Supplemental Information.

Appendix 1. Consensus Guidelines that were formulated to aid with management of patients with severe BPD.

Severe BPD Consensus Guidelines

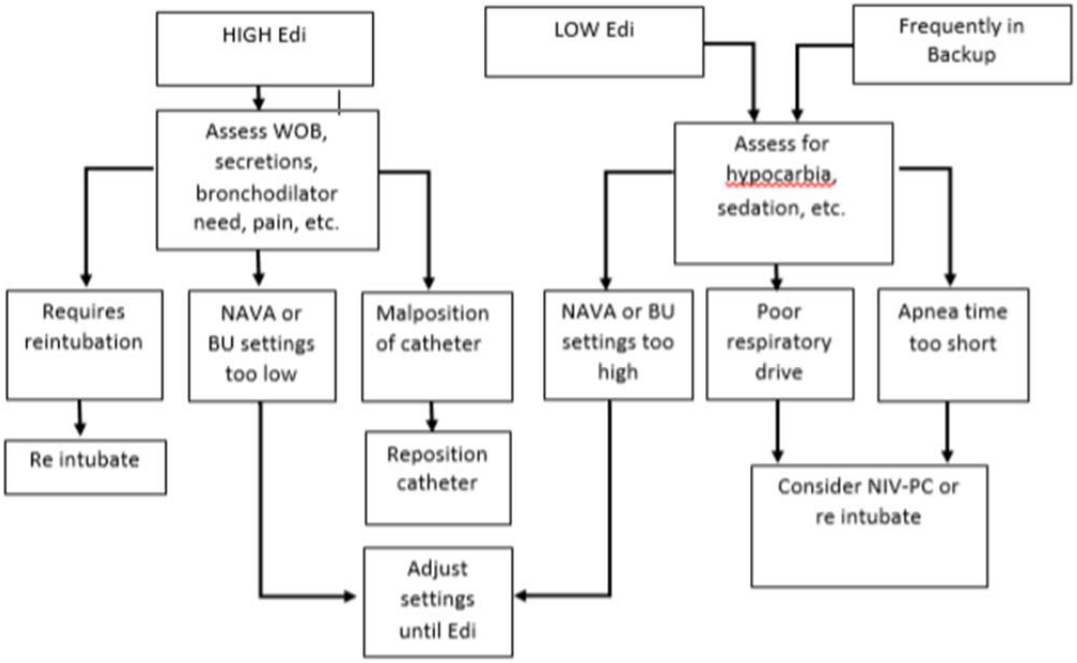
I. Ventilation strategy for infants with severe BPD (preferably at the time of BPD severity classification at 36 weeks PMA; and definitely by 39 - 40 weeks PMA)

1. **Low-rate, large tidal volume, longer I time strategy to achieve adequate minute ventilation (200-300 ml/kg/min)**
   (Rationale: Lung injury in severe BPD is very heterogenous and best described as "two-compartment" model. Focus mode of ventilation to address pulmonary function present in the damaged part of the lung (SLOW compartment or damaged compartment with high R and normal or near normal C). In severe BPD, 67% of tidal volume is from slow compartment. In addition, PFT in severe BPD is dominated by marked increase in R to airflow, meaning time constant is very long, therefore Respiratory Rate must be set low to allow for 5 expiratory time constants. Suggested settings: Rate 20's, Tidal volume 10-12 ml/kg, I time ≥0.5 sec)
2. **PEEP should be relatively high (> 6 to 8 cm H2O)**
   (Rationale: Higher PEEP is needed to optimize gas exchange, maintain FRC and avoid regional atelectasis. It should be even higher when tracheo- or bronchomalacia or TBM are present to keep airways open during active exhalation. TBM is found in 36% of infants with BPD. Higher PEEP in combination with low vent rate and sufficient expiratory time can avoid air trapping).
3. **Changes in Rate, tidal volume, inspiratory and expiratory times and pressures are highly interdependent.**
4. **Consider invasive NAVA if there is significant patient-ventilator asynchrony. The optimal NAVA level is the level that allows comfortable breathing with adequate tidal volume without excessively high peak inspiratory pressure. Edi level alone does not determine NAVA wean.**
   (Rationale: Edi, in conjunction with NAVA level controls NAVA ventilation. PIP = NAVA level X Edi (peak –min) + PEEP. Unlike PC and Volume-targeted ventilation, delivered Pressure during NAVA is continuously adjusted based on the neural feedback to the respiratory centers. Identify "breakpoint" NAVA level to avoid diaphragmatic atrophy and NAVA dependence).
5. **Adjust FiO2 to target spO2 90-95%**
6. **Accept the reality that severe BPD is physiologically STATIC and CHRONIC and will not change substantially over short period of time, therefore, do not wean vent support rapidly.**
7. **Goal is to provide OPTIMAL vent support that allows a.) patient to breath comfortably without evidence of air hunger, b.) weaning of FiO2, c.) adequate growth and d.) tolerance to age-appropriate developmental activities.**

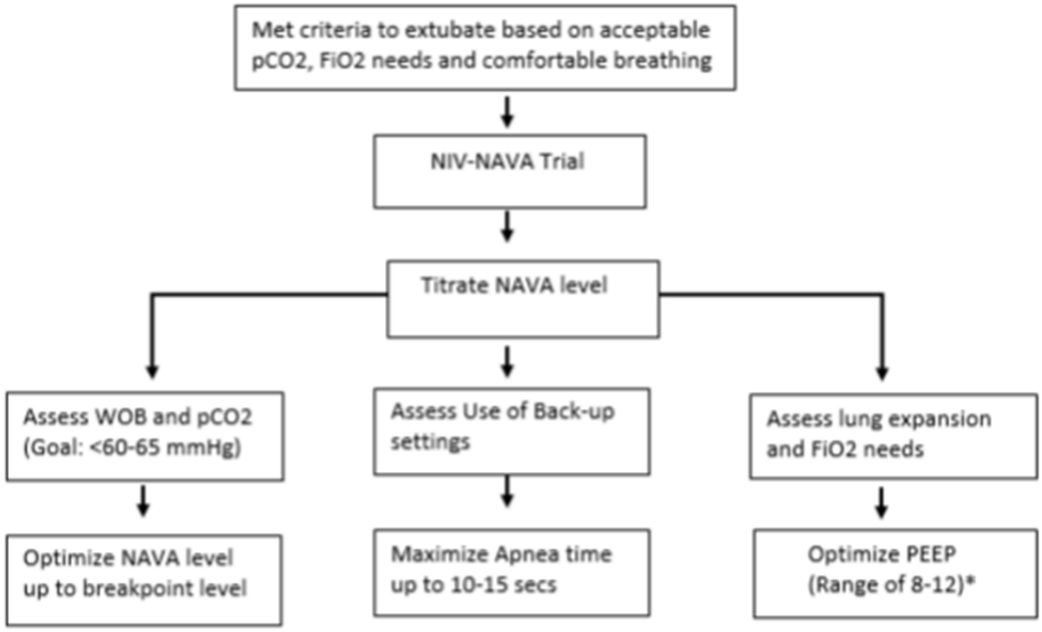
II. Non-invasive NAVA strategy for infants with moderate/severe BPD

1. Generally, not every infant with severe BPD can be maintained or supported adequately with NIV/CPAP/HFNC. Avoid the mentality that extubation to NIV support is being successful. Conversely, reintubation does not always mean a failure.
2. HFNC is less effective than CPAP and confers no advantage for infants who are positive pressure-dependent.
3. Synchronized NIV may be better than unsynchronized NIV and NAVA is a way to synchronize ventilation effectively.
4. With the Servo-U in NIV NAVA, the upper Pressure limit can now be set up to 60. The need for maximum upper Pressure limit must be on a case by case basis.
5. The only benefit of higher NAVA level at maximum pressures is to decrease the rise time delivering the flow faster to help alleviate flow hunger. Goal Edi peak <20 and Edi min <3. Set back up settings to closely match the support received on NIV-NAVA. When using small infant tubing interfaces compared to the larger circuit tubing, back pressure can be generated in the interface.
6. No preference for RAM cannula or nasal mask/prongs. However, RAM cannula is potentially associated with less BPD but at the same time with higher NIV failure rate. RAM cannula has an obligatory leak therefore it delivers lower pressures, therefore consider using higher pressures.
7. Stomach distension is an important part of clinical assessment during NIV.
8. Know when to re-intubate. Consider reintubation when:
    a. maximum NIV support is reached
    b. consistently with baseline pCO_2 >65-70 mmHg and/or FiO_2 >50-60%
    c. exacerbating factors have been explored and treated (infection, aspiration, etc)
    d. evidence of structural upper airway obstruction
    e. strong evidence of/or worsening BPD-associated pulmonary hypertension
9. Other markers of NIV failure include:
    a. persistent tachypnea
    b. increased work of breathing
    c. growth failure
    d. intolerance to perform age-appropriate developmental activities.

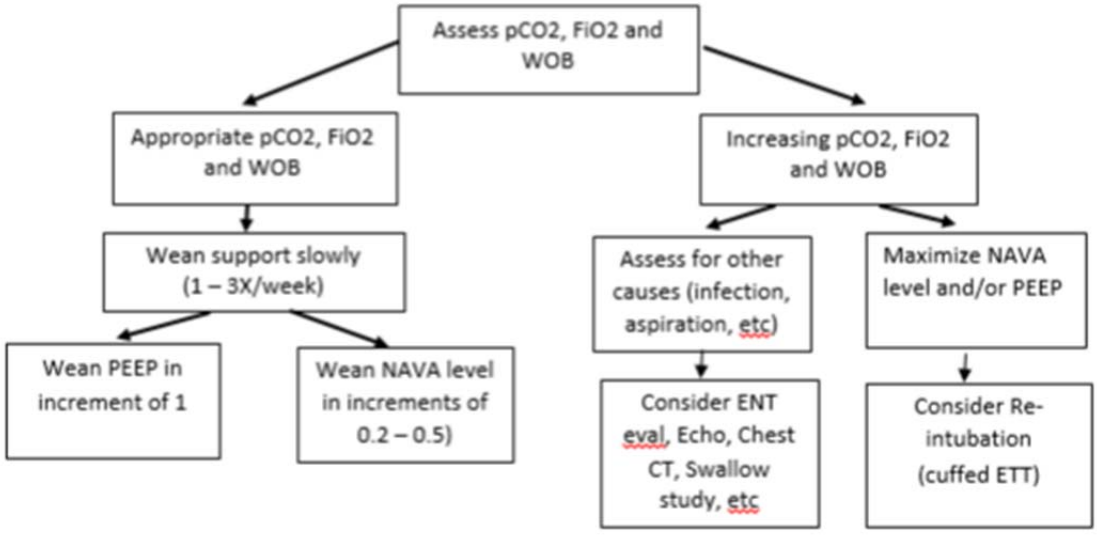
Troubleshooting Algorithm – NIV NAVA for BPD



Initiation Algorithm- NIV NAVA for BPD



Monitoring Algorithm – NIV NAVA for BPD



III Transition to Trilogy Home Ventilator

1. Optimize the patient clinical conditions prior to Trilogy vent trials with the following goals:
   a. to have a stable respiratory status, with normal pH, pCO_2 <60-65 with no significant metabolic alkalosis, and low Oxygen need, preferably <40% FiO_2
   b. adequate growth
   c. tolerance of routine developmental activities
   d. underlying primary lung pathology dictates the mode of ventilation on Trilogy ventilator
2. Understand the 3 most commonly used Modes of Ventilation on Trilogy
   a. PC-SIMV - prescribed pressure control at a **set rate** with variable tidal volumes depending on C and R. All breaths above the set Rate will be spontaneous at the set Pressure Support above the PEEP. Uses SIMV "window" to decide which type of breath (mandatory versus spontaneous) should be delivered. Ideal for infants with weight of less than 5 kg. Potential for air trapping if RR is set high with high I time.
   b. ST (Spontaneous Timed) – ideal for spontaneously breathing infant with relatively normal lungs and those with isolated upper airway anomaly or obstruction. Maybe used on NIV-ST mode with a mask for older infants. Apnea time set to determine when the backup rate/iTime is initiated.
   c. PC Mode – prescribed pressure control level with **each breath at a set I time.** Tidal volumes vary with changes in C and R. With **AVAPS** (average volume-assured pressure support) feature, PS is adopted to patient's needs to guarantee an average tidal volume. The tidal volume is maintained to be equal to or greater than the set target tidal volume by automatically controlling the PS provided to the patient. Inspiratory pressure changes slowly over several minutes (<1 cmH_2O/min up to max of 5 cmH_2O/min); set the AVAPS rate to 5 cmH_2O to avoid discomfort to the patient. Digital Auto-TRAK algorithm identifies leak by comparing with original baseline and new baseline is created. Attention to cuffed tubes with minimal leak inflation. Minimum tidal volume requirement of 50 ml. Set trigger sensitivity to ATS. Set rise time to 1. iPAP is adjusted to maintain true average patient tidal volume. Consider a wide range of inspiratory pressures (min iPAP and max iPAP) and adjust clinically based on RR, work of breathing and lung dynamic changes. As a starting point, the min IPAP should be close to the average PIP on conventional ventilation, then titrated down over time, as appropriate.
3. Transitioning from Servo-I PRVC to Trilogy
   a. Servo-I PRVC – set tidal volume is achieved by automatic breath-by-breath regulation. If the measured tidal volume increases/decreases, the pressure level adjusts between consecutive breaths in steps of a maximum of 3 cmH_2O (fast dynamic change)
   b. Simulate the Servo-I PRVC settings with slight increase to compensate for dead space and slower dynamic change in peak inspiratory pressure
   c. Trend peak inspiratory pressures while on Servo-I, keeping in mind that iPAP max on Trilogy can only be set up to 40 cmH_2O above PEEP.

4. Infants on NAVA, it is preferable to transition to Servo –I SIMV (PRVC) or straight PRVC first as a bridge to Trilogy ventilator.
   a. While on NAVA, decrease NAVA level to maintain Edi peak and min wnl; assess spontaneous Vte, VE and spontaneous pPeak and note the dynamic changes in pPeak. Consider adjusting NAVA trigger to strengthen inspiratory demand of diaphragm.
   b. Trial of SIMV-PRVC from NAVA- monitor edi signal, assess asynchrony and edi measurements. Perform expiratory hold, monitor end expiratory flow (Vee). Start with short periods of time and extend time based on patient's tolerance.

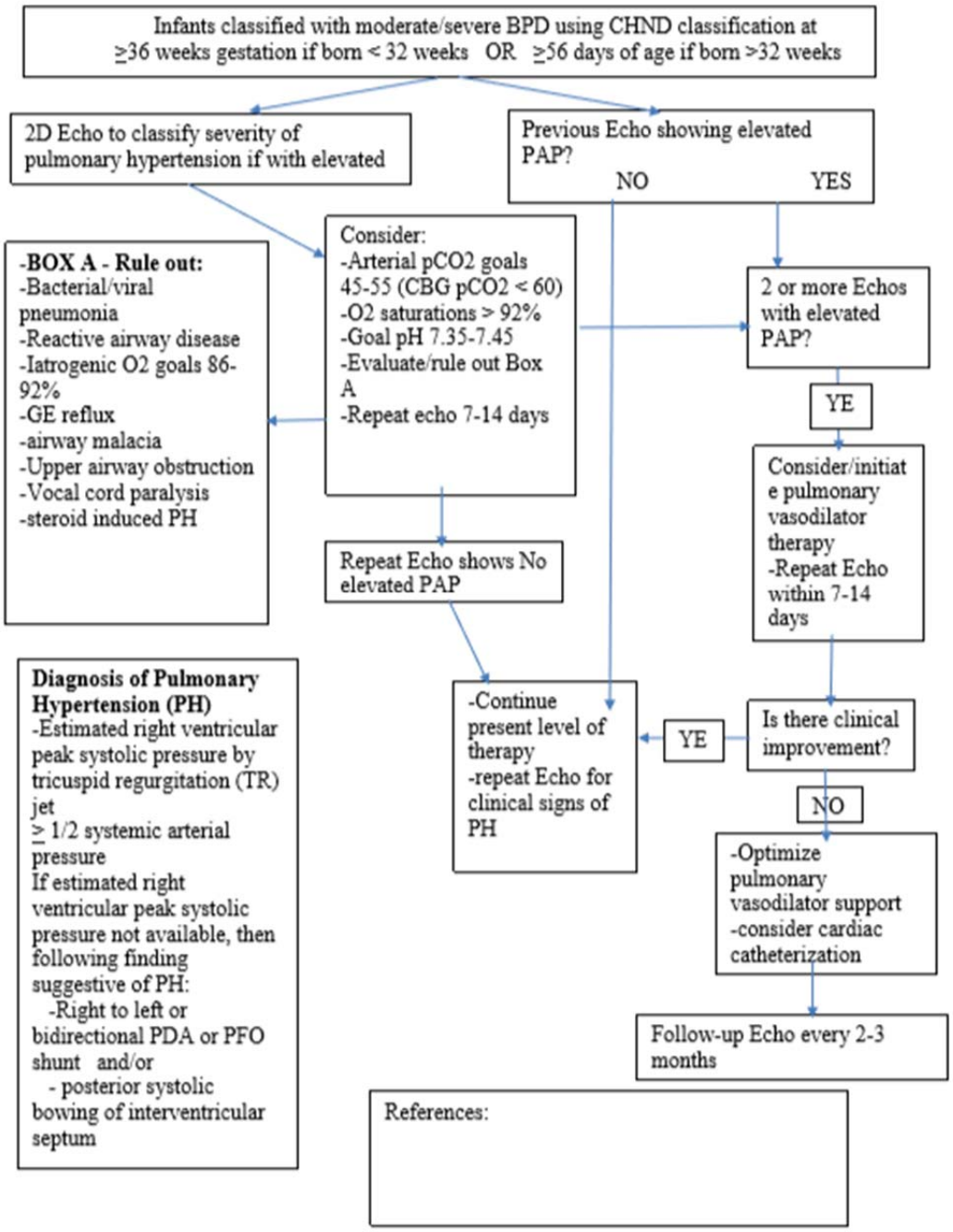
c. Trial of PRVC from NAVA – assess patient without PS breaths. Monitor pneumatic triggering capabilities, perform expiratory hold and monitor Vee.

5. Additional Practice Recommendation
   a. Start Trilogy trials slowly, from 1-2 hours up to 3-4 hours/day taking note of RR and work of breathing, pre/post end tidal CO2 and change in FiO2 requirement
   b. Obtain a ventilator download while on Trilogy vent to assess average RR, TV, minute ventilation and peak inspiratory pressures
   c. If Trilogy trials not tolerated for up to 4 hours at a time under optimal conditions, change back to baseline mode of ventilation (Servo-I PRVC or NAVA) and wait for 1 to 2 weeks to try again
   d. Use of in-line heat moisture exchange (HME)- to be initiated once infants are stable on Trilogy vent 24 hours/day for 1-2 weeks. Total duration of in line HME tolerance should be calculated based on time needed for travels plus anticipated duration of clinic visits. Once these trials are tolerated daily for the prescribed duration of hours/day for at least a week, the trials can be changed to 2 -3 times/week. Hold trials if clinical condition changes due to acute illness.
6. Potential Pitfalls during transition to trilogy vent
   a. Using lower ventilatory support on Trilogy compared to Servo-I
   b. Clinical condition not optimized to sustain transition
   c. Tendency to rush without consideration of the primary lung pathology

IV BPD-associated pulmonary hypertension

10. Between 20% and 40% of infants with BPD develop pulmonary hypertension (PH). The risk is related to the severity of BPD. The pathophysiologic mechanism of BPD-associated PH is not well defined.
11. All infants with moderate or severe BPD should be screened for PH using echocardiography performed at the time the formal diagnosis of BPD is made (see algorithm)
12. A presumptive diagnosis of PH by echocardiography is based on:
    a.) quantitative estimate of RV peak systolic pressure by TR jet or
    b.) demonstration of R to L or bidirectional shunting through PDA or PFO or posterior systolic bowing of interventricular septum
13. Evaluate for other underlying cardiovascular, airway or other treatable conditions (Algorithm Box A) at the time of PH assessment
14. The goals of treatment include:
    a.) optimizing BPD management by improving gas exchange
    b.) avoiding hypoxic pulmonary vasoconstriction
    c.) optimizing lung growth
    d.) preventing further lung injury
15. Infants with sustained PH after initial evaluation and management are candidates for targeted pharmacotherapy using Sildenafil
16. Pulmonary hypertension team should be involved in the management of ALL infants with BPD-associated PH

Evaluation of Pulmonary Hypertension in BPD/CLD patients



V - Nutritional support for severe BPD

Background: Nutrition and lung function are interdependent. Careful adjustment of parenteral nutrition and appropriate enteral feeding selection and progression are vital to enhancing growth. Nutritional success in patients with BPD/CLD is complicated by many factors. Resolution of lung disease and improvement in lung function depends on emphasizing nutritional strategies that enhance somatic and lung growth.

Recommendations:

1. Conservative fluid intake, while ensuring adequate delivery of nutrients and water to meet nutritional and physiological needs, usually in the range of 130-150 ml/kg/day. Fluid needs decrease over the first year of life.

2. Optimize energy intake, goal caloric intake of 130-150 kcal/kg/day, with careful balance of carbohydrate and lipid calories. Breastmilk is preferred, but fortification is needed to make up for protein and mineral deficiencies.

3. The goal for lipid intake should be the amount that prevents essential fatty acid deficiency, i.e., 40-55% of total energy intake. Supplementation with MCT oil may be needed.
4. Adequate protein intake should be provided according to corrected gestational age, aiming for higher range during catabolic and hypermetabolic states. Goal protein intake for patients with established BPD is 3.6 – 4 gm/kg/day. Supplementation with HMF, premature formula or liquid protein may be needed.
5. Diuretic therapy predisposes to Na and K depletion. Supplementation should be considered when serum Na <130 mEq/L and/or serum Cl <90 mEq/L.
6. Calcium intake of 120-140 mg/kg/d of highly bioavailable calcium salts; phosphorus intake of 60-90 mg/kg/d of phosphate; vitamin D intake of 800-1000 IU/d.

   Regular monitoring for metabolic bone disease should be done.
7. Patients with CLD/BPD have changing nutritional needs over time, during growth suppressive states, comorbidities, and during periods of high metabolic needs. The goal is to deliver adequate constituents that match the patient's specific needs. Nutritional intake should be titrated accordingly at least weekly in close collaboration with ICN dietician.
8. Growth assessments include weight gain and linear growth. Weight for length should be followed closely, with a target goal of ~50%. Weight can be influenced by fluid status.
9. Patients with moderate/severe BPD are at high risk for aspiration due to dysfunctional swallowing, GER and increased oropharyngeal secretions. Evaluation and ongoing assessment by OT and ST are highly recommended.
10. In patients with proven or high clinical suspicion of aspiration, a trial of transpyloric feedings should be considered for at least 2 weeks to determine if respiratory status (i.e. ventilatory and FiO2 requirements, CXR findings) improve.
11. Provide adequate respiratory support that would minimize energy expenditure and stress-induced growth suppression, allowing for tolerance of developmental activities and play.

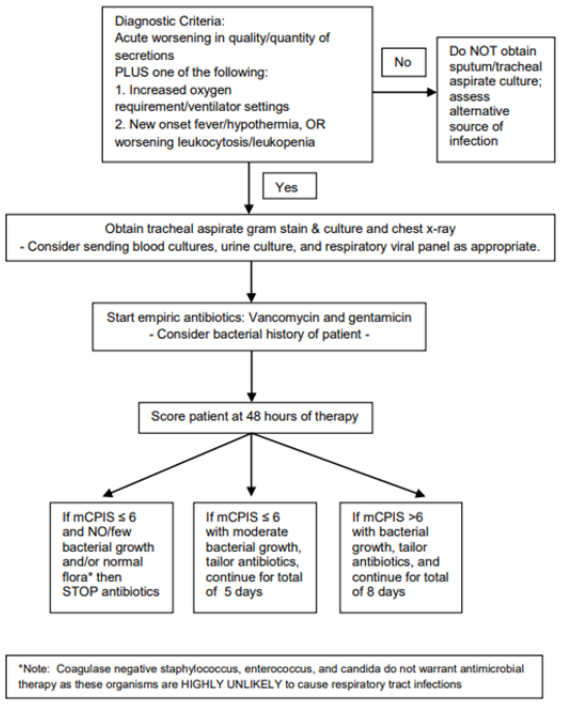
Appendix 2. The CLD team performed quarterly educational presentations to provide updated information relevant to the management of infants with CLD.

Education Roadmap for the CLD team	
2010	
February	-Pediatric Tracheostomy Home Care-review products from Bivona, Shiley, & Mallinckrodt -Facilitating consistent communication with families
April	-Review of LTV ventilator -minimal leak policy and technique -recommended inflation technique for Bivona TTS tracheostomy tube -CMH RT Guidelines: Monitoring artificial airway intracuff pressure/leak
May	-Indications for Tracheostomy -discussed indications for tracheostomy in BPD and other conditions -proposed assessment criteria/evaluations prior to tracheostomy consideration -listed subspecialty consultations
June	-Update on tracheostomy ordering -LTV Considerations for CLD and tips for home ventilation (demo)
July	-SERVO-I Theory, Techniques, and Applications
October	-Infant pulmonary function diagnostic system for infants -NAVA in the ICN
2011	
January	-Infant PFT estimation of lung volumes and pulmonary mechanics in infants
February	-Acute effects of Sildenafil treatment for pulmonary hypertension in infants with BPD
March	-Evaluation of pulmonary hypertension in BPD/CLD overview and guideline
July	-FRC Overview
August	-Neonatal Tracheobronchomalacia and its diagnosis by Tracheobronchography
2012	
January	-ICN communication committee (family groups, teaching, and parent to parent) -Telehealth
June	-Alternatives for Narcotic/Benzodiazepine weaning
2013	
March	-Feeding plans for ventilated infants
April	-Ventilation strategies for older CLD patients
June	-An alternative nutritional approach in an older CLD patient population
August	-Trilogy ventilator use in the ICN
October	-Palivizumab prophylaxis in the ICN for patients with CLD -Research study iNO in BPD/CLD -Synagis use update for 2013-2014 RSV season
2014	
January	-Multicenter BPD collaborative
February	-Role of occupational therapy in infants with BPD and/or ventilator dependence
April	-Multicenter BPD collaborative update
May	-Home Vent education video (viewing and public release)
August	-PHARM: Systemic steroids and BPD
November	-Respironics' Trilogy Ventilator Tool
2015	
January	-Updated to AAP recommendations for RSV prophylaxis
February	-Pediatric emergency forms -Montelukast and BPD -BPD collaborative update
November	-Inhaled nitric oxide for treatment of hypoxic respiratory failure in preterm infants -Infant pulmonary score for tracheitis
December	-Hearing screening guidelines in the NICU
2016	
February	-Short-term outcomes of infants with Chiari II malformation with tracheostomy and home ventilator-dependence -Case series of non-infectious parotitis in infants with BPD -Long term feeding outcomes trachs <24 months -Inhaled steroids
May	-Home visiting project for ventilator dependent infants
June	-Adrenal suppression in premature infants with BPD on inhaled fluticasone propionate HFA
July	-Inhaled corticosteroid formulary change
August	-Inhaled medications in the ICN: Dornase -Inhaled steroids study

September	-Tracheitis algorithm and inhaled medications in the ICN
October	-RT bagging concerns
2017	
January	-Environmental home health
February	-Four-dimensional CT for the diagnosis of tracheobronchomalacia in ventilator-dependent infants with BPD
March	-Factors leading to hospital readmission <2-year-old tracheostomized-ventilator dependents infants
May	-BPD collaborative update
June	-Oxygen saturation histograms in NICU care
August	-CLD patient transport: preparation, safety, and airway during transport
December	-Effect of Aerosol devices and administration techniques on drug delivery in a simulated spontaneous breathing pediatric tracheostomy model
2018	
	-General BPD ventilation principles -NAVA in BPD -NIV in BPD -Transition to trilogy home ventilator -BPD-associated pulmonary hypertension -Steroids and BPD -Growth and nutrition for BPD

Appendix 3. A QI initiative produced the Tracheitis algorithm to decrease antibiotic exposure of chronically intubated patients.

Evaluation and Diagnosis of Tracheitis in the Intensive Care Nursery



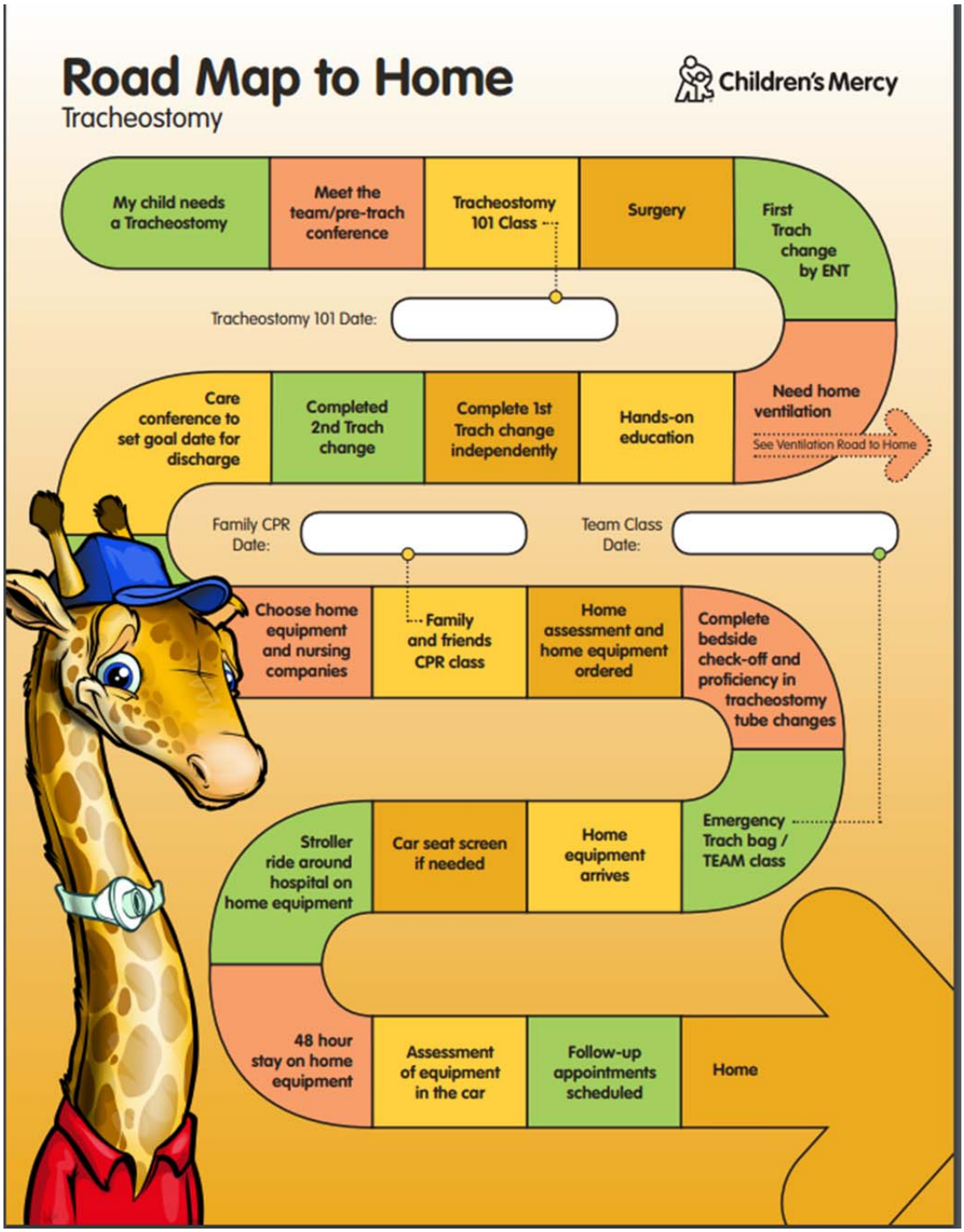
Calculating the Modified Clinical Pulmonary Infection Score (mCPIS)

	0 Point	1 Point	2 Points
Temp (° C)[a] *Age is based on chronological age*	< 3 months of age: 36.5-37.9 ≥ 3 months of age: 36.5 to 38.4	< 3 months of age: 38 to 38.4 ≥ 3 months of age: 38.5 to 38.9	< 3 months of age: ≤ 36.4 or ≥ 38.5 ≥ 3 months of age: ≤ 36.4 or ≥ 39
WBC (cells/mm^3)	4,000-11,000	<4,000 OR > 11,000 AND with I:T ratio ≥ 0.3	
Tracheal Secretions	None/Baseline	Increased but non-purulent	Increased AND Purulent
Chest X-Ray	Only atelectasis OR No new infiltrate	Diffuse or patchy infiltrates	Localized Infiltrate OR consolidation present
Progression of infiltrate	None		Progression
Tracheal Aspirate – WBC	No/Few/Rare WBCs	Moderate/Many WBCs	
Tracheal Aspirate - Growth	No growth OR known colonization OR > 1 organism	Moderate/heavy growth of a single organism OR moderate/heavy growth of a new organism	
Respiratory factors: 1. Escalation of any of the ventilatory settings (Pressure, Rate, MAP) OR switch to a different mode of ventilation 2. Sustained FiO_2 absolute increase of >20% from baseline[b] 3. Need for adjunctive respiratory therapy	Baseline (none of the factors present)	Presence of 1 respiratory factor	Presence of 2 or more respiratory factors

[a]Temp not due to environmental factors or antipyretic use

[b]Example: FIO_2 increase from 21% to 41%

Appendix 4. Families/caregivers must complete and be competent in skills training and receive education for discharge home. This image "Roadmap to home" is provided to families to track their progress.



Appendix 5. Representation of the locations of infants treated by the CLD team.