J Pediatr.*, 179(11):1665-1671.

[23]Selewski, D.T., Gist, K.M., Nathan, A.T., & et al. (2020). The impact of fluid balance on outcomes in premature neonates: a report from the AWAKEN study group. *Pediatr Res.*, 87(3):550-557.
[24]Starr, M.D., Griffin, R., Gist, K.M., & et al. (2022). Association of fluid balance with short- and long-term respiratory outcomes in extremely premature neonates: a secondary analysis of a randomized clinical trial. *JAMA Netw Open*, 5(12):e2248826.
[25]Soullane, S., Patel, S., Claveau, M., Wazneh, L., Sant'Anna, G., & Beltempo, M. (2021). Fluid status in the first 10 days of life and death/bronchopulmonary dysplasia among preterm infants. *Pediatr Res,* 90(2):353-358.
[26]Patel, A.L., Johnson, T.J., Robin, B., & et al. (2017). Influence of own mother's milk on bronchopulmonary dysplasia and costs. *Arch Dis Child Fetal Neonatal Ed*., 102(3):F256-F261.

Intermediate Management Practices (DOL 7-28)

For all babies (no matter extubation status), we recommend continued adherence to the following, as discussed above:

- **Permissive hypercapnia** (targeting CO2 50-60 in this time period) has been used in other respiratory care bundles of premature infants.[1,2] Though the evidence of its utility is limited when evaluated of its own merit, it has not been shown to be harmful and results in less invasive respiratory support. It is especially important to avoid hypocarbia (CO2 <40) as described in the IVH bundle. Participating NICUs are encouraged to incorporate use of permissive hypercapnia into their bundles especially as a part of RT-driven weaning protocols to encourage earlier extubation. Transcutaneous CO2 monitoring can assist with more frequent weaning and expedite extubation.
- **Caffeine:** Early use of caffeine and maintenance of appropriate caffeine dosing (10 mg/kg/day) reduces risk of apnea and increased extubation success.[3-8] Maintaining high dose (10mg/kg/day) with routine dose adjustments is recommended until 33-34 weeks PMA.

For babies that remain intubated despite use of the strategies described above, we recommend the following:

- **Weaning/Extubation Guidelines:** We recommend the multi-disciplinary development of guidelines meant to facilitate weaning and extubation from mechanical ventilation. Given the variability in ventilator strategies used within this diverse group of babies, it is important for each unit to develop guidelines to identify when there is agreement among providers that it is time for a trial of extubation. Developing a consensus among the group increases consistency between providers and allows the multidisciplinary team to both be aware and help prepare baby and parents for the timing of this attempt. Suggestions for components of those guidelines include mean airway pressure, FiO2, rate and status of apnea; we recommend evaluating the use of the Extubation Success Calculator, developed by Wayne State University (**http://extubation.net/**) as part of this guideline.[9] Extubation failure is considered as re-intubation within 7 days of intentional extubation. Extubation failure rates will be tracked as part of this project.
- **Non-Invasive ventilation:** Extubation to non-invasive ventilation (as discussed above) reduces the risk of extubation failure as compared to extubation to CPAP alone. If synchronization is available, it likely confers added benefit, but data is limited in the comparison between modes of non-invasive. All participating units should include use of non-invasive support in their extubation guidelines.[10,11]
- **Postnatal Steroids:** Use of dexamethasone facilitates extubation of infants from mechanical ventilation, reduces risk of mortality and of BPD.[12,13] If babies remain intubated at ≥14 days of life, we recommend development of a unit-specific guideline for use of postnatal steroids (DART; dexamethasone cumulative dose 0.89 mg/kg over 10 days) to facilitate extubation. We recommend use of the BPD estimator tool available at

https://neonatal.rti.org/index.cfm.[14] If an individual baby's combined risk for grade 2, grade 3 BPD and death is estimated to be ≥ 50%, we recommend a course of DART following documentation of discussion with parents.

- **Unplanned Extubation:** Participating hospitals should evaluate their rates of unplanned extubation (defined as the inadvertent loss of the ETT in the absence of obstruction of the ETT). Unplanned extubation can lead to a longer course of invasive ventilation, respiratory morbidity and mortality. Participating hospitals should consider the development of guidelines intended to reduce the risk of unplanned extubation with consideration to ETT securement and position, patient handling/positioning, ETT suctioning, sedation, etc.[15,16]

References:

[1]Ryu, J., Haddad, G. and Carlo, W.A. (2012). Clinical effectiveness and safety of permissive hypercapnia. *Clin Perinatol*., 39(2012):603-612.
[2]Sant'Anna, G.M., Keszler, M. (2012). Developing a neonatal unit ventilation protocol for the preterm baby. *Early Human Development.* 88(2012): 925-929.
[3]Schmid, B., Roberts, R.S., Davis, L., & et al. (2006). Caffeine therapy for apnea of prematurity. *N Engl J Med*., 354(20):2112- 2121.
[4]Davis, P.G., Schmidt, B., Roberts, R.S., & et al. (2010). Caffeine for Apnea of Prematurity trial: benefits may vary in subgroups. *J Pediatr.*, 156(3):382-387.
[5]Dobson, N.R., Patel, R.M., Smith, P.B., et al. (2014). Trends in caffeine use and association between clinical outcomes and timing of therapy in very low birth weight infants. *J Pediatr.,*164(5):992-998.e3.
[6]Lodha, A., Seshia, M., McMillan, D.D., & et al. (2015). Association of early caffeine administration and neonatal outcomes in very preterm neonates. *JAMA Pediatr*, 169(1):33-38.
[7]Vliegenthart, R., Miedema, M.,. Hutten, G.J., van Kaam, A.H., & Onland, W. (2018). High versus standard dose caffeine for apnoea: a systematic review. *Arch Dis Child Fetal Neonatal Ed*, 103(6):F523-F529.
[8]Lamba, V., Winners, O., & Fort, P. (2021). Early high-dose caffeine improves respiratory outcomes in preterm infants. *Children (Basel)*,8(6):501.
[9]Gupta, D., Greenberg, R.C., Sharma, A. (2019). A predictive model for extubation readiness in extremely preterm infants. *J Perinatol.* 39(12)1663-1669.
[10]Lemyre, B., Deguise, M.O., Benson, P., Kirpalani, H., De Paoli, A.G., & Davis, P.G. (2023). Nasal intermittent positive pressure ventilation (Nippv) versus nasal continuous positive airway pressure (Ncpap) for preterm neonates after extubation. *Cochrane Database Syst Rev*., 7(7):CD003212.
[11]Kidman, A.M., Manley, B.J., Boland, R.A., Malhotra, A., Donath, S.M., Beker, F., Davis, P.G., & Bhatia, R. (2023). Higher versus lower nasal continuous positive airway pressure for extubation of extremely preterm infants in Australia (ÉCLAT): a multicentre, randomized, superiority trial. *The Lancet Child & Adolescent Health*, 2023.
[12]Doyle, L.W., Davis, P.G., Morley, C.J., et al. 2006. Low dose dexamethasone facilitates extubation among chronically ventilator-dependent infants: A multicenter, international, randomized, controlled trial. *Pediatrics.* 117(1):75-83.
[13]Doyle, L.W., Cheong, J.L., Hay, S., et al. 2021. Late (> 7 days) systemic postnatal corticosteroids for prevention of bronchopulmonary dysplasia in preterm infants. *Cochrane Database Syst Rev*. 11(11):CD001145.
[14]Laughon, M.M., Langer, J.C., Bose, C.L., et al. 2011. Prediction of bronchopulmonary dysplasia by postnatal age in extremely premature infants. *Am J Respir Crit Care Med.* 183(12):1715-1722.
[15]Klugman, D., Melton, K., Maynord, P.O., et al. 2020. Assessment of an unplanned extubation bundle to reduce unplanned extubations in critically ill neonates, infants and children. *JAMA Pediatr.* 174(6):e200268.
[16]Igo, D.A., Kingsley, K.M., Malaspina, E.M., et al. 2021. Decreasing unplanned extubations in the neonatal ICU. *Respir Care.* 66(7):1059-1062.

Late Management Practices (DOL >28)

For babies who have been extubated and continue non-invasive support:

- **Caffeine:** The evidence of caffeine use has been discussed above. We recommend that caffeine continue to be used until 34 weeks PMA. Participating hospitals can consider discontinuation of caffeine at that time per their unit-specific guidelines.

- **CPAP/Non-Invasive Support:** We recommend consideration of continued use of CPAP until 32 weeks PMA. Between 32-34 weeks PMA, we recommend trialing room air in the appropriate infant (free of apnea, clinically stable, on 21% FiO2).
- **Room Air Trial:** Participating hospitals should consider a trial of room air for babies who remain on respiratory support (any flow rate of nasal cannula) between 35 5/7 and 36 0/7 weeks PMA.[1] Care should be taken to wean support incrementally over the course of time instead of immediate discontinuation.

Should a baby continue invasive ventilation or higher levels of support than above it is important to continue to utilize aspects discussed above and take advantage of opportunities to trial of extubation should they arise. We recommend maintaining appropriate caffeine dosing and adjusting the ventilator strategy as necessary for evolution of lung disease.

References:
[1]Walsh, M.C., Yao, Q., Gettner, P., et al. (2004). Impact of a physiologic definition on bronchopulmonary dysplasia rates. *Pediatrics.* 114(5):1305-1311.

Universal Interventions

- **Avoidance of hyperoxia (aim for 21% by DOL 28):** Oxygen toxicity is a hyperoxia mediated lung damage that is an important risk factor in the development of BPD. All efforts should be made to reduce exposure to hyperoxia, Bapat et al showed that through QI methodology and emphasizing the goal of being on 21% oxygen by DOL 28 (0.21 by 28), they were able to show significant improvement in BPD. TIPQC suggests that each unit should follow the best practices of:
    - Standardizing oxygen targets/limits
    - Education and audits to assess adherence. Use of pulse ox histograms where available.
    - Aim to wean all infants to 21% by DOL 28 with adjustment of peep to address optimal FRC/atelectasis.
    - If an infant weaned from CPAP 21% to nasal cannula requires an FiO2 >30% in the immediate weaning period, the infant should be placed back on CPAP to minimize oxygen requirement.
- **Vitamin A for BPD:** Prophylactic vitamin A to prevent BPD has been well studied with several trials including the one by the Neonatal Research Network [1,2]. These trials have been summarized in a Cochrane review: 12-dose regimen with 5000 IU of vitamin A administered IM 3 days per week for the first 4 weeks of life showed a marginal reduction in the incidence of BPD or death at 36 weeks PMA, with a number needed to treat of 20 (95% CI 10 to 100) [3]. However, the incidence of BPD in the placebo arm of the NICHD study was 62% and Tolia et al [4] showed that in a retrospective cohort with decreasing Vitamin A supplementation in a group where 48% of infants had BPD, there was no difference with decreasing use of Vitamin A. Based on this evidence, TIPQC recommends that prophylactic Vitamin A may be considered for use in centers with baseline rates of BPD in the highest quartile.
- **Management by Team:** TIPQC recommends that all members of the team collaborate in the management of Chronic Lung Disease. It is imperative that the Parents, RN, Speech Therapist, Dietician, Respiratory Therapist, Pharmacist, APRN/NNP and Neonatologist work hand in hand to provide the key components listed below to assist in maintaining the highest quality of life for the infant.[5,6]
    - Utilization of respiratory therapist driven protocols allows RRT to expand their scope, while increasing autonomy of the NICU RRT.[7] Having the expertise of an RRT to initiate, manage, and wean allows for decrease ventilator days and help reduction of mortality.
        - Respiratory therapists not only play an important role in initiation of ventilation, but also in the weaning and continual care of the neonate. Appendix 2 provides an RT driven weaning ventilator protocols that could be adapted to any NICU setting in low-risk patients.

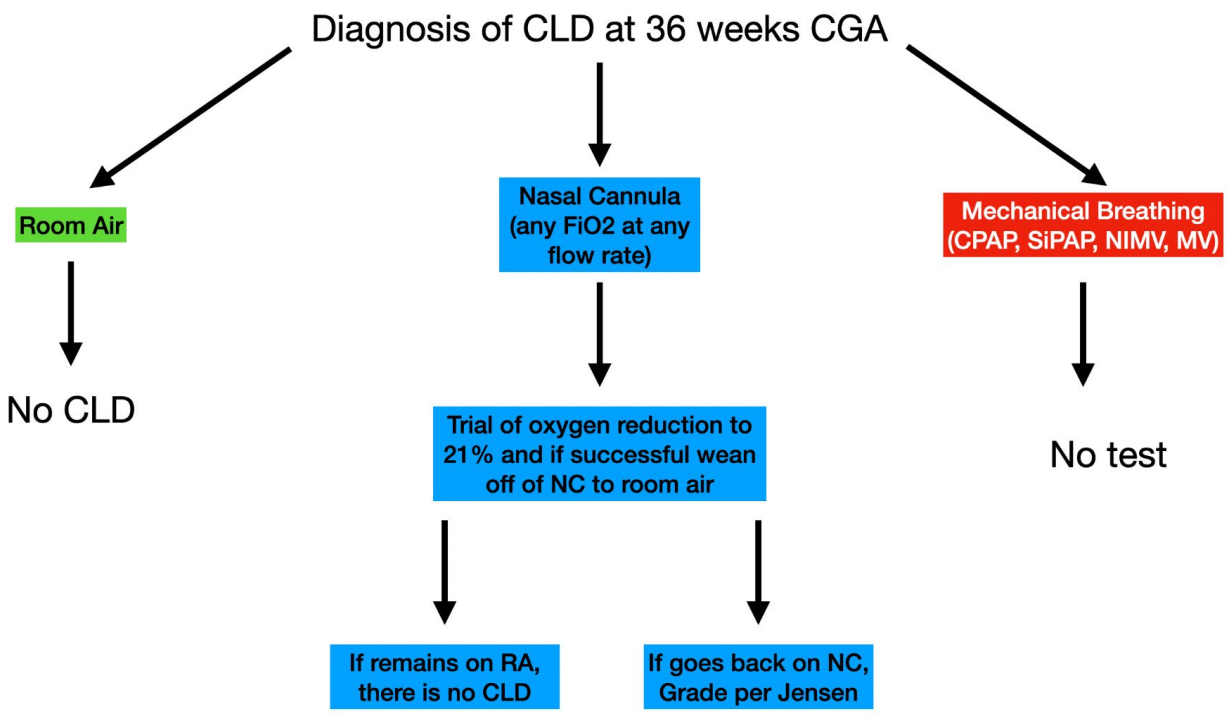
        - As part of the care team, the respiratory therapist is continually monitoring the neonate's lung compliance, dynamics, and monitoring for volutrauma/barotrauma and searching for the safest modality to decrease CLD and mortality.
        - **Cases where immediate intervention is necessary that is counterintuitive of the baby's condition should immediately be discussed with the attending provider.**
    - Neonatal Dietician Support: Support from specialist neonatal dietitian (if available) should be sought for collaborative nutritional management of all preterm infants.
    - Neonatal physiotherapy: Support from experienced neonatal physiotherapy team (if available) should be sought for collaborative management of the ventilated infant.
    - Speech and Language Therapy: Support from experienced Speech and Language therapy (SALT) team should be sought to assess and support feeding progression for babies on respiratory support.
    - Parents: Parents should be viewed as partners in care and supported with accurate and individualized information throughout the neonatal stay, including in decision making around respiratory support, and BPD.

References:
[1]Tyson, J.E, Wright, L.L., Oh, W., et al. Vitamin a supplementation for extremely-low-birth-weight infants. National institute of child health and human development neonatal research network. N Engl J Med. 1999;340(25):1962-1968.
[2]Ambalavanan, N., Tyson, J.E., Kennedy, K.A, et al. Vitamin A supplementation for extremely low birth weight infants: outcome at 18 to 22 months. Pediatrics. 200.5;115(3):e249-254.
[3]Darlow, B.A., Graham, P.J., Rojas-Reyes, M.X. Vitamin A supplementation to prevent mortality and short- and long-term morbidity in very low birth weight infants. Cochrane Database Syst Rev. 2016;2016(8):CD000501.
[4]Tolia, V.N., Murthy, K., McKinley, P.S., Bennett, M.M., Clark, R.H. The effect of the national shortage of vitamin A on death or chronic lung disease in extremely low-birth-weight infants. JAMA Pediatr. 2014;168(11):1039-1044.
[5]Sarafidis, K., Chotas, W., Agakidou, E., Karagianni, P., Drossou, V. The Intertemporal Role of Respiratory Support in Improving Neonatal Outcomes: A Narrative Review. Children (Basel). 2021 Oct 2;8(10):883. doi: 10.3390/children8100883. PMID: 34682148; PMCID: PMC8535019.
[6]Pano, C., Barta, W., Couillard, S., Halvorson, K., Wingert, J., Zettler, E. Safe Implementation of a Respiratory Therapist-Driven NICU Ventilator Weaning Protocol. Respiratory Care. 2019;64(Suppl 10). Accessed December 6, 2023. https://rc.rcjournal.com/content/64/Suppl_10/3237953

Identification & Diagnosis

- The Jensen criteria is the preferred definition of CLD and will be used for this project.[1] All participating NICUs should adopt these criteria. BPD is assessed at 36 weeks or at discharge based on the oxygen requirement at that time. There is no 28-day evaluation.
    - No respiratory support = No CLD/BPD
    - Nasal cannula $\leq$ 2LPM and any amount of oxygen = Grade 1 CLD/BPD
    - Nasal cannula > 2LPM, NCPAP, or NIPPV = Grade 2 CLD /BPD
    - Invasive PPV = Grade 3 BPD

- In order to make the diagnosis of CLD, a room air trial should be adopted as a part of a respiratory therapist driven NICU protocol, for any infant who is on nasal canula at 35 5/7 and 36 0/7 weeks PMA. This is required to correctly diagnose CLD, and proper diagnosis may lead to a decrease in CLD rates across the state.[2]



Adapted from PROP study

References:

1. Jensen, E.A., Dysart, K., Gantz, M.G., et al. The Diagnosis of Bronchopulmonary Dysplasia in Very Preterm Infants. An Evidence-based Approach. *Am J Respir Crit Care Med*. 2019;200(6):751-759. doi:10.1164/rccm.201812-2348OC
2. Walsh, M.C., Yao, Q., Gettner, P., et al. Impact of a physiologic definition on bronchopulmonary dysplasia rates. *Pediatrics*. 2004;114(5):1305-1311. doi:10.1542/peds.2004-0204

Measures: *How will we know that a change is an improvement?*

Target population

Infants born *29.6 or less weeks gestation* admitted to one of the participating NICUs for care. This includes all infants including transfers admitted within 24 hours of birth.

Outcome measures

Use the following definitions of BPD when capturing data on these Outcome Measures:

BPD is defined as:

- No BPD = no support at 36 weeks PMA
- Grade 1 BPD = nasal cannula ≤2 LPM at 36 weeks PMA
- Grade 2 BPD = nasal cannula >2 LPM or noninvasive positive airway pressure at 36 weeks PMA; and
- Grade 3 BPD = invasive mechanical ventilation at 36 weeks PMA

#1. Percent of targeted infants with **any BPD** at 36 weeks PMA.
  #1a. Percent of targeted infants with **Grade 1 BPD** at 36 weeks PMA
  #1b. Percent of targeted infants with **Grade 2 BPD** at 36 weeks PMA
  #1c. Percent of targeted infants with **Grade 3 BPD** at 36 weeks PMA

#2. Percent mortality of targeted infants with any BPD

#3. Percent mortality of targeted infants with Grade 3 BPD

#4. Percent of 'Final Disposition' of Infants with BPD (Home – no oxygen, Home with oxygen, transfer to another hospital)

#5. Percent mortality of targeted infants prior to 36 weeks

#6. Percent of infants discharged home prior to 36 weeks, discharged home on oxygen

These outcome measures will be calculated from the captured data collected on the "TIPQC TTB-CLD Case Report" form and entered into the SimpleQI platform. See data form for details.

Baseline data: Retrospective data source: VON or Jensen criteria.

- Participating NICUs will retrospectively capture and report **annual** baseline data for the previous 3 years (2020, 2021, 2022) including:
    - Annual CLD/BPD rates among infants born ≤ 29.6 weeks.
    - Annual Grade 3 CLD/BPD rates among infants born ≤ 29.6 weeks.
    - Annual mortality rate of CLD/BPD among infants born ≤ 29.6 weeks.
    - Annual Mortality rate of infants born prior to 36 weeks.
- This baseline data will serve as the "institutional baseline" for measuring a planned 25% relative reduction in rates.

Process measures

- Percent of mothers (of targeted infants) receiving any antenatal steroids
- Percent of mothers (of targeted infants) receiving *2 doses* of antenatal steroids
- Percent of mothers (of targeted infants) receiving any magnesium sulfate (MgSO4)
- Percent of targeted infants receiving continuous positive airway pressure (CPAP) at +5 to +6 cm of H2O pressure in the delivery room
- Percent of targeted infants with RDS (FiO2 > 0.30 on CPAP ≥ 6 cm of H2O pressure or need for mechanical ventilation within the first 2 hours of life)
    - Percent of targeted infants diagnosed with RDS receiving surfactant within 2 HOL
- Percent of targeted infants receiving caffeine within 24 hours of birth
- Percent of targeted infants receiving dexamethasone for BPD
    - Of infants receiving dexamethasone, DOL medication initiated
- Percent of targeted infants with extubation failure (reintubated within 7 days of elective extubation)
    - Of infants with extubation failure, DOL on first planned extubation attempt
- Percent of infants receiving a Room Air Trial between the ages of 35 weeks 5 days and 36 weeks and 0 days.

These process measures will be calculated from the captured data collected on the "TIPQC TTB-CLD Case Report" form. See TIPQC CLD Data Entry Form for details.

In addition, participating NICUs will report the following Process measures *quarterly*:

- Provider education

    - Cumulative proportion of providers, including Neonatologists and NNPs, who have completed an education program on CLD Prevention that includes the unit-standard protocols
        - Report estimates in 10% increments (0%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%)
- Nursing and Respiratory Staff education
    - Cumulative proportion of neonatal nurses and respiratory staff who have completed an education program on CLD Prevention that includes the unit-standard protocols
        - Report estimates in 10% increments (0%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%)

These Process measures (provider and nursing education) will be entered directly into the Simple QI platform. See Data Collection below.

Balancing measures

- Percent of targeted infants with a pneumothorax
- Percent of targeted infants with Grade 3 or 4 IVH
- Percent of targeted infants receiving dexamethasone for BPD
- Annual mortality rate of infants prior to 36 weeks PMA among the target population.

These Balancing measures will be calculated from the captured "TIPQC TTB-CLD PROJECT Case Report form" and entered directly into the SimpleQI platform.

Structure measures

- *Frequency of collection & reporting*: quarterly
- Unit Guidelines for early surfactant administration - reviewed and updated in the last 2-3 years.
    - Report % complete implementation of guidelines and a process for reviewing and updating every 2-3 years.
        - Report estimates in 10% increments (0%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%)
- Unit Guidelines for extubation criteria, post extubation support - reviewed and updated in the last 2-3 years.
    - Report % complete implementation of guidelines and a process for reviewing and updating every 2-3 years.
        - Report estimates in 10% increments (0%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%)
- Hospital has a patient/family partner who engaged in appropriate education, e.g., Momma's Voices' Training, and is actively participating on the improvement team.
    - Report completion progress on 3-point Likert scale.
        - 1 = Not Started
        - 3 = Started
        - 5 = Fully in Place

Data Collection

Participating NICUs will capture data on each infant using the provided "TIPQC TTB- CLD PROJECT Case Report form" and through direct data entry in the SimpleQI platform. See appendix for form details. SimpleQI data entry training will be conducted prior to the start of the project. Each team will determine the process in which the data will be collected (e.g., on paper at the bedside and/or from the targeted infant's EMR).

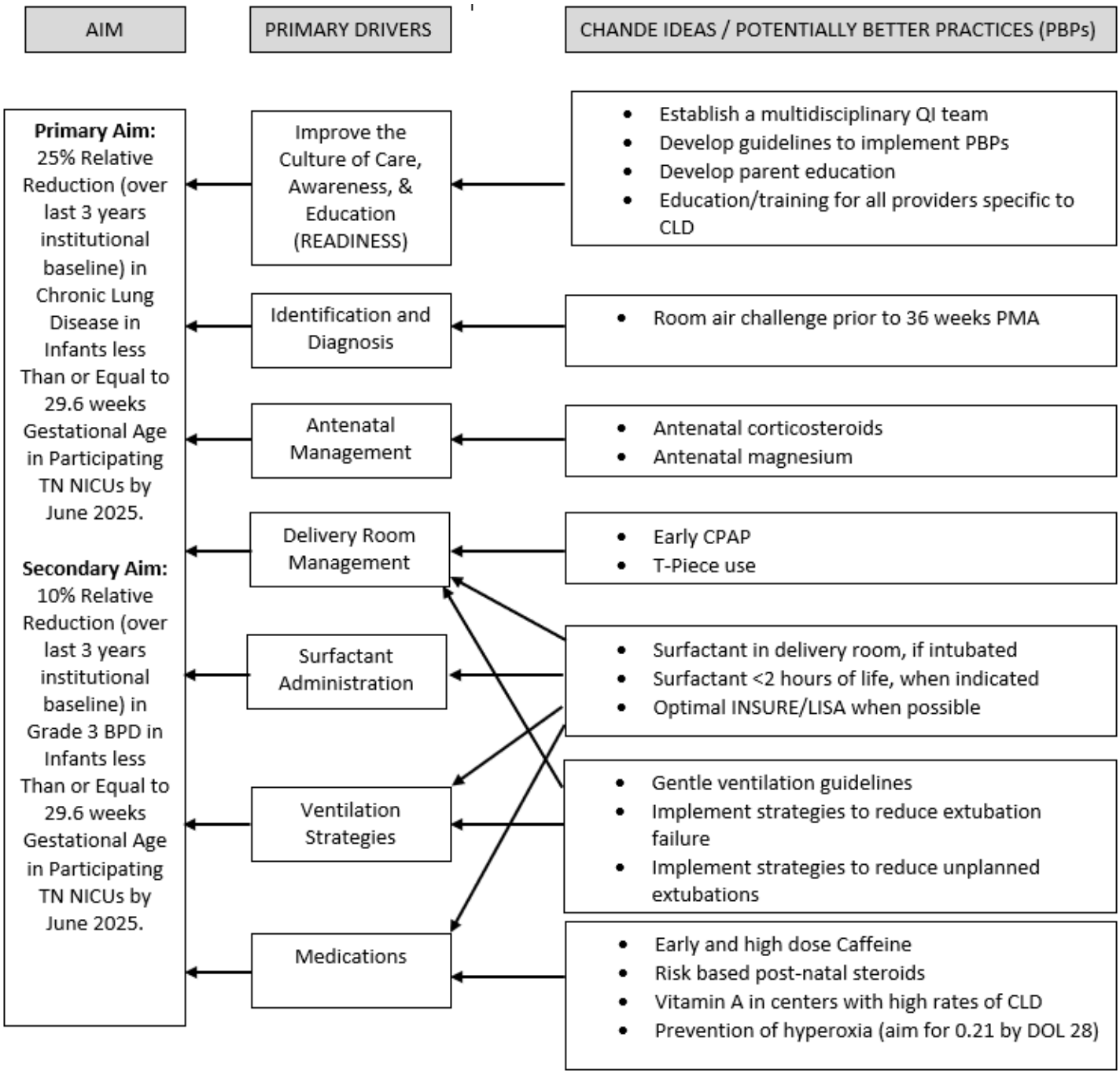
Measures that are calculated from the Infant Case report form captured in SimpleQI will have accompanying data visuals (graphs) within 24-48 hours of the case report form being finalized (finalized = all data is entered and complete for the individual infant).

The two education Process measures and Structure measures will be entered directly into SimpleQI. See data entry instructions and screenshots in the Appendix. Data reports will be available immediately with each data point entered. For details on data collection methods, see Data Collection Form.

Key Driver Diagram

A driver diagram is a visual display of a QI collaborative's (or team's) theory of what "drives," or contributes to, the achievement of the project aim – that is, the project's "theory of change." The far-right column of the driver diagram lists the specific *change ideas to test* using PDSA cycles.

Key Driver FLOW Diagram


AIM
PRIMARY DRIVERS
CHANDE IDEAS / POTENTIALLY BETTER PRACTICES (PBPs)
Primary Aim: 25% Relative Reduction (over last 3 years institutional baseline) in Chronic Lung Disease in Infants less Than or Equal to 29.6 weeks Gestational Age in Participating TN NICUs by June 2025.
Secondary Aim: 10% Relative Reduction (over last 3 years institutional baseline) in Grade 3 BPD in Infants less Than or Equal to 29.6 weeks Gestational Age in Participating TN NICUs by June 2025.
Improve the Culture of Care, Awareness, & Education (READINESS)
Establish a multidisciplinary QI team
Develop guidelines to implement PBPs
Develop parent education
Education/training for all providers specific to CLD
Identification and Diagnosis
Room air challenge prior to 36 weeks PMA
Antenatal Management
Antenatal corticosteroids
Antenatal magnesium
Delivery Room Management
Early CPAP
T-Piece use
Surfactant Administration
Surfactant in delivery room, if intubated
Surfactant <2 hours of life, when indicated
Optimal INSURE/LISA when possible
Ventilation Strategies
Gentle ventilation guidelines
Implement strategies to reduce extubation failure
Implement strategies to reduce unplanned extubations
Medications
Early and high dose Caffeine
Risk based post-natal steroids
Vitamin A in centers with high rates of CLD
Prevention of hyperoxia (aim for 0.21 by DOL 28)

Appendix 1 - Pathways Shared Courtesy of Vanderbilt NICU

NICU Respiratory Care Pathways

Purpose: The purposes of the NICU Respiratory Care Pathways are to provide evidence-based recommendations for the use of mechanical ventilation based upon a patient's pathophysiology. By standardizing the respiratory care provided, we intend to create a shared mental model amongst all team members about the pathology necessitating mechanical ventilation and the goals of ventilation.

Rationale: Observational evidence suggests that standardized respiratory care improves overall short- and long-term respiratory outcomes in the NICU. 1,2 Currently substantial practice variation exists in the Vanderbilt NICUs regarding the initiation, escalation, weaning and discontinuation of mechanical ventilation. This variation in practice makes it difficult to standardize the respiratory care that is provided. These pathways will attempt to use the available evidence and local expert consensus to standardize ventilator care.

Caveats:

- These recommendations do not replace clinical judgment and will not fit all clinical scenarios.
- These settings should be altered if the medical providers and the respiratory therapists (RTs) deem more appropriate settings.
- An individual patient's pathology and physiology may change frequently and abruptly, and the use of these pathways should not be rigid.
- Constant consideration and multi-disciplinary discussion about the continuing need for mechanical ventilation and the goals of mechanical ventilation therapy is critically important in tailoring therapy to the individual needs of each infant.
- Respiratory care in the NICU is a dynamic field and these pathways will be updated with new evidence as this becomes available.

Special Considerations:

- Most of the pathways recommend a volume-targeted ventilation (VTV) mode with the evidence for these recommendations cited below.

  Use of a VTV mode can safely be accomplished with our current ventilators (Dräger Evita® Infinity® V500), which employ a flow sensor at the proximal end of the endotracheal tube.
- VTV modes can be used immediately after placing an endotracheal tube (and before obtaining a chest x-ray to confirm endotracheal tube position) provided that the correct tidal volume is set, and an appropriate pressure limit is entered. This will theoretically limit lung injury due to both barotrauma and volutrauma.
- Dräger Evita® Infinity® V500 ventilators can compensate for most endotracheal tube leaks (<80%). Should an endotracheal tube leak be greater than 80%, consideration should be given to: 1) attempting extubation should this be clinically appropriate, 2) exchanging the endotracheal tube for a larger size, or 3) using a pressure limited ventilation mode. Tidal volume will not be reliably known with the latter option.

Default settings: (settings to be entered if conversation is unable to occur between RT and provider)

a. Mode: PC-PSV with volume guarantee
b. Initial set tidal volume: 5 cc/kg
c. Pressure limit: Set at 23 cm H2O (to limit at 18 cm H2O)
d. Inspiratory time max: 0.6 seconds
e. PEEP: 5 cm H2O.
f. Respiratory rate: High enough to ensure minute ventilation of 200-300 cc/kg/min. Approximately 40-50 breaths per minute

Diagnosis-based Respiratory Care Pathways

1) Prematurity/Respiratory Distress Syndrome (RDS)- <700 grams
   a) Initiation of ventilator support 3-7
      i) Mode: PC-AC with volume guarantee (alternatively PC-PSV with volume guarantee)
      ii) Initial set tidal volume: 5.5-6 cc/kg
         (1) Infants <750g may require tidal volumes 5.5-6 cc/kg due to relatively large instrumental deadspace8,9
      iii) Pressure limit:
         (1) Initial: Set at 23 cm H2O (to limit at 18 cm H2O).
         (2) After CXR confirmation: Set at 25-30 cm H2O (to limit at 20-25 cm H2O)
      iv) Inspiratory time: 0.3 seconds
      v) PEEP: 5-6 cm H2O. Adjust based on clinical exam, CXR, and oxygen requirement
      vi) Respiratory rate: High enough to ensure minute ventilation of 200-300 cc/kg/min. Approximately 40-50 breaths per minute
      vii) Additional considerations: If the infant meets criteria, consider surfactant administration as soon as possible after intubation.

2) Prematurity/Respiratory Distress Syndrome (RDS)- 700-2500 grams
   a) Initiation of ventilator support 3-7
      i) Mode: PC-PSV with volume guarantee (alternatively PC-AC with volume guarantee)
      ii) Initial set tidal volume: 4-5 cc/kg
      iii) Pressure limit:
         (1) Initial: Set at 23 cm H2O (to limit at 18 cm H2O).
         (2) After CXR confirmation: Set at 25-30 cm H2O (to limit at 20-25 cm H2O)
      iv) Inspiratory time max: 0.4-0.6 seconds
      v) PEEP: 5-6 cm H2O. Adjust based on clinical exam, CXR, and oxygen requirement
      vi) Respiratory rate: High enough to ensure minute ventilation of 200-300 cc/kg/min. Approximately 40-50 breaths per minute
      vii) Additional considerations: If the infant meets criteria, consider surfactant administration as soon as possible after intubation.

3) Term RDS/Pneumonia/Meconium aspiration syndrome with poor aeration on CXR
   a) Initiation of ventilator support 10
      i) Mode: PC-PSV with volume guarantee
      ii) Set tidal volume: 4-4.5 cc/kg
      iii) Pressure limit:
         (1) Initial: Set at 25 cm H2O (To limit at 20 cm H2O)
         (2) After CXR confirmation: Set at 30 cm H2O (To limit at 25 cm H2O)
      iv) Inspiratory time max: 0.4-0.6 seconds
      v) PEEP: 5-6 cm H2O. Adjust based on clinical exam, CXR and oxygen requirement.
      vi) Respiratory rate: High enough to ensure minute ventilation of 200-300 cc/kg/min. Approximately 40-50 breaths per minute
      vii) Additional considerations: If the infant meets criteria, consider surfactant administration as soon as possible after intubation.

4) Chronic lung disease (CLD)
   a) Initiation of ventilator support 11-13
      i) Mode: PC-AC with volume guarantee
      ii) Set tidal volume: 6-12 cc/kg
      iii) Pressure limit:
         (1) Initial: Set at 30 cm H2O (To limit at 25 cm H2O)
         (2) After CXR confirmation: Set at 30-35 cm H2O (To limit at 25-30 cm H2O). May require higher pressure limit depending upon the severity of the lung disease.
      iv) Inspiratory time: Consider longer I-times (0.5-1). Adjust in concert with rate to allow at least 1:2 or 1:3 I:E ratio
      v) PEEP: 5-6 cm H2O. Adjust based on clinical exam, CXR and oxygen requirement
      vi) Respiratory rate: High enough to ensure minute ventilation of 200-300 cc/kg/min. Approximately 30-40 breaths per minute depending on set tidal volume.
      vii) Additional considerations: The chronologic age at which a chronically ventilated preterm infant should be considered to have lung pathophysiology that requires a larger tidal volume strategy is not known. Evidence suggests that these changes may occur after only 2-3 weeks of mechanical ventilation.14

5) Post-operative/post-procedural/neurologic disease/apnea
   a) Initiation of ventilator support
      i) Mode: PC-PSV with volume guarantee
      ii) Set tidal volume: 4-5 cc/kg
      iii) Pressure limit:
         (1) Initial: Set at 25 cm H2O (To limit at 20 cm H2O)
         (2) After CXR confirmation: Set at 30-35 cm H2O (To limit at 25-30 cm H2O)
      iv) Inspiratory time: 0.4 seconds
      v) PEEP: 5-6 cm H2O. Adjust based on clinical exam, ventilator loops, CXR and oxygen requirement
      vi) Respiratory rate: High enough to ensure minute ventilation of 200-300 cc/kg/min. Approximately 40-50 breaths per minute

6) Special Circumstances
   a) Congenital diaphragmatic hernia
      i) Consider using Term RDS pathway with a lower pressure limit (20-25 cm H2O)

ii) Alternatively, consider prophylactic treatment with HFOV.15 See Congenital Diaphragmatic Hernia protocol for further details.

b) Mechanical ventilation for pulmonary over-circulation in infants with ductal dependent congenital heart disease

i) Use Term RDS pathway.

ii) Target lower minute ventilation to manage over-circulation. See Ductal Dependent Congenital Heart Disease protocol for further details.

c) Pulmonary hypoplasia

i) Consider using primary high frequency ventilation mode

d) Pulmonary airleak syndrome (Pulmonary interstitial emphysema [PIE], pneumothorax, bronchopleural fistula, tracheoesophageal fistula)

i) Consider high frequency ventilation mode

References:

[1]Hermeto. F., Bottino, M.N., Vaillancourt, K., Sant'Anna, G.M. Implementation of a respiratory therapist-driven protocol for Neonatal ventilation: impact on the premature population. Pediatrics. 2009;123(5):e907-916.
[2]Mola, S.J, Annibale, D.J., Wagner, C.L., Hulsey, T.C., Taylor, S.N. NICU bedside caregivers sustain process improvement and decrease incidence of bronchopulmonary dysplasia in infants < 30 weeks gestation. Respir. Care. 2015;60(3):309-320.
[3]Peng, W., Zhu, H., Shi, H., Liu, E. Volume-targeted ventilation is more suitable than pressure-limited ventilation for preterm infants: a systematic review and meta-analysis. Arch. Dis. Child. Fetal Neonatal Ed. 2014;99(2):F158-165.
[4]Wheeler, K., Klingenberg, C., McCallion, N., Morley, C.J., Davis, P.G. Volume-targeted versus pressure-limited ventilation in the neonate. The Cochrane database of systematic reviews. 2010(11):Cd003666.
[5]Wheeler, K.I., Klingenberg, C., Morley, C,J., Davis, P.G. Volume-targeted versus pressure-limited ventilation for preterm infants: A systematic review and meta-analysis. Neonatology. 2011;100(3):219-227.
[6]Klingenberg, C., Wheeler, K.I., Davis ,P.G., Morley, C.J. A practical guide to neonatal volume guarantee ventilation. J. Perinatol. 2011;31(9):575-585.
[7]Abubakar K., Keszler, M. Effect of volume guarantee combined with assist/control vs synchronized intermittent mandatory ventilation. J. Perinatol. 2005;25(10):638-642.
[8]Nassabeh-Montazami, S., Abubakar, K.M., Keszler M. The impact of instrumental dead-space in volume-targeted ventilation of The extremely low birth weight (ELBW) infant. Pediatr. Pulmonol. 2009;44(2):128-133.
[9]Neumann, R.P., Pillow, J.J, Thamrin, C., Larcombe, A.N., Hall, G.L., Schulzke, S.M. Influence of gestational age on dead space and alveolar ventilation in preterm infants ventilated with volume guarantee. Neonatology. 2015;107(1):43-49.
[10]Bhat, P., Chowdhury, O., Shetty, S., et al. Volume-targeted versus pressure-limited ventilation in infants born at or near term. Eur. J. Pediatr. 2016;175(1):89-95.
[11]Abman, S.H. Management of the infant with severe BPD. In: Banalari ED, ed. The newborn lung: Neonatology questions and controversies. Philadelphia Elsevier; 2012:21.21–21.19.
[12]Abman, S.H., Collaco, J.M., Shepherd, E.G., et al. Interdisciplinary Care of Children with Severe Bronchopulmonary Dysplasia. J. Pediatr. 2017;181:12-28 e11.
[13]Gien, J., Kinsella, J., Thrasher, J., Grenolds, A., Abman ,S.H., Baker, C.D. Retrospective Analysis of an Interdisciplinary Ventilator Care Program Intervention on Survival of Infants with Ventilator-Dependent Bronchopulmonary Dysplasia. Am. J. Perinatol. 2017;34(2):155-163.
[14]Keszler, M, Nassabeh-Montazami ,S., Abubakar, K. Evolution of tidal volume requirement during the first 3 weeks of life in infants <800 g ventilated with Volume Guarantee. Arch. Dis. Child. Fetal Neonatal Ed. 2009;94(4):F279-282.
[15]Snoek, K.G., Capolupo, I., van Rosmalen, J., et al. Conventional Mechanical Ventilation Versus High-frequency Oscillatory Ventilation for Congenital Diaphragmatic Hernia: A Randomized Clinical Trial (The VICI-trial). Ann. Surg. 2016;263(5):867-874.
[16]"Neonatal Ventilator Weaning Guidelines: ACUTE Care Patients."

Respiratory Management of 22 0/7 – 24 6/7-week infants through First 28 Postnatal Days of Age Using the High Frequency Jet Ventilator

The following recommendations apply to the initial respiratory management of all infants at 22 0/7 to 24 6/7 weeks gestational age born at Vanderbilt or transferred to the NICU within 24 hours of age. The underlying philosophy of the following recommendations includes minimizing positive pressure breaths by use of the high frequency jet ventilator (HFJV), optimizing lung inflation, avoiding both atelectasis and over-distension, tolerating moderate hypercapnia after 72 hours of age, maintaining oxygen saturation within a narrow range, and weaning toward extubation once an infant has achieved a period of relative stability. The frequency and magnitude of ventilator changes outlined in the protocol are initial guidelines; larger, smaller, or more frequent ventilatory changes may be required to maintain infants in the target ranges. It is essential that every effort be made to rapidly return infants to the target ranges if they have "drifted" outside these ranges.[1-5]

To be clear, these recommendations are only intended for first-intention ventilation in infants 22 0/7 weeks – 24 6/7 weeks gestation. Different strategies/settings may be needed for use of HFJV as a rescue therapy in older infants. These recommendations should not replace clinical judgment.

Delivery Room Respiratory Management:

- 22 0/7 – 23 6/7 weeks gestation: Intubation with 2.5 endotracheal tube (ETT), surfactant administration, ventilation with the HFJV per protocol below.
- 24 0/7- 24 6/7 weeks gestation: Placement of Bubble Continuous Positive Airway Pressure (bCPAP) and trial of non-invasive support per protocol. Should intubation be necessary, infant should be intubated with 2.5 ETT, given surfactant, and ventilated with the HFJV per protocol below.
- Target oxygen saturations should be congruent with NRP guidelines and oxygen titrated to meet saturation goals
- For infants requiring intubation, a 2.5 ETT should always be the first choice and a 2.0 ETT should only be placed after the most experienced intubation provider has been unable to place a 2.5 ETT (assuming infant stability for attempts). 2.0 ETTs have exponentially higher resistance and there currently is not 2.0 ETT adapter for the HFJV.
- For infants who are intubated in the delivery room, the minimum Neopuff settings (18/5) needed to obtain target oxygen saturations should be used. Once admitted to the NICU, the HFJV should be the initial mode of ventilation
- Chest X-ray (CXR) prior to surfactant administration is not indicated if ETT depth is consistent with NRP guidelines. NRP guidelines for ETT depth at 23-24 weeks gestational age is 5.5 centimeters. Alternatively, the nasal septum to ear tragus length + 1 cm can be used for guidance on ETT depth.6

Target Oxygenation/Ventilation Ranges:

- Oxygen saturations: 90- 95% after the five minutes of age per NRP guidelines6
- pH: 7.2- 7.45. If metabolic acidosis, shouldn't increase HFJV settings to manage pH
- Arterial PCO2: 45-60 mmHg in patients without pulmonary interstitial emphysema (PIE), gross air leak, hyperinflation, chronic changes on CXR
- Venous or capillary PCO2: 50-65 mmHg in patients without PIE, gross air leak, hyperinflation, chronic changes on CXR
- Arterial PCO2: 50-65 mmHg in patients with PIE, air leak, or hyperinflation on CXR
- Venous or capillary PCO2: 55-70 mmHg in patients with PIE, air leak, or hyperinflation on CXR
- PCO2 ranges should be strictly followed during the first week of life and consideration for some "wiggle-

room" in the ranges may be considered after postnatal age 7.

Target Oxygenation/Ventilation Ranges:
"Ideal" lung inflation is defined as the top margin of the dome of the right hemidiaphragm located between the bottom of the eighth rib and no more than midway between the ninth and tenth ribs on an appropriately positioned CXR. The major focus will be avoidance of atelectasis and hyperinflation. In addition to overexpansion, small heart and flat diaphragms may also indicate hyperinflation. Patients with PIE or air leak should be managed with a lower-pressure strategy, defined as the dome of the diaphragm between the bottom of the seventh and bottom of the eighth ribs.2

Routine Blood Gas and CXR Monitoring:

- During initial stabilization, repeat arterial blood gas at least every 2 hours until the PaCO2 is within the target range for 2 subsequent gases. If no arterial or venous access is available, check capillary blood gases every 4 hours until the PCO2 is within target range for 2 subsequent gases.
- Once PCO2 is in target range, decrease frequency of blood gases to every 6 hours for the first 24 hours, then every 12 hours for hours 24-72, and daily for the remaining duration of ventilation (up to day 28 of age if remains ventilated).
- If PCO2 is outside of target ranges, adjust ventilator settings and repeat subsequent gas. Frequency of recheck after ventilator adjustment should be left to the discretion of the clinical team taking into consideration the clinical situation.
- CXR on admission to the NICU and then q6h until optimal lung inflation/oxygenation is achieved. Daily for first 7 days.
- If FiO2 changes by ≥ 0.1 and is sustained for >30 minutes, repeat a CXR and blood gas to evaluate lung inflation and ventilation.

High Frequency Jet Ventilation (HFJV) Strategy:

Initial HFJV settings. Initiate HFJV at these settings:

- HFJV Peak Inspiratory Pressure (PIP): 20-22 or whatever is needed to create chest "bounce"
- Positive End Expiratory Pressure (Set PEEP): 7 cm H2O on Dräger ventilator
- HFJV Rate: 360 breaths per minute
- HFJV Inspiratory time (I-time): 0.02 seconds
- Back-up ventilator mode: SPN-CPAP
- Back-up rate (BUR): 0 breaths per minute

Adjusting HFJV settings to optimize lung inflation. The initial goal on HFJV is to optimize lung inflation without overdistention. The optimal position of the right hemidiaphragm is between 8 and 9.5 ribs. Diaphragm position is primarily determined by extrinsic and/or intrinsic PEEP. Delivered PEEP is best measured by the measured PEEP which appears on the HFJV face and adjusting PEEP recommendations should be based on the measured PEEP. It is not uncommon for the measured PEEP to fluctuate, and it is not recommended to "chase" the measured PEEP if the infant is otherwise doing well. If top dome of right diaphragm is:

- Below the 11th rib, decrease PEEP by 1 cm H2O, decrease HFJV rate to 240-300, ensure no BUR is in use, and recheck CXR in 6 hours;
- Between the 10th and 11th rib, decrease HFJV rate to 300, consider decreasing PEEP by 0.5 cm H2O, ensure no BUR is in use, and recheck CXR in 12 hours;

- Between 8 and 9.5 ribs, no change;
- Above the eighth rib, increase PEEP by 0.5 cm H2O and recheck CXR in 12 hours;
    - Above the eighth rib, but infant FiO2 < 0.25, increasing PEEP is optional.
- Above the seventh rib, increase PEEP by 1 cm H2O and recheck CXR in 6 hours;
    - Above the seventh rib, but infant FiO2 < 0.25, increasing PEEP is optional.

Adjusting HFJV settings based on FiO2. Assuming acceptable lung inflation (defined as position of the right hemidiaphragm between 8 and 9.5 ribs), adjust PEEP based on FiO2:

- FiO2 ≥ 0.40, increase PEEP by 1 cm H2O;
- FiO2 0.30 to 0.39, may increase PEEP by 0.5 cm H2O or make no change, depending on CXR;
- FiO2 < 0.30, decrease PEEP by 0.5cm H2O or make no change, depending on CXR.
    - If FiO2 < 0.30 AND infant meets extubation criteria, consider extubation. See section below.
- Should an infant require FiO2 ≥ 0.40 but lung expansion is adequate by CXR, clinical team should consider alternate pathophysiologic reasons for hypoxemia that will not be improved by increasing PEEP/MAP (i.e. infection, pulmonary hypertension, patent ductus arteriosus, etc.)
- As much as possible, positive-pressure breaths using a BUR on the conventional ventilator should be minimized. If infant has hypoxemia and poor lung expansion/atelectasis on CXR, a BUR at 5-10 breaths per minute can be considered for a short period of time (~1 hour) while adjusting PEEP.

Adjusting HFJV settings to optimize ventilation. Assuming a constant HFJV rate, PaCO2 is primarily determined by the size of the tidal volume which is determined by the HFJV PIP and I-time (For venous or capillary blood gases, all targets below should be adjusted up by 5 mmHg):

Managing PIP:

- PaCO2 < 35 mmHg, decrease HFJV PIP by 4;
- PaCO2 35 to 44 mmHg, decrease HFJV PIP by 2;
- PaCO2 45 to 60 mmHg, no change in HFJV PIP is necessary
    - If PaCO2 has been 45 to 60 mmHg for > 12 hours, consider weaning HFJV. See section below.
- PaCO2 61 to 69 mmHg, increase HFJV PIP by 2;
- PaCO2 > 70 mmHg, increase HFJV PIP by 4;

Managing HFJV I-time and Rate:

- HFJV I-time should be maintained at 0.02 seconds in this specific population with rare exceptions. Only consider increasing the HFJV I-time in the setting of poor ventilation with HFJV PIP > 40. Increasing HFJV I-time increases the HFJV tidal volume as well as the distance down the airway that the HFJV pressure wave is transmitted. In infants at risk for PIE or other air leak syndromes, minimizing pressure fluctuations transmitted to the distal airway may be prudent.
- In contrast to the high-frequency oscillator ventilator, the I-time on the HFJV is set and does not change with changes in the rate. As HFJV rate decreases and HFJV I-time remains unchanged, expiratory time increases.
- In some situations, increasing HFJV rate can be effective in eliminating CO2 but this should only be done after thorough discussion with the clinical team.

HFJV management of air leak (PIE, pneumomediastinum, pneumothorax) with “lower-pressure” strategy. If the infant has PIE, pneumothorax, or pneumomediastinum, change to a “lower-pressure” strategy. The goal of the “lower-

pressure" strategy is to reduce distal transmitted airway pressure sufficiently to allow for healing at the site(s) of the air leak while accepting higher pCO2 and lower SpO2 limits.

- Decrease airway pressure as able in the following order: Ensure no BUR is in use, Decrease HFJV rate to 240-300 bpm, adjust HFJV PIP to allow for higher PCO2, and finally adjust PEEP to target diaphragm level between seventh and eighth ribs
- FiO2: Temporarily accept FiO2 necessary to maintain lower target oxygen saturations (85%-95%)
- Target PaCO2: As long as pH is in target range, arterial pCO2 50-65 mmHg or venous or capillary PCO2 55-70 mmHg
- Unilateral PIE, patient should be positioned with affected side down (at 90-degree angle to bed). Attempt to keep the infant primarily in this position until PIE is resolved and limit turning as needed to maintain skin integrity. To ensure stable cerebral blood flow in this position, the nose should be kept in line with the umbilicus when the patient is lying on one side.
- Once PIE or air leak has resolved for 24- 48 hours, consider return to optimal lung volume strategy.

HFJV management of patients with hyperinflation and/or chronic changes of evolving lung disease on CXR.

· Some patients with early chronic changes can have relative hyperinflation. This should be treated by weaning of HFJV rate (first), HFJV PIP, and adjusting PEEP based on the underlying pathophysiology of the hyperinflation, as well as by accepting a higher target PCO2 range
    - Patients with obvious chronic changes on chest radiograph should be treated by accepting a higher target PCO2 range.
- Hyperinflation may decrease with lower HFJV rates (240-300 bpm);

Weaning HFJV. The goal is to wean infants toward extubation to non-invasive ventilation (NIV) as soon as they are ready:

· If PCO2 remains in target range for > 12 hours and patient is stable, wean HFJV PIP by 2. However, if PCO2 remains in the upper 5 mmHg of the range, weaning is optional.
- If oxygen saturation and lung inflation remain in target range > 12 hours, wean PEEP by 0.5 to 1.0 cm H2O, unless this results in a sustained increase in FiO2 ≥ 0.05. If this occurs, return to PEEP at which the infant had stable oxygenation.
- Avoid weaning PEEP faster than every 6-12 hours, particularly if weaning PEEP is associated with increasing FiO2.
- Consider adding transcutaneous CO2 measurement in this population when entering the weaning phase

Additional Considerations for using back-up rates on the HFJV.

- Since one of the goals for using the HFJV in this population is to minimize the amount of positive-pressure breaths, a BUR on the conventional ventilator should not be routinely used.
- If a BUR is needed to re-recruit alveoli while awaiting the effect of increasing PEEP, two potential strategies are recommended:
  o BUR of 5 breaths per minute, BUR PIP of 70-80% of HFJV PIP (maximal BUR PIP of 25), and BUR I-time of 0.35 seconds
  o BUR of 5-10 breaths per minute, BUR PIP 5-6 above set PEEP, and BUR I-time of 0.4 seconds
- A BUR should have an order documented by a provider and the order should specify the amount of time the BUR is to be used. A BUR should not be used indefinitely and in the absence of a specified amount of time, a BUR will time out after 4 hours.

- If the HFJV must be paused to perform a physical exam, the HFJV should be placed in standby and a BUR of 30 should be applied for the time needed to perform the exam. As able, one collaborative exam should be completed each morning (or at the beginning of a shift) to minimize the amount of time the infant is off the HFJV.

Extubation Attempt, Post-extubation support, and Reintubation:

Initial trials of extubation. Extubation should be considered when the infant is stable on minimal ventilator settings, without significant work of breathing or ongoing hemodynamic instability, and the infant can be safely supported with existing NIV equipment. Limited data suggests that infants who are extubated from high-frequency ventilation to an NIV modality without a trial of conventional ventilation have improved pulmonary outcomes 7 though this should be at the discretion of the clinical team. If an infant meets all the following criteria for 6-12 hours with stable blood gas and oxygenation, extubation from HFJV should be strongly considered:

- FiO2 < 0.3 or higher if infant is >14 days of age and oxygen requirement has been stable over 3-5 days
- Measured PEEP ≤ 7-8 cm H2O

HFJV PIP ≤ 20-24 cm H2O

Pharmacologic therapy to facilitate separation from mechanical ventilation. Caffeine should be routinely used in this population of infants after admission to the NICU.

- Caffeine should be administered within 24 hours of extubation attempt.

Post-extubation respiratory support. Infants should be routinely extubated to one of the following modalities:

- NCPAP of 6-8 cm H2O
- Nasal intermittent positive-pressure ventilation (NIPPV) generated through the Dräger ventilator with a PEEP of 6-8 cm H2O, PIP of 15-20 cm H2O, and rate of 10 breaths per minute

Criteria for re-intubation. Infants should be considered for re-intubation if any of the following criteria are met:

- Worsening hypoxemia: FiO2 >0.5 to maintain pulse oximeter saturations of 85-95% after optimizing lung inflation using a PEEP/CPAP of 6-8 cm H2O on NIPPV/bCPAP
    - If FiO2 > 0.1 higher than pre-extubation, repeat CXR to evaluate lung inflation and consider increasing PEEP by 1 cm H2O (to a max of 8 cm H2O).
    - Hypercarbia: Arterial PCO2: > 65 mmHg or venous/capillary PCO2: > 70 mmHg on two consecutive blood gas' 2-4 hours apart
- Repeat CXR to assess lung inflation and increase PEEP if under-inflated
- If patient is on bCPAP, consider changing to NIPPV if lung inflation is optimized

· Recurrent apnea with bradycardia and/or desaturation < 85% requiring resuscitation for recovery

References:
1Courtney, S.E., Durand, D.J., Asselin, J.M., et al. High-frequency oscillatory ventilation versus conventional mechanical ventilation for very-low-birth-weight infants. N Engl J Med. 2002;347(9):643-652.
2Durand, D.J., Asselin, J.M., Hudak, M.L., et al. Early high-frequency oscillatory ventilation versus synchronized intermittent mandatory ventilation in very low birth weight infants: a pilot study of two ventilation protocols. J Perinatol. 2001;21(4):221-229.

[3]Keszler, M., Modanlou, H.D., Brudno, D.S,, et al. Multicenter controlled clinical trial of high-frequency jet ventilation in preterm infants with uncomplicated respiratory distress syndrome. Pediatrics. 1997;100(4):593-599.
[4]Keszler, M., Donn, S.M., Spitzer, A.R. High-frequency jet ventilation in respiratory distress syndrome. J Pediatr. 1991;119(2):340-341.
[5]Keszler, M., Donn, S.M., Bucciarelli, R.L., et al. Multicenter controlled trial comparing high-frequency jet ventilation and conventional mechanical ventilation in newborn infants with pulmonary interstitial emphysema. J Pediatr. 1991;119(1 Pt 1):85-93.
[6]Weiner, G.M., Kattwinkel, J., editors. Textbook of Neonatal Resuscitation. 7th ed. Elk Grove Village, IL: American Academy of Pediatrics and American Heart Association; 2016.
[7]Clark, R.H., Gerstmann, D.R,. Null, D.M., Jr., deLemos, R.A. Prospective randomized comparison of high-frequency oscillatory and conventional ventilation in respiratory distress syndrome. Pediatrics. 1992;89(1):5-12.
[8]Finer, N.N., Carlo, W.A., Walsh, M.C., et al. Early CPAP versus surfactant in extremely preterm infants. N Engl J Med. 2010;362(21):1970-1979.

Appendix 2 - RT Driven Vent Weaning for Stable Patients Towards Extubation. Shared Courtesy of LeBonheur NICU

Protocol for:

Weaning from conventional mechanical ventilation

Patient Type:

Neonatal Intensive Care patients who have been identified by the NICU attending physicians and team to be hemo-dynamically stable and with a pulmonary condition suitable for weaning from the ventilator towards extubation in the next 24-48 hours. An order will be entered: **NICU Ventilator Weaning Protocol-Acute**.

Equipment Needed:

Conventional Mechanical Ventilator, TcPCO2 I-STAT, ABG kits, Stethoscope, cardio-respiratory and hemo-dynamic monitor, pulse oximeter.

Basic Sequence: