

# Chronic Neonatal Lung Disease

“ A Pulmonologist's perspective”

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## Which region are you from?

Singapore

ASEAN

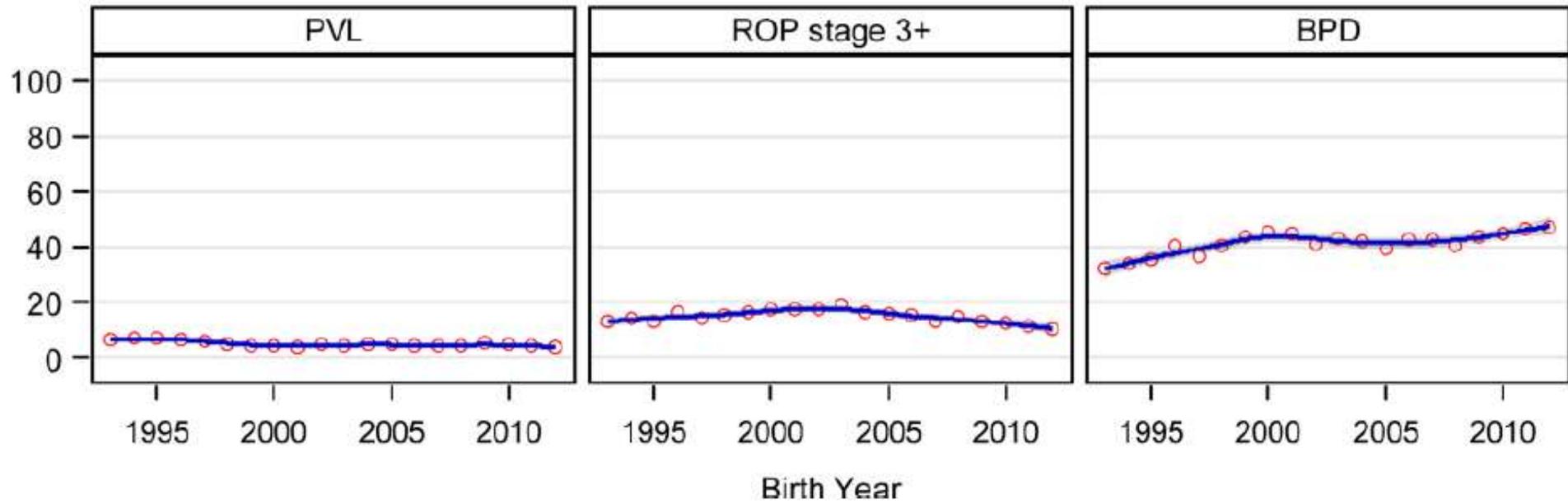
Beyond  
ASEAN

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## Definition of bronchopulmonary dysplasia: Diagnostic criteria 2001 NICHD consensus workshop

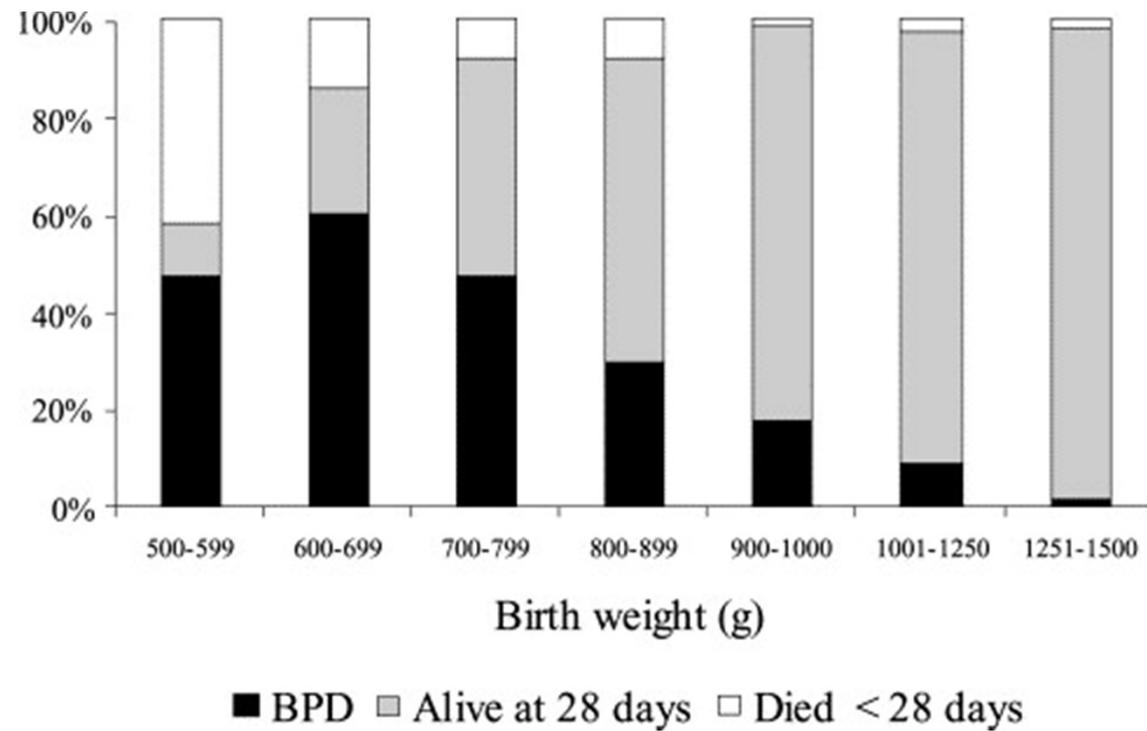
	Gestational age	
	<32 weeks	≥32 weeks
Time point of assessment	36 weeks PMA or discharge to home, whichever comes first	>28 days but <56 days postnatal age or discharge to home, whichever comes first
	<b>Treatment with oxygen &gt;21 percent for at least 28 days plus</b>	
Mild BPD	Breathing room air at 36 weeks PMA or discharge, whichever comes first	Breathing room air by 56 days postnatal age or discharge, whichever comes first
Moderate BPD	Need* for <30 percent oxygen at 36 weeks PMA or discharge, whichever comes first	Need* for <30 percent oxygen at 56 days postnatal age or discharge, whichever comes first
Severe BPD	Need* for ≥30 percent oxygen and/or positive pressure (PPV or nCPAP) at 36 weeks PMA or discharge, whichever comes first	Need* for ≥30 percent oxygen and/or positive pressure (PPV or nCPAP) at 56 days postnatal age or discharge, whichever comes first

# Incidence of BPD

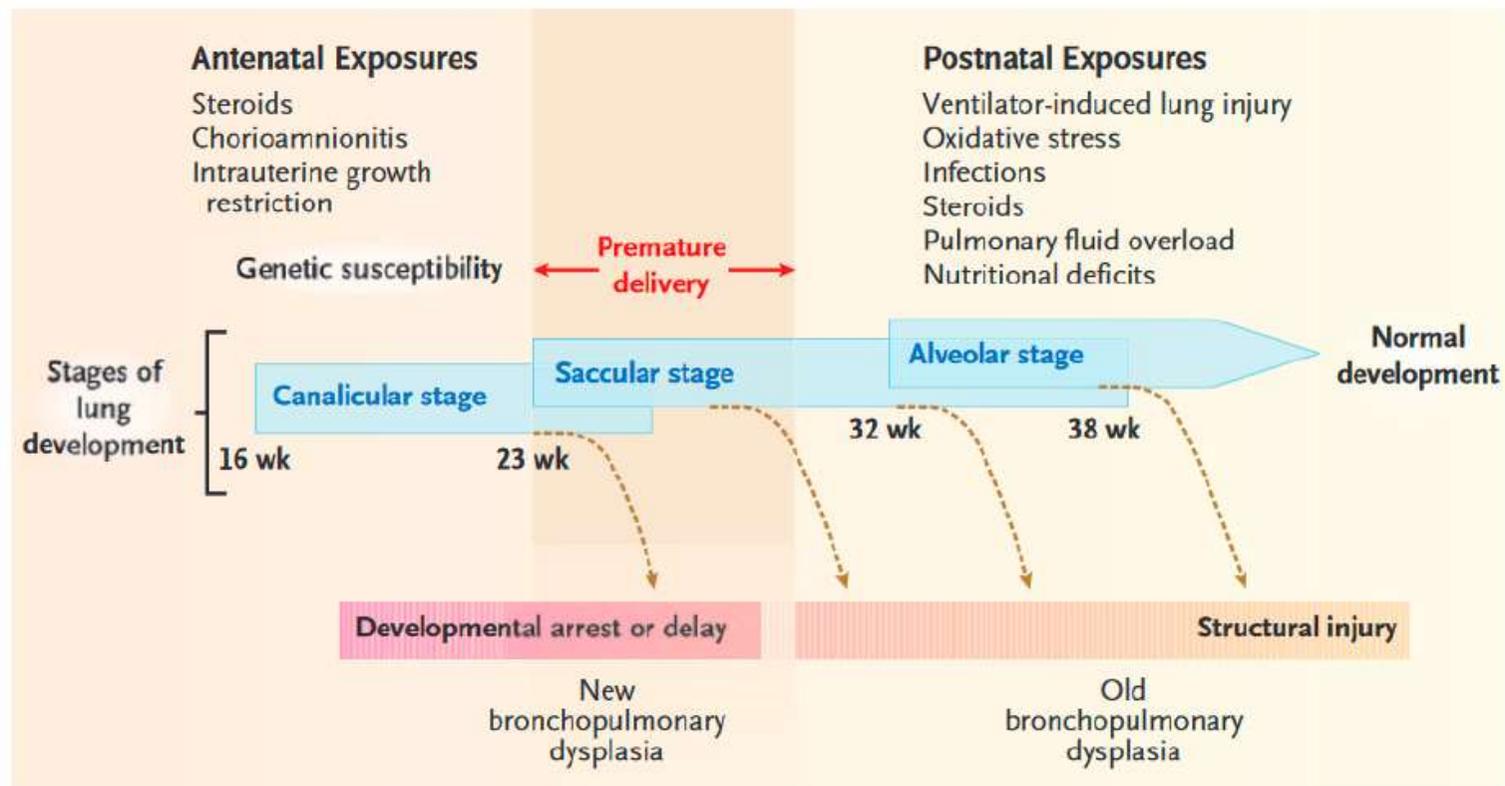


Stoll BJ, Hansen NI, Bell EF; et al. Trends in care practices, morbidity, and mortality of extremely preterm neonates, 1993-2012. *JAMA*.  
 doi:10.1001/jama.2015.10244

# Incidence of BPD by birth weight



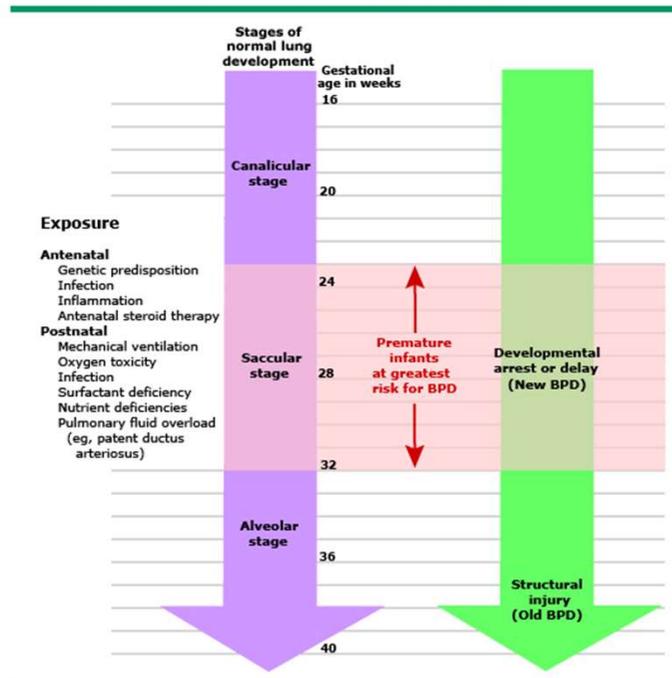
# Stages of lung development, potentially damaging factors and types of lung injury



Lauren M. Davidson and Sara K. Berkelhamer \* *J. Clin. Med.* 2017, 6, 4; doi:10.3390/jcm6010004

# Pathology of BPD

## Pathogenesis of bronchopulmonary dysplasia (BPD)



Exposure to antenatal pulmonary insults during the saccular state of lung development result in developmental arrest or delay in pulmonary maturation ("new" bronchopulmonary dysplasia [BPD]), whereas postnatal insults cause structural pulmonary injury ("old" BPD).  
 Adapted from: Baraldi E, Filippone M. Chronic lung disease after premature birth. *N Engl J Med* 2007; 357:1946.

### New BPD

- Decreased septation and alveolar hypoplasia lead to fewer and larger alveoli
- Dysregulation of pulmonary vasculature development with abnormal distribution of alveolar capillaries and thickening of muscle layer resulting in increasing pulmonary resistance
- Increased elastic tissue and thickening of interstitium which in turn compromises capillary development.

### Old BPD

- Airway injury, Airway inflammation and parenchymal fibrosis due to mechanical ventilation and oxygen toxicity



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# Post neonatal effects of BPD

In the first year of life, 118 of 238 (49%) infants with BPD were re-hospitalized which was more than twice the non BPD population, 309 of 1359 (23%)

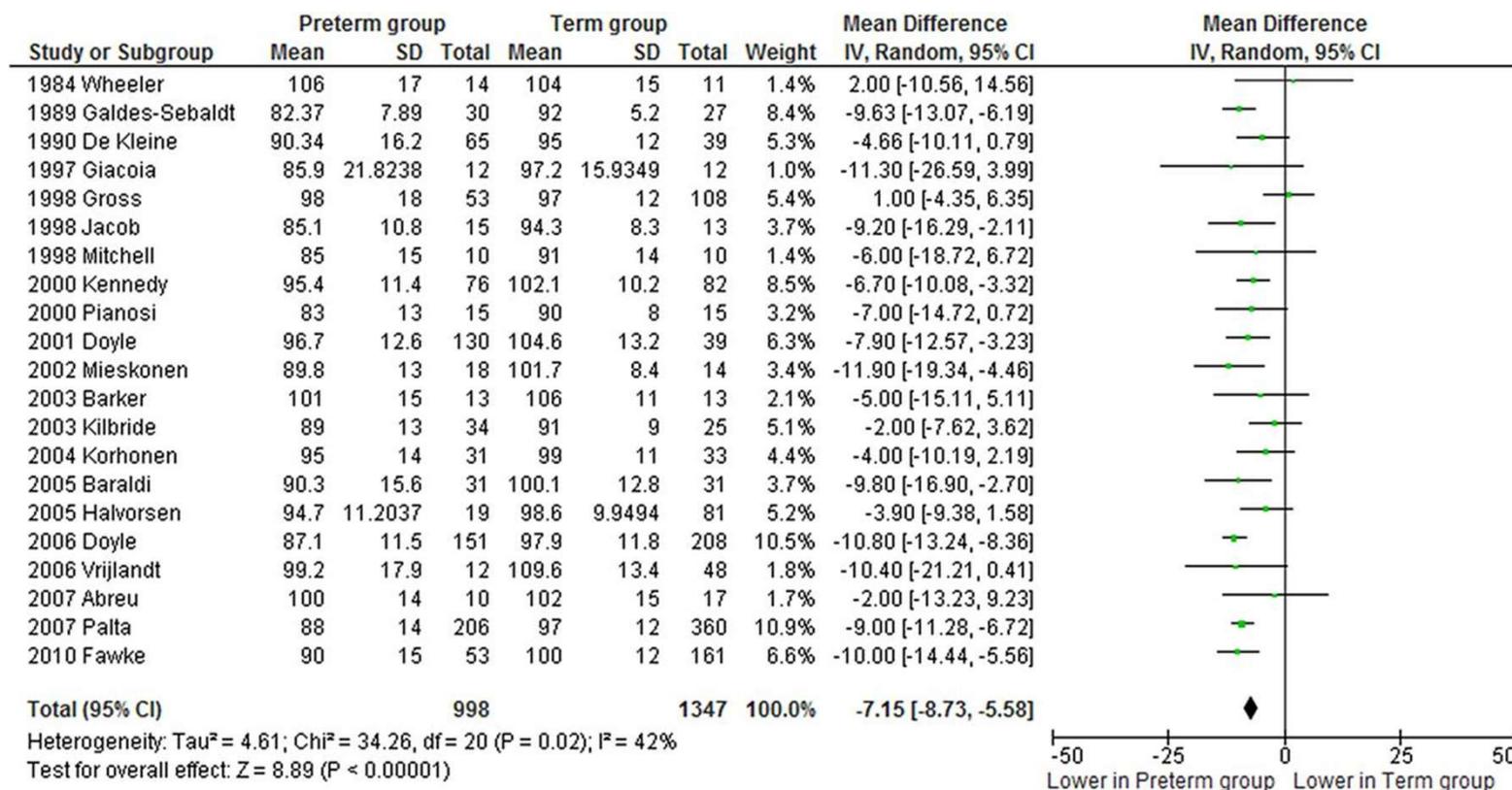
[Rehospitalization in the first year of life among infants with bronchopulmonary dysplasia.](#) Smith VC, Zupancic JA, McCormick MC, Croen LA, Greene J, Escobar GJ, Richardson DK. J Pediatr. 2004 Jun;144(6):799-803

Follow up studies of child and young adult survivors demonstrate concerns of:

- Compromise Pulmonary function
- Pulmonary defenses
- Asthma like symptoms
- Exercise intolerance with altered responses to hypoxia
- Pulmonary hypertension

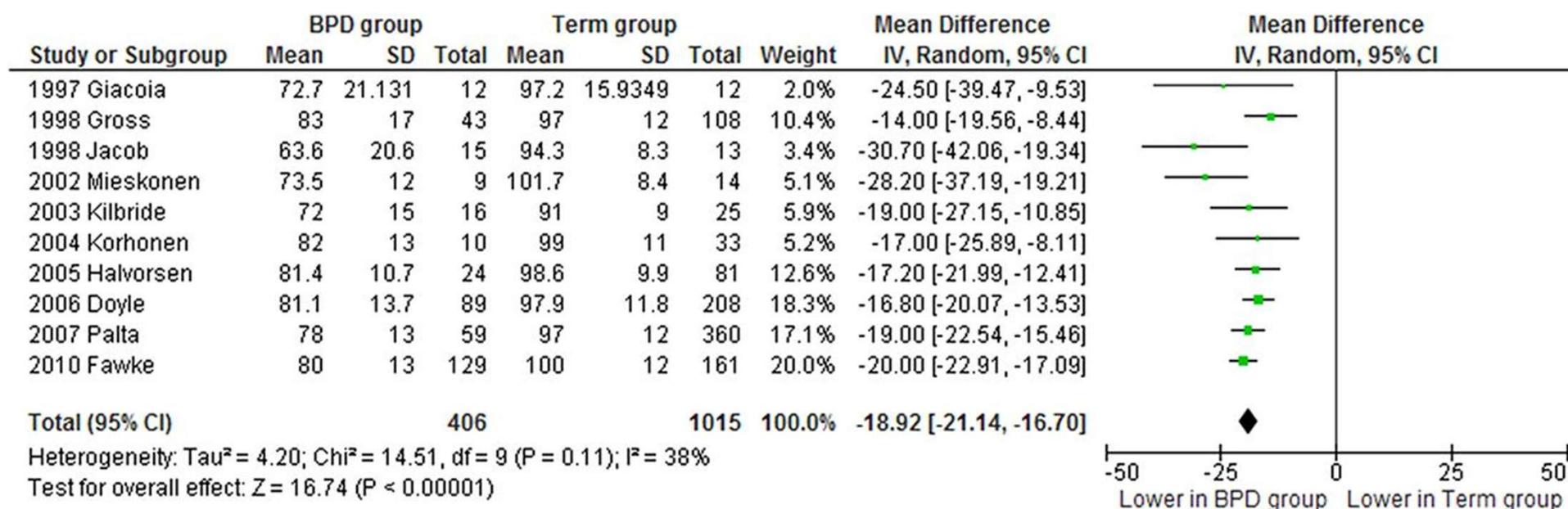
# Compromised Lung Function

## Percentage predicted forced expiratory volume in 1 s (%FEV<sub>1</sub>) of the premature group (no bronchopulmonary dysplasia, BPD) compared with term control group



Kotecha SJ, Edwards MO, Watkins WJ, *et al*, Effect of preterm birth on later FEV<sub>1</sub>: a systematic review and meta-analysis  
*Thorax* 2013;**68**:760-766

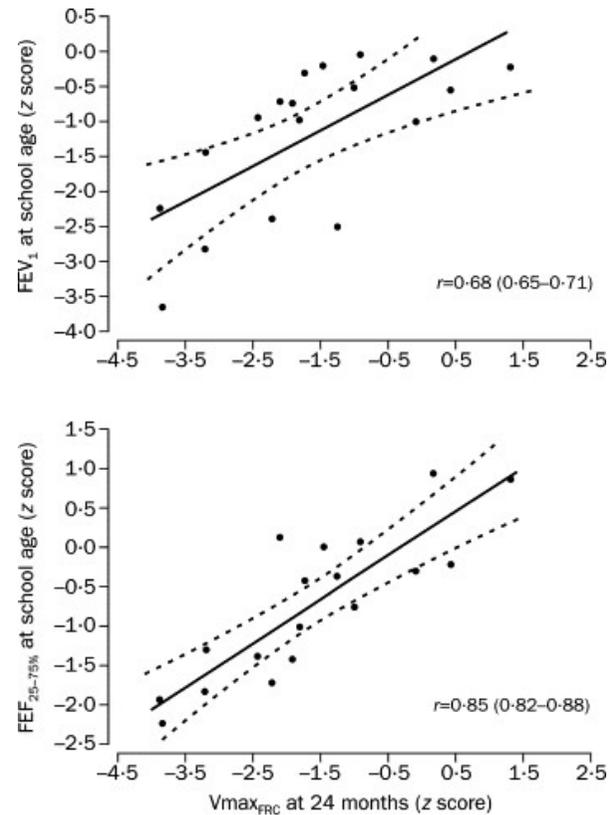
Percentage predicted forced expiratory volume in 1 s (%FEV<sub>1</sub>) of the bronchopulmonary dysplasia (BPD) group (supplemental oxygen dependency 36 weeks postmenstrual age) compared with term control group



Longitudinal PFT of BPD infants at 6 months CGA and one year later showed decreased FVC, FEV at 0.5 seconds and Forced expiratory flows without any catch up during the period.

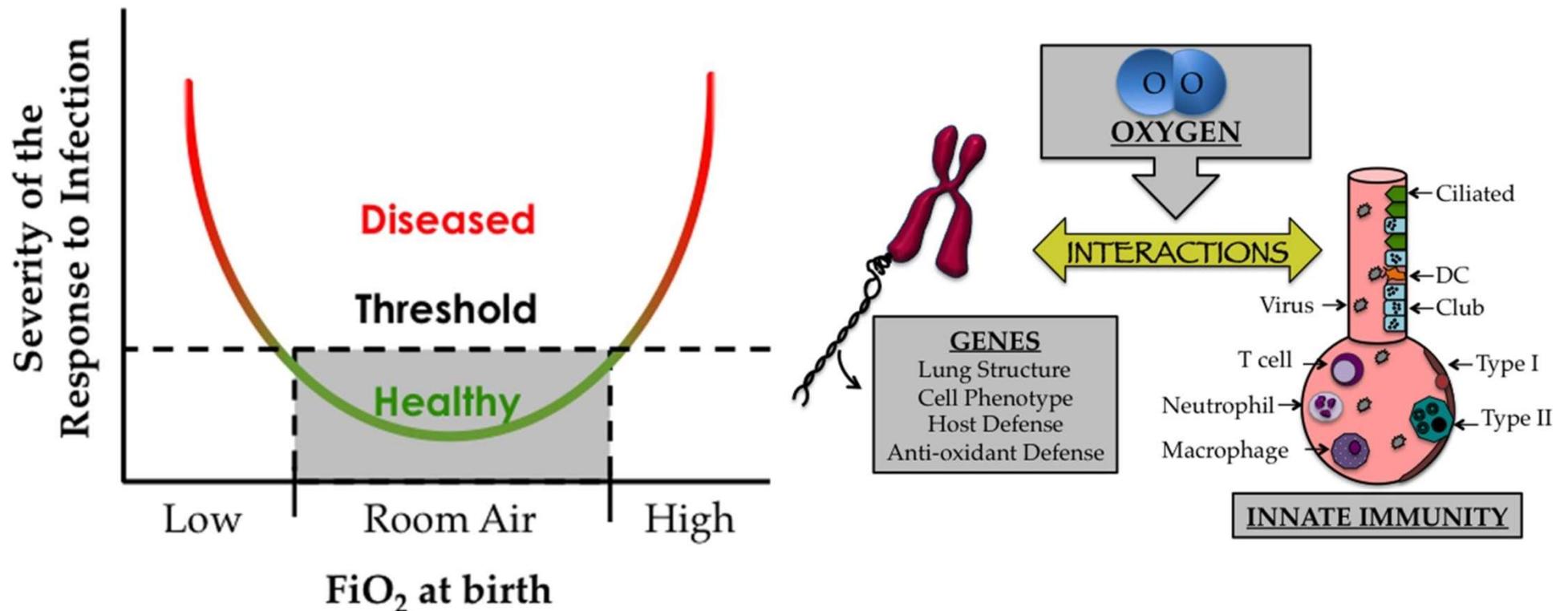
[Lung function gain in preterm infants with and without bronchopulmonary dysplasia.](#) Sanchez-Solis M, Perez-Fernandez V, Bosch-Gimenez V, Quesada JJ, Garcia-Marcos L. *Pediatr Pulmonol.* 2016 Sep;51(9):936-42. doi: 10.1002/ppul.23393. Epub 2016 Feb 10.

# Flow limitation in infants with bronchopulmonary dysplasia and respiratory function at school age



# Pulmonary defenses

# Affect of early life oxygen exposure on proper lung development and response to respiratory viral infections



# Asthma like symptoms in CLD

# Lung function and respiratory symptoms at 11 years in children born extremely preterm: the EPICure study

- Many survivors of BPD demonstrate a component of reactive airway disease
- Long term follow up of infants born <26 weeks gestation identified that 25% had an asthma diagnosis at 11 years of age (13% in controls).
- 56% of preterm infants had low baseline spirometry and 27% had positive bronchodilator response.
- Less than half of this group were on medications

# Asthma like symptoms

- Co-morbid tracheo-broncho malacia in ex-preterm infants can result in exacerbated wheezing with use of bronchodilator therapy.
- ICS are also thought to be less consistent for children with BPD as compared to those with asthma
- School age children who had CLD in infancy had exercise induced bronchoconstriction that responded significantly to bronchodilation.
- Reversible exercise induced bronchoconstriction is common in children who experienced CLD in infancy and should be actively assessed for and treated.

[Exercise-induced bronchoconstriction in school-aged children who had chronic lung disease in infancy.](#)

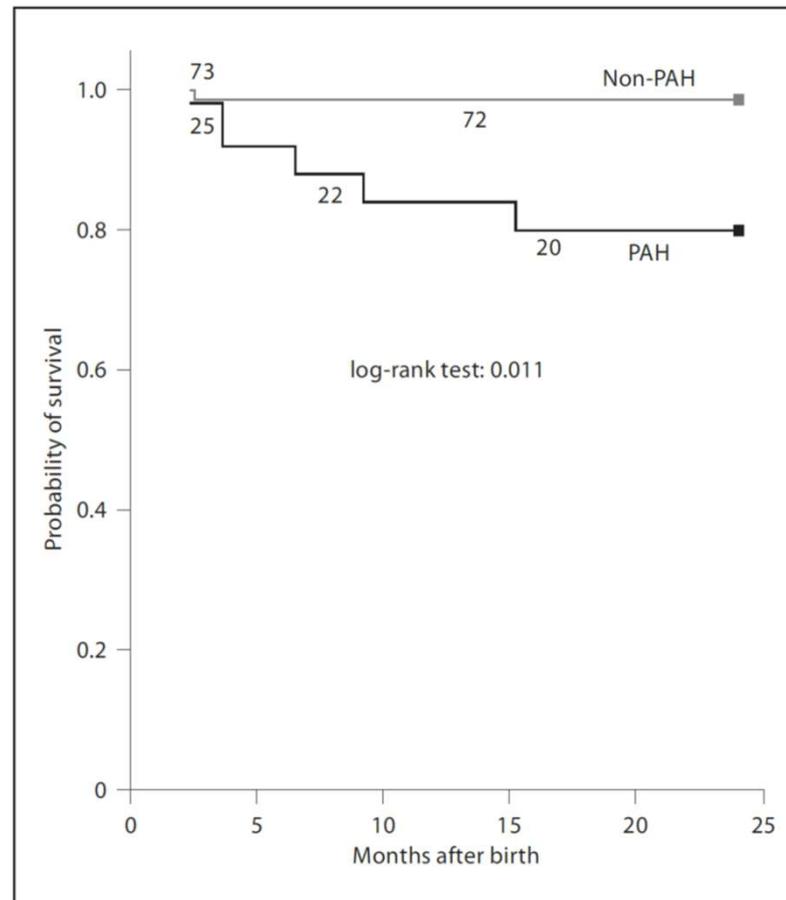
Joshi S, Powell T, Watkins WJ, Drayton M, Williams EM, Kotecha S., J Pediatr. 2013 Apr;162(4):813-818.

# Other Respiratory compromises in CLDI

- Treadmill exercise testing identify reduced gas transfer at rest and during activity.
- Higher oxygen uptake during activity has been observed, which could contribute to early fatigability during prolonged exercise.
- Peak exercise resulted in hypoxemia in 60% of BPD children with concomitant increase in PCO<sub>2</sub> suggestive of alveolar hypoventilation

## Pulmonary Arterial Hypertension (PAH)

- Dysmorphic pulmonary vasculature and compromised angiogenesis with BPD results in increased risk of elevated pulmonary pressures.
- Compromised lung growth with pulmonary pruning represent “fixed component” of PAH
- Abnormal vascular tone and vasoreactivity may be more responsive to therapy.



Kaplan-Meier curve demonstrating the probability of survival from the time of birth for the study patients with moderate or severe BPD (n = 98), including infants with PAH (n = 25) and those without PAH (n = 73).

# Risk factors for PAH

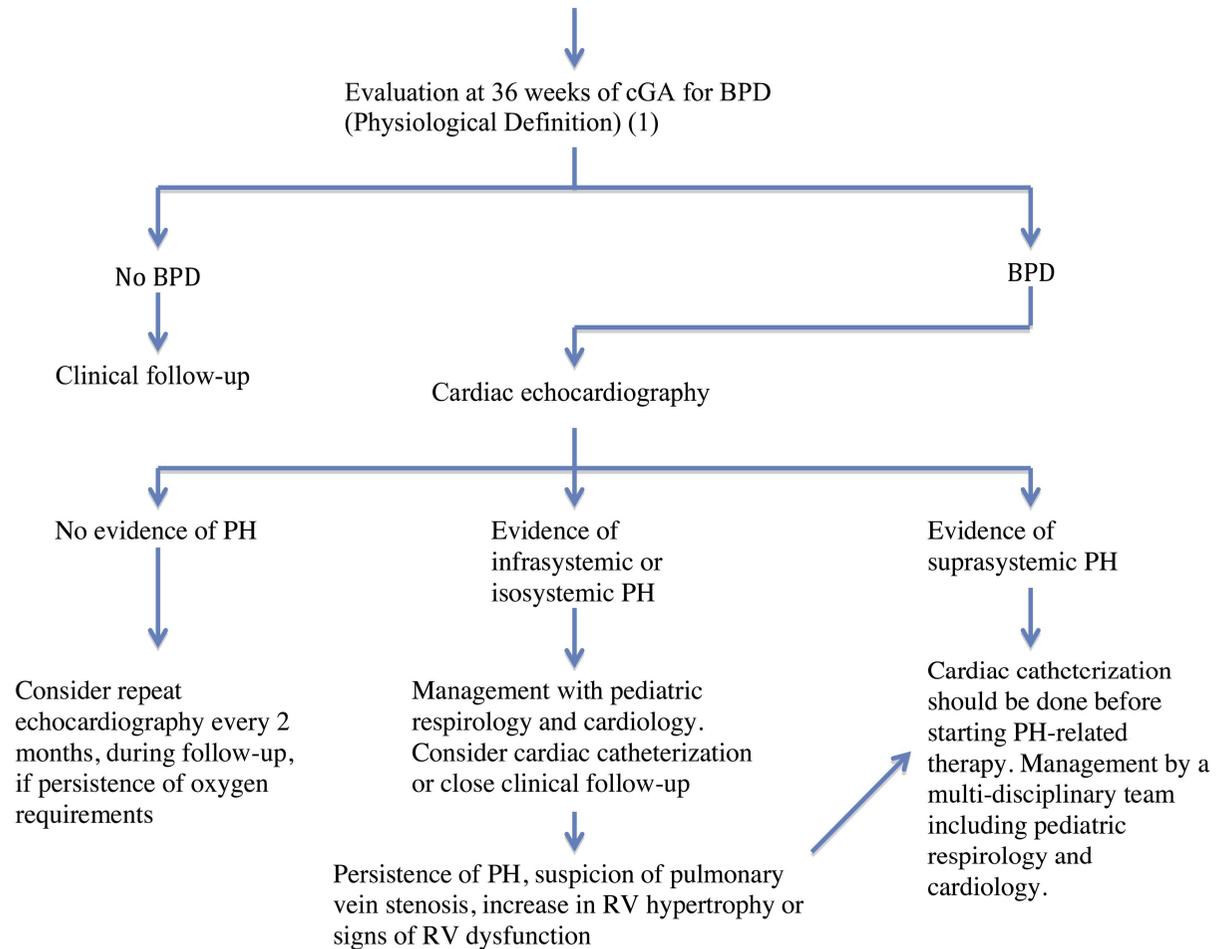
**Table 2.** Risk factors for the development of PAH in each group determined by binary logistic regression analysis

Clinical characteristics	Unadjusted RR (95% CI)	p values	Adjusted <sup>1</sup> RR (95% CI)	p values
Birth weight <3rd percentile for age	2.9 (1.1–7.5)	0.031	3.0 (0.1–1.9)	0.282
5-min Apgar scores, ≤6	1.4 (1.1–1.8)	0.015	6.2 (1.4–28.0)	0.017
Oligohydramnios	4.9 (2.0–12.0)	0.001	7.7 (2.0–29.6)	0.030

<sup>1</sup> Adjusted for birth weight <3rd percentile for age, 5-min Apgar scores (≤6), and oligohydramnios in all subjects included in this study.

Kim, D.H.; Kim, H.S.; Choi, C.W.; Kim, E.K.; Kim, B.I.; Choi, J.H. Risk factors for pulmonary artery hypertension in preterm infants with moderate or severe bronchopulmonary dysplasia. *Neonatology* 2012, 101, 40–46.

Extremely premature infants (less than < 28 weeks of CGA or  $\leq 1250$  grams)



# What are the preventative steps that can reduce the incidence of Pulmonary hypertension in children with BPD?

Both antenatal steroids and surfactant administration reduce rates of Respiratory distress syndrome and improve survival, however, neither has been shown to reduce incidence of BPD.

# Prevention of BPD

- Ventilation strategies
  - Gentle ventilation
  - Decreased ventilation and early CPAP
  - NIPPV
- Saturation targets (low – 85%-89%, High 91%-95%)
  - Surfactant, positive pressure and Oxygenation Randomization Trial (SUPPORT) found slightly lower rates of BPD (38% vs 41.7%) in the low saturation group without statistical significance
  - Benefits of Oxygen Saturation Trials (BOOST II) – found similar trends with rates of 39.5% and 44.7% in the low and high groups, again without statistical significance.
  - However, many units use higher saturations based on improved survival.

# Prevention of BPD

- Corticosteroids
  - Concerns of systemic steroids
  - ? Role for low dose short course steroids
  - ? Role for inhaled steroids
- Caffeine
- Vitamin A

**What are the take home points you have all learnt today from this talk? !!!!!**

# 4<sup>TH</sup> NUHKids PAEDIATRIC FLEXIBLE BRONCHOSCOPY COURSE

26 to 27 August 2019 | Khoo Teck Puat-Advanced Surgical Training Centre (ASTC),  
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- ❖ A hands-on intensive workshop for paediatricians and paediatric pulmonologists.
- ❖ The course provides hands-on bronchoscopic experience (on live animals) with lectures and video workshops to give participants an in-depth understanding and exposure to the art of flexible bronchoscopy in children.
- ❖ Open to both beginners and advanced learners.



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*Dr Rina Triasih - Indonesia*

*"Unique course for paediatric flexible bronchoscopy.  
Hands on experience on live animals gave me a  
totally real experience. Excellent teachers  
who taught me the finer aspects too!"*

*Dr. Sagar Warankar - India*

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Associate Professor Daniel Goh  
Dr Michael Lim

United Kingdom  
Dr Gary Connett

India  
Dr Ilin Kinzhi

Thank you

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