Severe Bronchopulmonary Dysplasia

Ventilator Strategies and Concepts of Care

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Objectives

- Define and describe BPD
- Discuss concepts of care in BPD
- Evaluate data from PASSIVE study

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Abbreviations

- BPD, Bronchopulmonary Dysplasia
- RDS, Respiratory Distress Syndrome
- PEEP, Positive End Expiratory Pressure
- PPV, Positive Pressure Ventilation
- NICU, Neonatal Intensive Care Unit
- PICU, Pediatric Intensive Care Unit
- GA, Gestational Age at birth
- PMA, Postmenstrual Age
- wk, weeks
- SGA, Small for Gestational Age
- IQR, Interquartile Range
- SIMV, Synchronized Intermittent Mandatory Ventilation
- AC, Assist Control
- VT/VC, Volume-Targeted/Volume-Control
- PC, Pressure Control
- NAVA, Neurally Adjusted Ventilatory Assist
- CPAP, Continuous Positive Airways Pressure
- PIP, Peak Inspiratory Pressure
- MAP, Mean Airway Pressure
- Ti, inspiratory Time
- HFNC, High Flow Nasal Cannula
- LFNC, Low Flow Nasal Cannula
- NIV, Noninvasive Ventilation
- NIPPV, Noninvasive intermittent positive pressure ventilation
- Vt, tidal volume
- RR, respiratory rate

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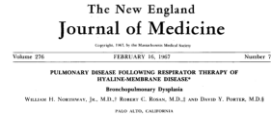
BPD: History

- 1967 Northway described a **heterogenous lung disease** with **fibrosis** and **cor pulmonale** in surviving infants born prematurely and treated with high airway pressures and FiO_2.


The New England Journal of Medicine

Volume 276 FEBRUARY 16, 1967 Number 7

PULMONARY DISEASE FOLLOWING RESPIRATOR THERAPY OF HYALINE-MEMBRANE DISEASE*
Bronchopulmonary Dysplasia

- The **spectrum** of BPD has **broadened**, and the **incidence** of BPD has **increased**.

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BPD: Features

- **Radiographiphic features** –Heterogenous hyperinflation, atelectasis, densities extending to periphery
- **Pathologic features** –Alternating **emphysematous/cystic** and **collapsed** areas, interstitial fibrosis and edema, dilated tortuous **lymphatics**, **vascular** medial muscle hypertrophy
  - **Decreased surface area** for gas exchange –Marked decrease in number of alveoli and capillaries

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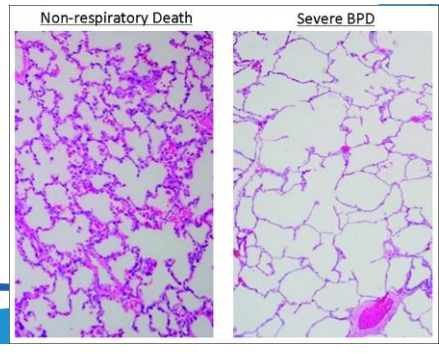

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BPD Classifications

- Improved survival, changes in clinical practice (low flow high FiO_2, HFNC, NIPPV), and knowledge of outcomes necessitate a new classification with prognostic implications.
- Simple new classification system linked to 2-year outcomes data.

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BPD Classifications

- **1978** NHLBI criteria, published by Tooley and Bancalari 1979
  - Oxygen use at 28 days of life
- **1988** Shennan tailored diagnosis to predict outcomes at 2 years
  - Oxygen use at 36wks PMA
- **2001** NHLBI Severity-based categories
  - Mild (RA), moderate (<30% O_2), or severe (>30% O_2 or CPAP/PPV) at 36wk PMA or discharge
- **2018** NICHD Workshop
  - Grades 0-3 based on FiO_2 and type of support at 36wk PMA or discharge
  - Reflects current respiratory management, but not outcomes-based.
- **2019** Jensen Definition
  - **Outcomes-based**. Simple. N =2677.

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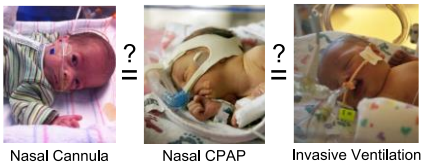
Are these cases equally "severe"?

GA = 28 weeks PMA = 36 weeks



Nasal Cannula 1L/min 35% FiO_2

Nasal CPAP 6cm H_2O 35% FiO_2

Invasive Ventilation Vt 7mL/kg / PEEP 6 35% FiO_2

*Slide from presentation by Erik Jensen CHOP CLD Conference 3-13-2019

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2018 NICHD Workshop BPD Classification

Table I. Suggested refinements to the definition of BPD

A premature infant (<32 weeks' gestational age) with BPD has persistent parenchymal lung disease, radiographic confirmation of parenchymal lung disease, and at 36 weeks PMA requires 1 of the following FiO_2 ranges/oxygen levels/O_2 concentrations for ≥3 consecutive days to maintain arterial oxygen saturation in the 90%-95% range.

Grades	Invasive IPPV*	N-CPAP, NIPPV, or nasal cannula ≥ 3 L/min	Nasal cannula flow of 1–<3 L/min	Hood O_2	Nasal cannula flow of <1 L/min
I	—	21	22-29	22-29	22-70
II	21	22-29	≥30	≥30	>70
III	>21	≥30			
III(A)	Early death (between 14 days of postnatal age and 36 weeks) owing to persistent parenchymal lung disease and respiratory failure that cannot be attributable to other neonatal morbidities (eg, necrotizing enterocolitis, intraventricular hemorrhage, redirection of care, episodes of sepsis, etc).				

*Excluding infants ventilated for primary airway disease or central respiratory control conditions.
Values are percents.
CPAP, continuous positive airway pressure; *IPPV*, intermittent positive pressure ventilation; *N-CPAP*, nasal continuous positive airway pressure; *NIPPV*, noninvasive positive pressure ventilation.

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Variability Among "NIH Severe BPD"

- High variability within category of "NIH Severe BPD"
- Additional phenotyping and Jensen definitions are helpful
- Descriptive data will facilitate further study

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Optimal BPD Definition

Treatment with the following respiratory support at 36 weeks PMA or discharge home if earlier:						
Room Air No 28 day O_2 assessment	NC ≤ 2L/min "low" flow		NC > 2L/min "high" flow		nCPAP NIPPV	Invasive PPV
	FiO_2 <30%	FiO_2 ≥30%	FiO_2 <30%	FiO_2 ≥30%	Any FiO_2	FiO_2 <30%	FiO_2 ≥30%
No BPD	Grade 1		Grade 2			Grade 3	

- Best predictor of both composite study outcomes
- No need to assess for 28 days of oxygen therapy
- Severity graded based on the **mode of support at 36 weeks PMA**, irrespective of oxygen level

NICHD Neonatal Research Network

*Slide from presentation by Erik Jensen CHOP CLD Conference 3-13-

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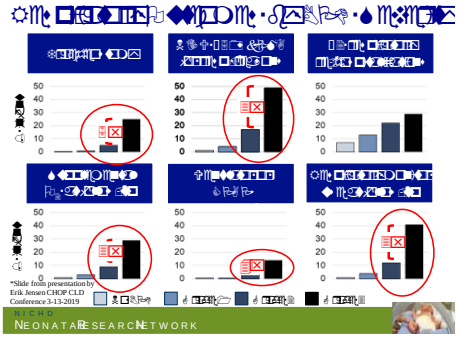

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Management Strategies in Severe Bronchopulmonary Dysplasia

- No large-scale studies
- Heterogenous disease
- Need to shift from **acute care strategies** designed to minimize exposure to positive pressure to **long-term strategies** designed to promote growth and development

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BPD Management: Overview

- Support growth and development while minimizing further lung damage
- Need to consistently apply what we know while developing and investigating optimal strategies

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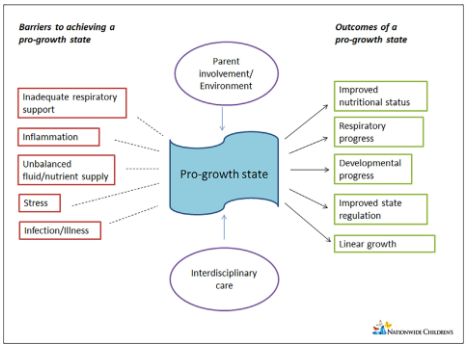

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Open Lung Strategy

- Optimize distribution of ventilation
- Identify appropriate tidal volume and PEEP
- Minimize atelectasis and V/Q mismatch
- Minimize oxygen toxicity

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"Whole Baby" Approach

- Gas exchange may be acceptable despite poor lung parenchymal and vascular growth, abnormal pulmonary and airways smooth muscle remodeling, and stalled injury repair
- Inadequate data to suggest optimal $PaCO_2$ and SpO_2

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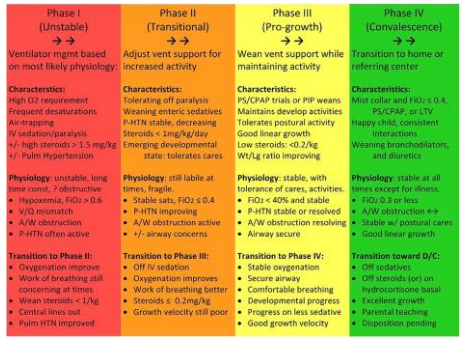

Phase I (Unstable) →→	Phase II (Transitional) →→	Phase III (Pro-growth) →→	Phase IV (Convalescence) →→
Ventilator mgmt based on most likely physiology:	Adjust vent support for increased activity	Wean vent support while maintaining activity	Transition to home or referring center
Characteristics: High O2 requirement Frequent desaturations Air-trapping IV sedation/paralysis +/- high steroids > 1.5 mg/kg +/- Pulm Hypertension	**Characteristics:** Tolerating off paralysis Weaning enteric sedatives P-HTN stable, decreasing Steroids < 1mg/kg/day Emerging developmental state: tolerates cares	**Characteristics:** PS/CPAP trials or PIP weans Maintains develop activities Tolerates postural activity Good linear growth Low steroids: <0.2/kg Wt/Lg ratio improving	**Characteristics:** Mist collar and FiO2 ≤ 0.4, PS/CPAP, or LTV Happy child, consistent interactions Weaning bronchodilators, and diuretics
Physiology: unstable, long time const, ? obstructive • Hypoxemia, FiO2 > 0.6 • V/Q mismatch • A/W obstruction • P-HTN often active	**Physiology**: still labile at times, fragile. • Stable sats, FiO2 ≤ 0.4 • P-HTN improving • A/W obstruction active • +/- airway concerns	**Physiology**: stable, with tolerance of cares, activities. • FiO2 < 40% and stable • P-HTN stable or resolved • A/W obstruction resolving • Airway secure	**Physiology**: stable at all times except for illness. • FiO2 0.3 or less • A/W obstruction ←→ • Stable w/ postural cares • Good linear growth
Transition to Phase II: • Oxygenation improve • Work of breathing still concerning at times • Wean steroids < 1/kg • Central lines out • Pulm HTN improved	**Transition to Phase III:** • Off IV sedation • Oxygenation improves • Work of breathing better • Steroids ≤ 0.2mg/kg • Growth velocity still poor	**Transition to Phase IV:** • Stable oxygenation • Secure airway • Comfortable breathing • Developmental progress • Progress on less sedative • Good growth velocity	**Transition toward D/C:** • Off sedatives • Off steroids (or) on hydrocortisone basal • Excellent growth • Parental teaching • Disposition pending

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Blood Gases

- Physical examination is at least as informative to guide weaning/escalation of support
- Avoid using permissive hypercarbia merely to avoid endotracheal intubation in infant with increased work of breathing and extrauterine growth failure

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Physical Examination

- Assessing work of breathing while sleeping may underestimate the degree of respiratory distress encountered during activity.
- Tolerance of therapies (or the Behavioral Sign of Respiratory Instability Scale) is an important indicator of adequacy of support.

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Noninvasive Respiratory Support

- Goal is to encourage growth and development.
- Goal is not primarily to avoid invasive ventilation
- Monitor for poor growth, worsening pulmonary hypertension, inability to tolerate activities, and repeated hypoxemic spells

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Weaning Strategies

- **RDS**
  - Rapid weaning corresponding to rapid improvement
- **BPD**
  - Slow weaning corresponding to gradual improvement
  - Avoid daily changes
  - Signs of inadequate support may be subtle, gradually develop, easily overlooked

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BPD Spells

- Acute, severe hypoxemia with airway collapse and/or pulmonary hypertensive crisis often associated with agitation or stooling
- Brief periods of higher PEEP may help
- Developing an individualized bedside plan is helpful

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Ventilation Strategies in Severe Bronchopulmonary Dysplasia

- No large-scale studies
- Heterogenous disease
- Different lung mechanics from RDS
- Need to shift from **acute care strategies** designed to minimize exposure to positive pressure to **long-term strategies** designed to promote growth and development

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RDS

- Low compliance, near-normal resistance
- Homogenous disease
- Goal is to minimize exposure to mechanical ventilation
- Frequent blood gases and adjustments

BPD

- Low compliance, high resistance
- Heterogenous disease
- Goal is to support growth and development, promote healing
- Less frequent gases and adjustments

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Parameter	Healthy	RDS	BPD
Compliance ($mL/cm\ H_2O$)	3-5	0.5-1	<1
Resistance ($cm\ H_2O/L/s$)	20-40	>40	>150
Time Constant (s)	0.09-0.15	0.05	>0.15

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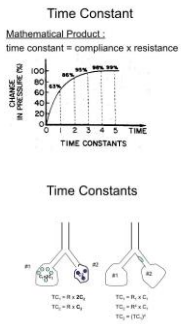
Time Constant (TC) = Resistance x Compliance

- How quickly lung volumes change
- In 1 TC, alveoli empty 63%.
- 2 TC, 84%. 3 TC, 95%.
- **3**-5 TCs required for adequate inspiration or expiration.
- *0.09 – 0.15s in healthy newborns, 0.05s in RDS, >0.15s in CLD.



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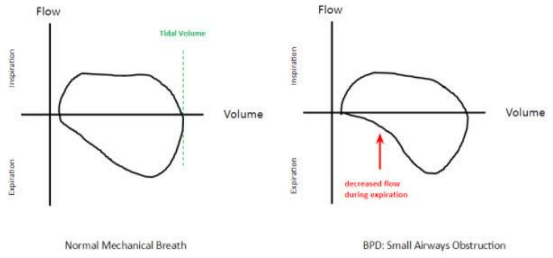
Airways Resistance



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The Ventilator is our Friend

- Holistic care, where management of lung disease and changes to level of support include consideration of strategies to improve somatic growth and neurodevelopment
- Optimize gas exchange, minimize dead space, limit excessive work of breathing, avoid intermittent hypoxemia

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BPD Phenotypes

1. Lung **parenchymal**
2. Pulmonary **vascular**
3. Small/large **airway** dysfunction

- Often a **mixed** phenotype with components of all three.

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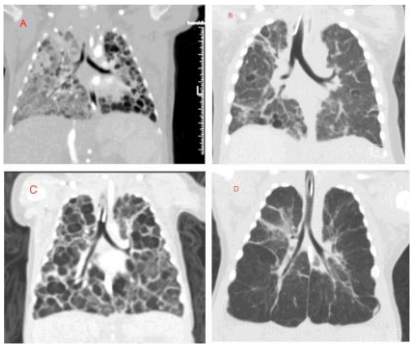

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Ventilator Strategies by Phenotype

- **Airways malacia**
  - Prevent airway collapse with optimal PEEP
- **Parenchymal disease**
  - Prevent atelectasis with adequate tidal volume, inspiratory time, and PEEP
- **Pulmonary vascular disease**
  - Decrease pulmonary vascular resistance

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Intrinsic PEEP ("Auto-PEEP" or PEEPi)

- Expiration prolonged by high airways resistance then interrupted by the subsequent inspiration
- High end-expiratory lung volumes cause hyperinflation
- Infant must overcome PEEPi to pneumatically trigger a spontaneous breath

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WASTED EFFORTS

*Slide from presentation by Natalie Napolitano at CHOP CLD Conference 3-13-2019

Children's Hospital of Philadelphia

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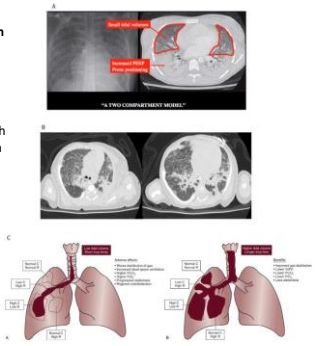
Two Compartment Model for Ventilation in Severe BPD

Illustration of **A,** 2-zone disease vs **B,** multizone (heterogeneous) disease. **A,** Chest CT with 2 zones in a patient with acute respiratory distress syndrome. **B,** Chest CT in a patient with type 2 sBPD and diffuse, heterogeneous disease. **C,** Schematic illustrating concept of multizone disease. Time constant, T = resistance x compliance.



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Multicenter Point Prevalence Study

McKinney RL, Napolitano N, Levin JJ, Kielt M, Abman SH, Guaman MC,Rose RS, Courtney SE, Matlock D, Agarwal A, Leeman KT, Sanlorenzo LA, Sindelar R, Collaco JM,Baker CD, Hannan KE, Douglass M, Eldredge LC, Lai K, McGrath-Morrow SA, Tracy MC, Truog W, Lewis T, Murillo AL, Kessler M, on behalf of the BPD Collaborative, Ventilatory Strategies in Infants WithEstablished Severe Bronchopulmonary Dysplasia: A Multicenter Point Prevalence Study, The Journal of Pediatrics (2021), doi: https://doi.org/10.1016/j.jpeds.2021.10.036.

- Point prevalence study to describe respiratory management practices of infants with severe BPD
- Ventilator support:
  - Type
  - Settings
- 187 infants, 15 centers, US and Sweden, 51% invasively ventilated

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Methods

- 8 AM October 29th, 2019
- Eligibility Criteria:
  - <24 months chronologic age
  - **Never discharged**
  - Severe BPD (2001 NIH): <32 weeks GA, >28 days of support required, ≥0.30 FiO_2 or PPV at 36 weeks
- Exclusion Criteria:
  - Requiring support due to surgical, neurologic, or anatomic reasons

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Results

- 16 hospitals (15 institutions) in US and Sweden
- 192 eligible infants (complete data from 187)
- Median PMA 46 weeks
- **86% in NICU**, 6% in PICU, 6% "Stepdown," 2% General Ward

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Results

- 27% s/p tracheostomy (53% of invasive group)
  - Median PMA 52wks
- **60% male**
- Median GA 25 weeks
- Median birth weight 710 grams

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BPD Classification

- Severe BPD **Type I**: Requiring noninvasive support at 36 wks PMA
- Severe BPD **Type II**: Requiring invasive support at 36 wks PMA

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BPD Classification

- **Type II** infants (Invasively Ventilated at 36wk):
  - **Lower birthweight** (631g vs 780g, p=0.003)
  - **Higher FiO_2** requirements at 36 and 40 weeks PMA
  - No difference in other demographics

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Support at 36 weeks PMA

- 91 of 176 were on noninvasive support at 36 weeks, **23 of these 91 were on invasive support at the time of the study.**
- 74% of those invasively ventilated at 36 weeks remains on ventilator on the study day (median PMA 46 weeks).

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Invasive Support on Study Day

- Invasive ventilation:
  - SIMV (64%), AC (21%)
  - VT/VC (50%), PC (43%)
- Noninvasive ventilation:
  - Nine modes, varied significantly by center

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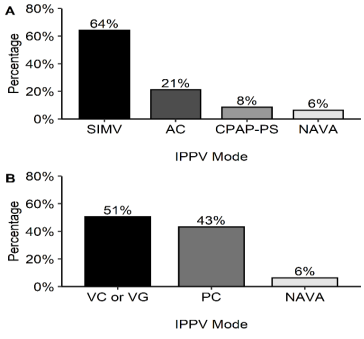

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Median (IQR) Invasive Ventilator Settings

- PIP: 32 (25.5-50.5)
- PEEP: 10 (8-11)
- FiO_2: 0.33 (0.29-0.4)
- MAP: 17 (13.8-20)

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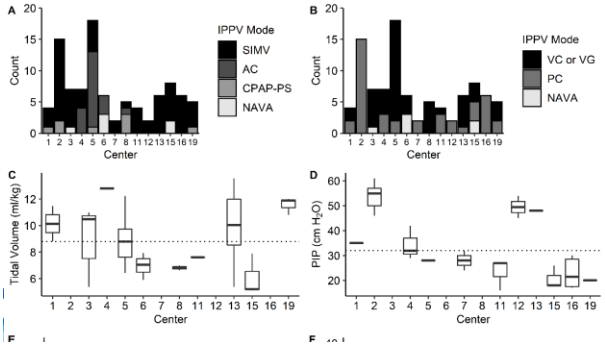

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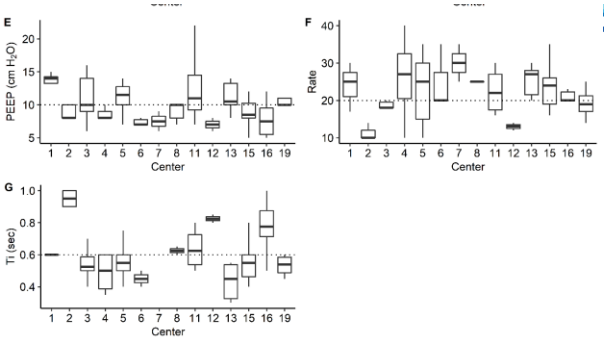

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Table III

Comparison of ventilator strategies and goals during progression of early disease to established sBPD (modified from Abman and Nelin[29])

Early (prevention)	Strategies to prevent acute lung injury	Low tidal volumes (3–5 mL/kg)
		Short inspiratory times (0.2–0.3 seconds)
		Increased PEEP for lung recruitment without overdistension
	Strategies for gas exchange	Adjust FiO_2 to target SpO_2 (range: 91%–95%)
		Permissive hypercapnia
Late (established BPD)	Strategies for gas exchange	Marked regional heterogeneity
		Larger tidal volumes (10–12 mL/kg)
		Longer inspiratory times (≥0.6 s)
		Airways obstruction
		Slower rates allow for better emptying, especially with larger tidal volumes (10–20 bpm)
		Complex roles for PEEP with dynamic airway collapse
		Interactive effects of ventilator strategies
		Changes in rate, tidal volume, inspiratory and expiratory times, and pressure support are highly interdependent
		Overdistension can increase agitation and paradoxically worsen ventilation
	Strategies for gas exchange	Adjust FiO_2 to target higher SpO_2 (92%–95%)
		Permissive hypercapnia to facilitate weaning

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Noninvasive Ventilator Settings

- 5 Modes: HFNC (41%), LFNC (28%), CPAP (26%), NIV NAVA (**3%**), NIPPV (**2%**)
- HFNC used most commonly
- Very few babies on NIPPV or NIV NAVA

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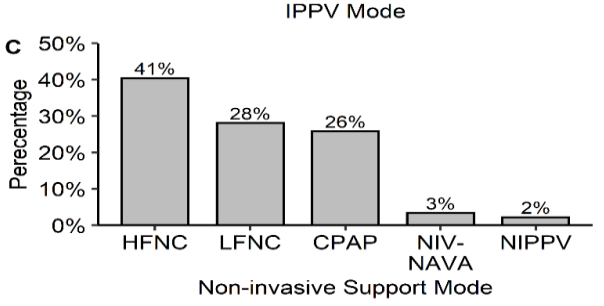

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High Variability in Modes and Settings

- Partially attributable to lack of prospective randomized controlled trials comparing:
  - –Mode of support
  - –Optimal PEEP
  - –Synchronization

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Conclusions

- A team-based, holistic approach will give a babies with BPD the best outcomes.
- Collaboration among centers will help us improve our care of patients with BPD.

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Thank You!

- https://base.uams.edu/redcap/surveys/?s=TTE7FXCRPW
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