

# Preventing Bronchopulmonary Dysplasia: Knowledge, Implementation and Attitudes

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# Disclosure

- Neither I nor any member of my immediate family has a financial relationship or interest with any proprietary entity producing health care goods or services related to the content of this CME activity.
- I do not intend to discuss an unapproved or investigative use of commercial products or devices.

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- Other families

# This Talk

Basic  
Science

Clinical  
evidence

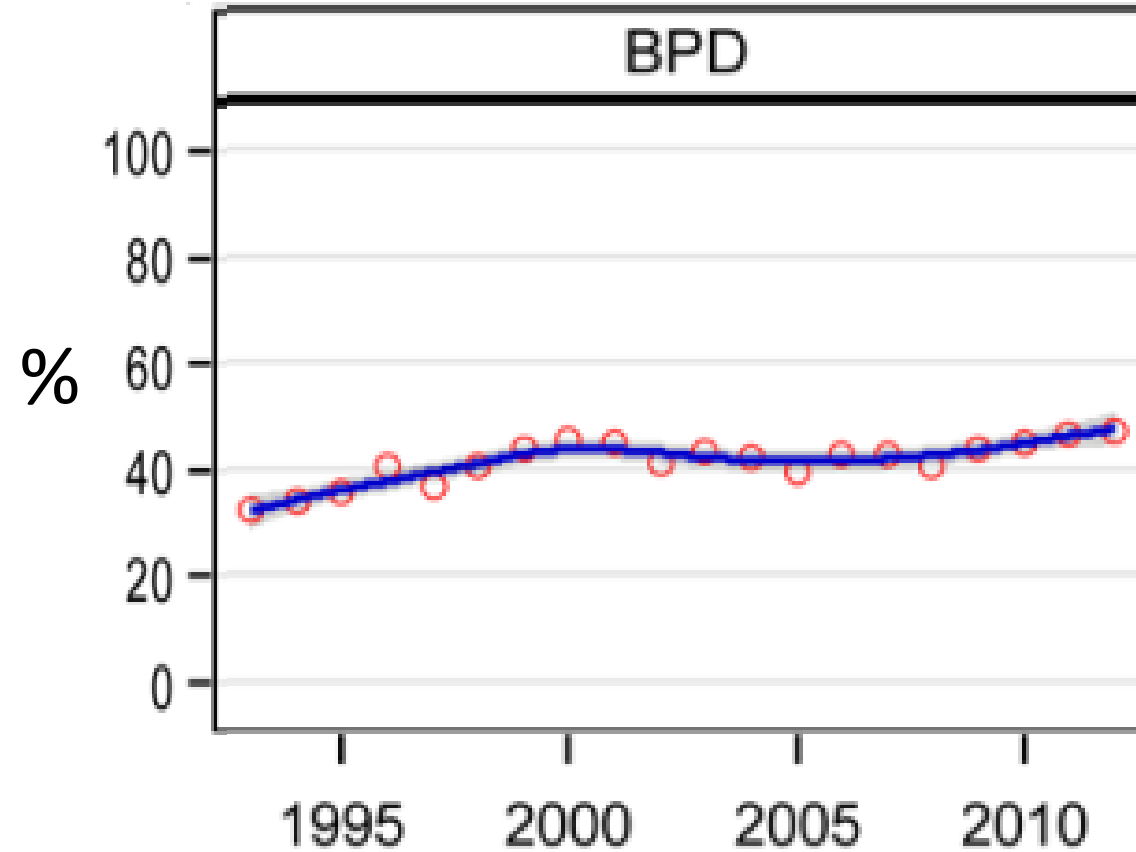
Quality  
Improvement  
findings

Opinion,  
hypotheses,  
ideas



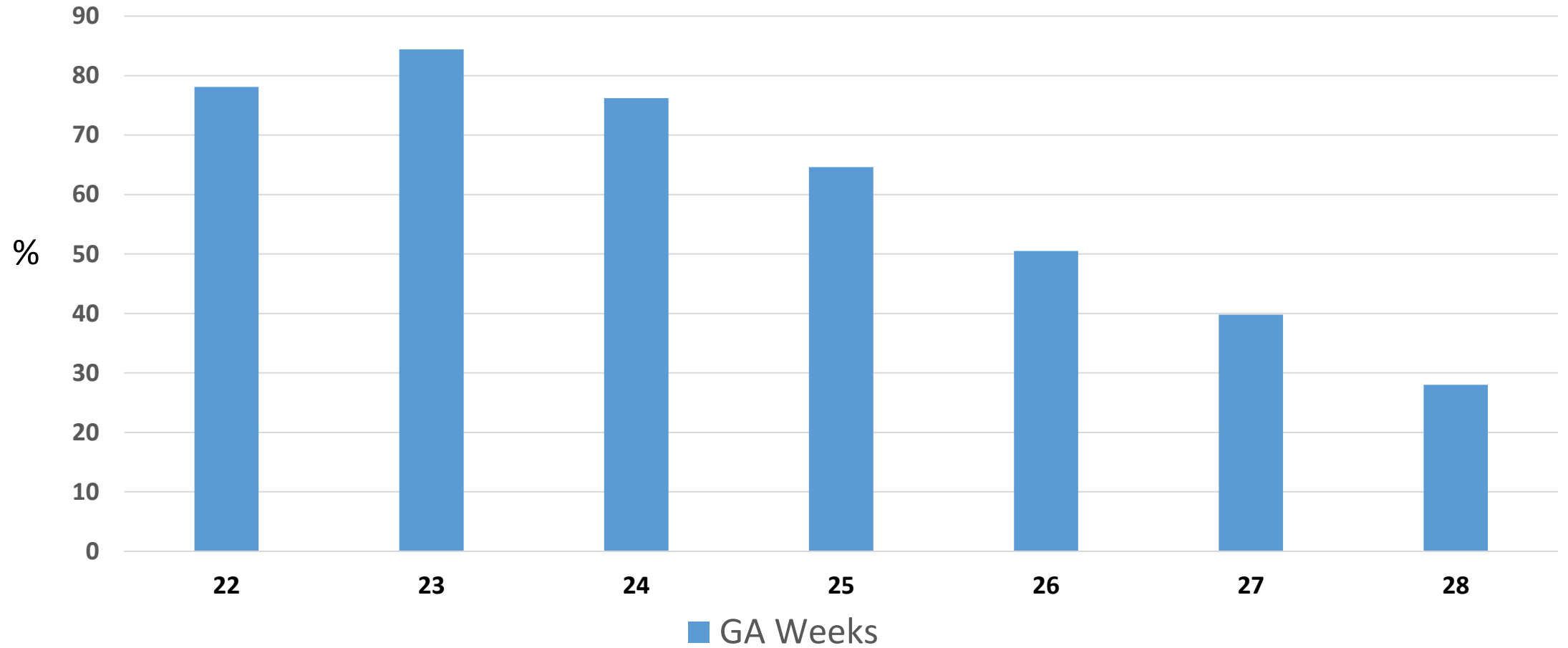
# NRN: BPD by birth year

Infants born at GA 22–28 weeks 1993–2012



Circles show the percent of infants born each year diagnosed with BPD and a smoothed curve shows the trend.

### NRN: BPD Incidence by Gestation at Birth



# NRN: BPD Incidence in Two Epochs GA 22 – 28 weeks

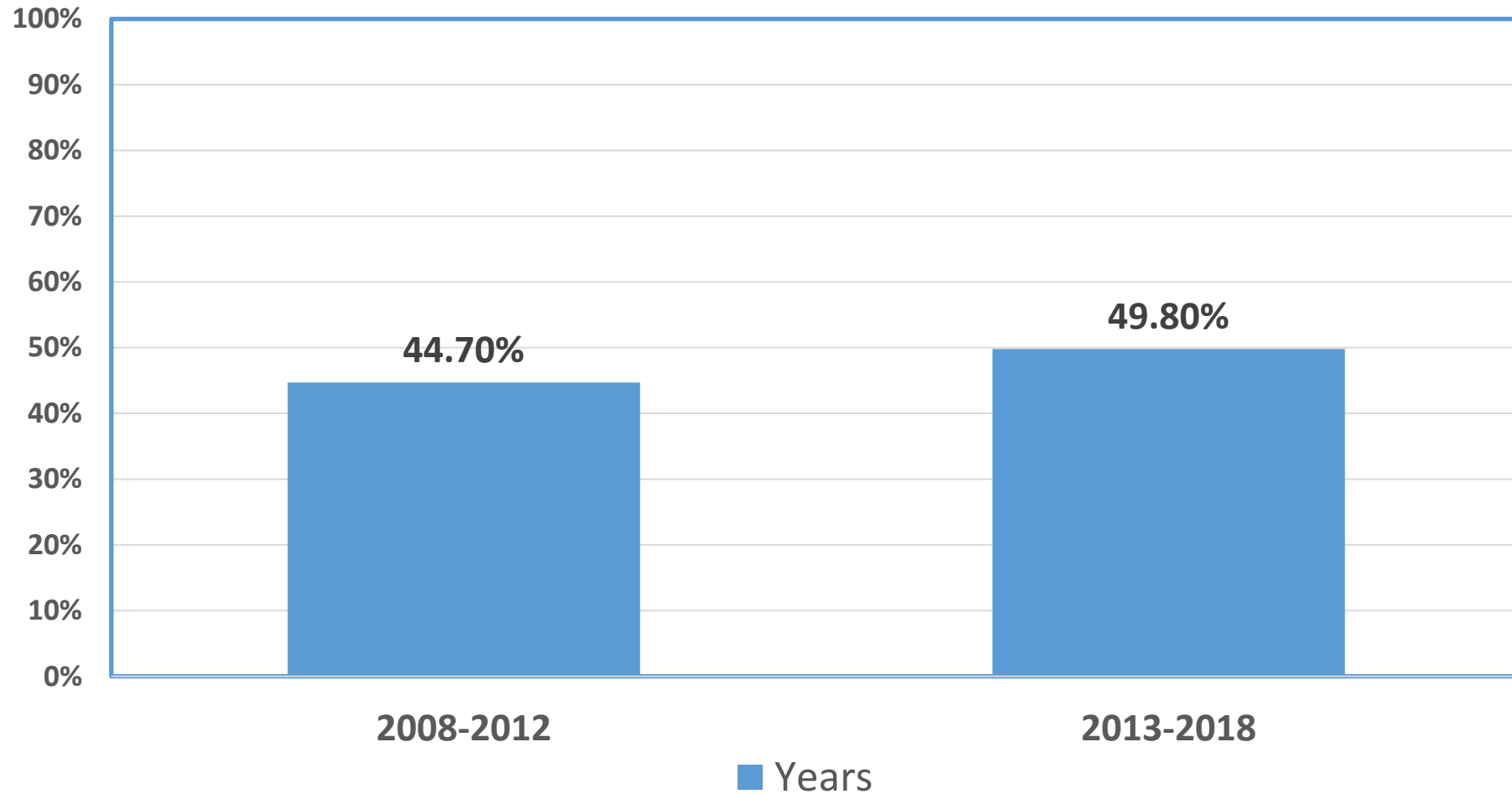
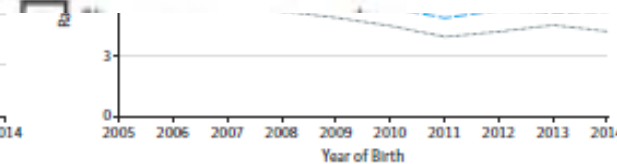
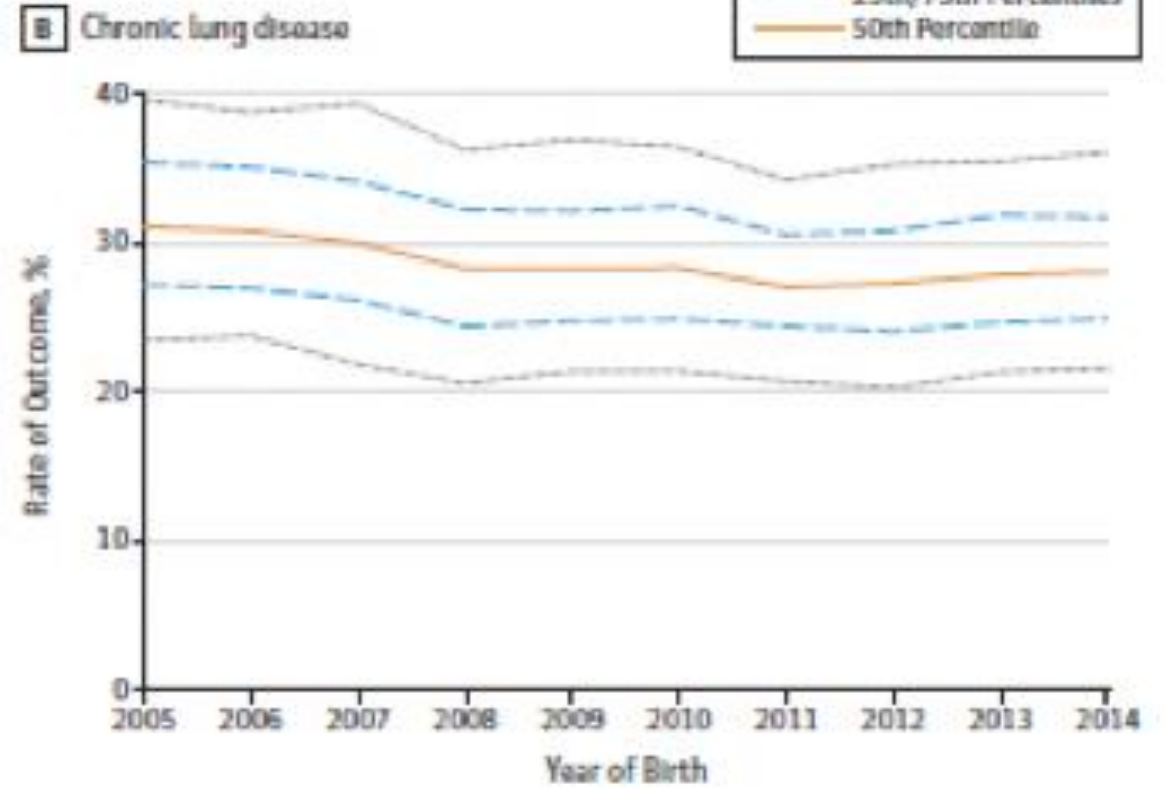
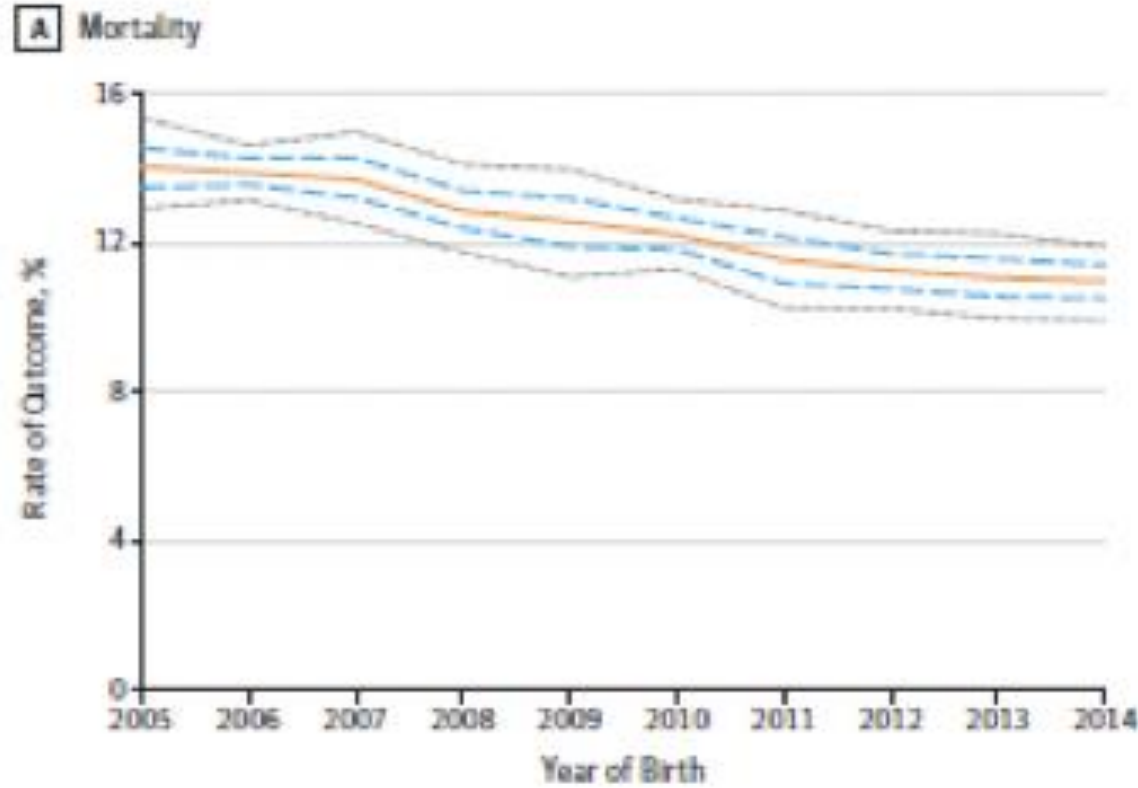
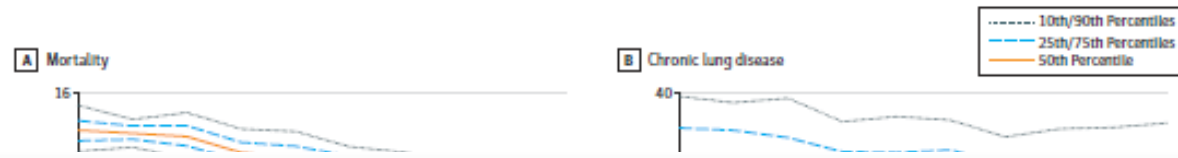


Figure 1. Risk-Adjusted Rates of Outcomes in the Neonatal Intensive Care Unit at the 10th, 25th, 50th, 75th, and 90th Percentiles, 2005-2014

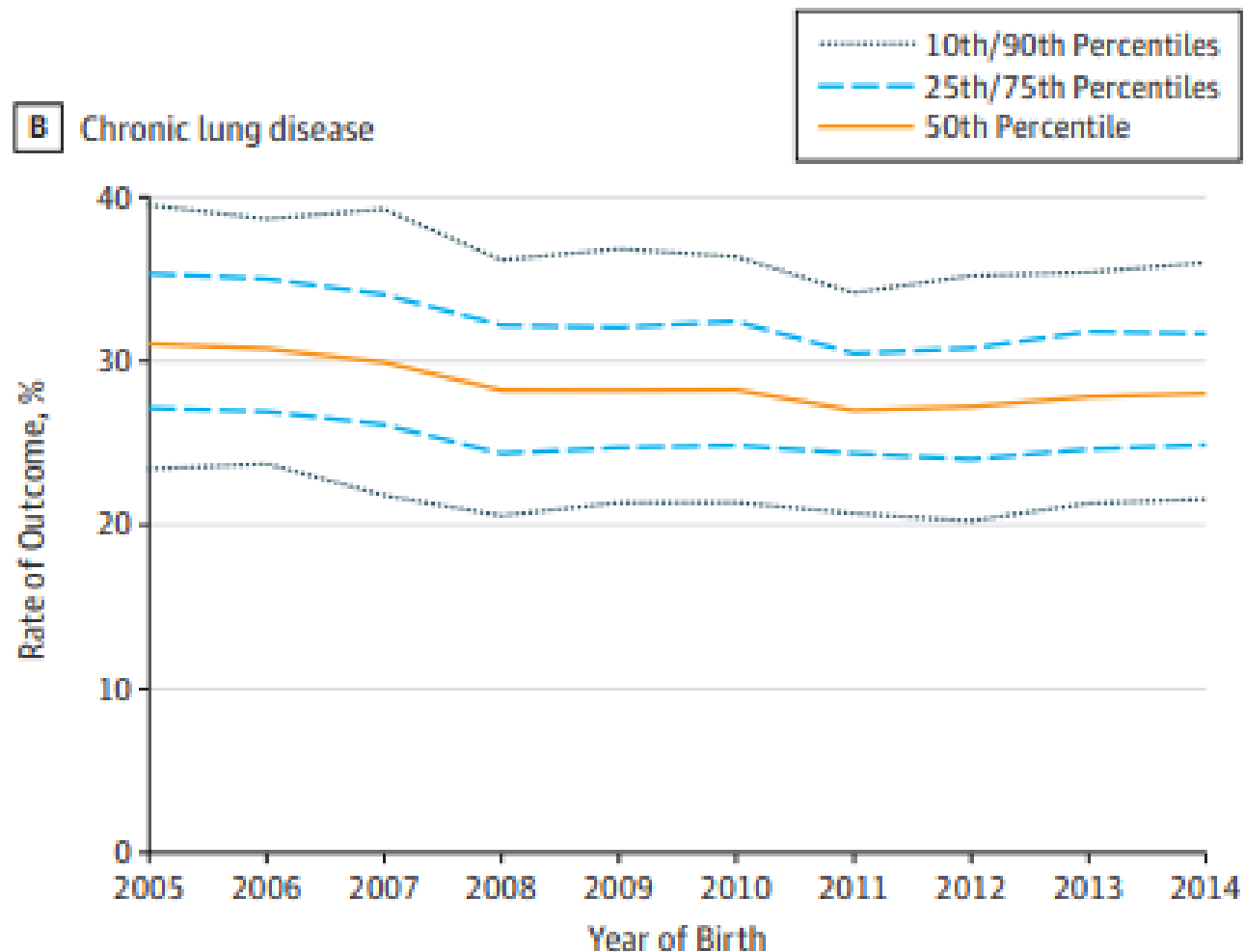


These charts illustrate percentiles of risk-adjusted rates for mortality and neonatal morbidities by year. A, Mortality. B, Chronic lung disease. C, Late-onset infection.



# Chronic Lung Disease

Risk-Adjusted Rates, Birth Weight 501 – 1500 grams, 2005-2014



Data from Vermont Oxford Network. Horbar et al JAMA Pediatrics 2017

# Chronic Lung Disease

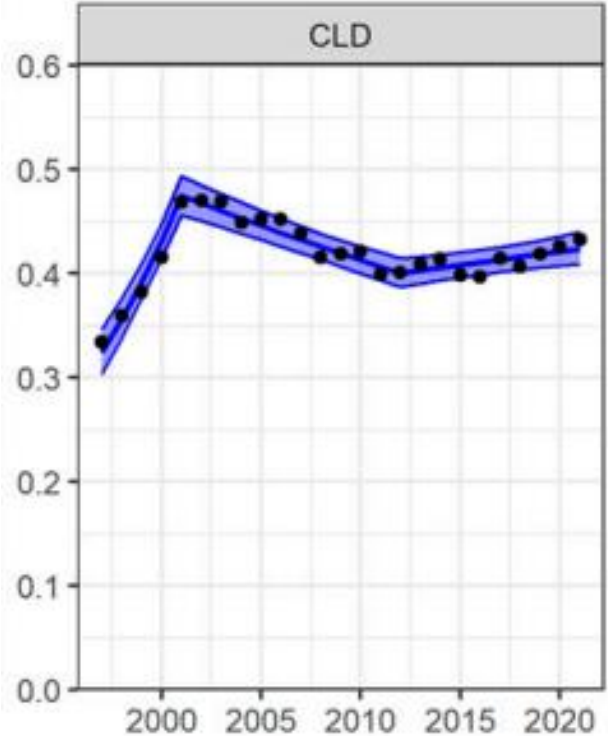
24 – 28 weeks GA, 1997 - 2021

Adjusted Annual Percentage Change

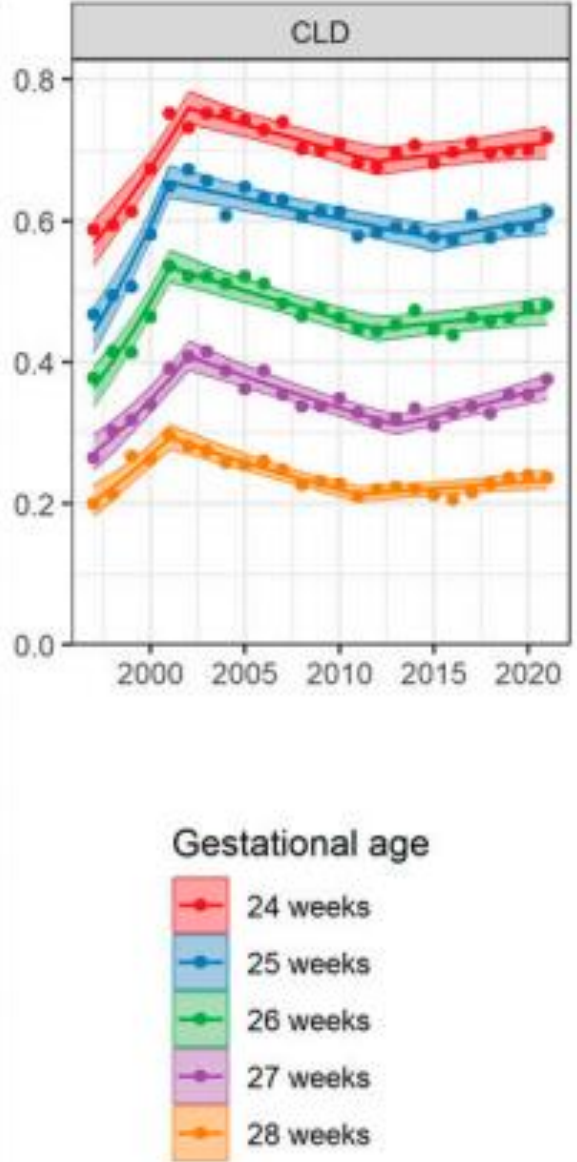
Years	aAPC	95% CI
1997-2001	10.0	(8.2 to 11.8) <sup>b</sup>
2001-2012	-1.7	(-2.1 to -1.3) <sup>a</sup>
2012-2021	0.6	(0.1 to 1.0) <sup>b</sup>

a: Indicates increase

b: Indicates stable



Observed rate (dot) and fitted trend with 95% CI (shaded area)  
 CI adjusted for clustering of infants within hospitals



Data from Vermont Oxford Network. Horbar et al Pediatrics 2024

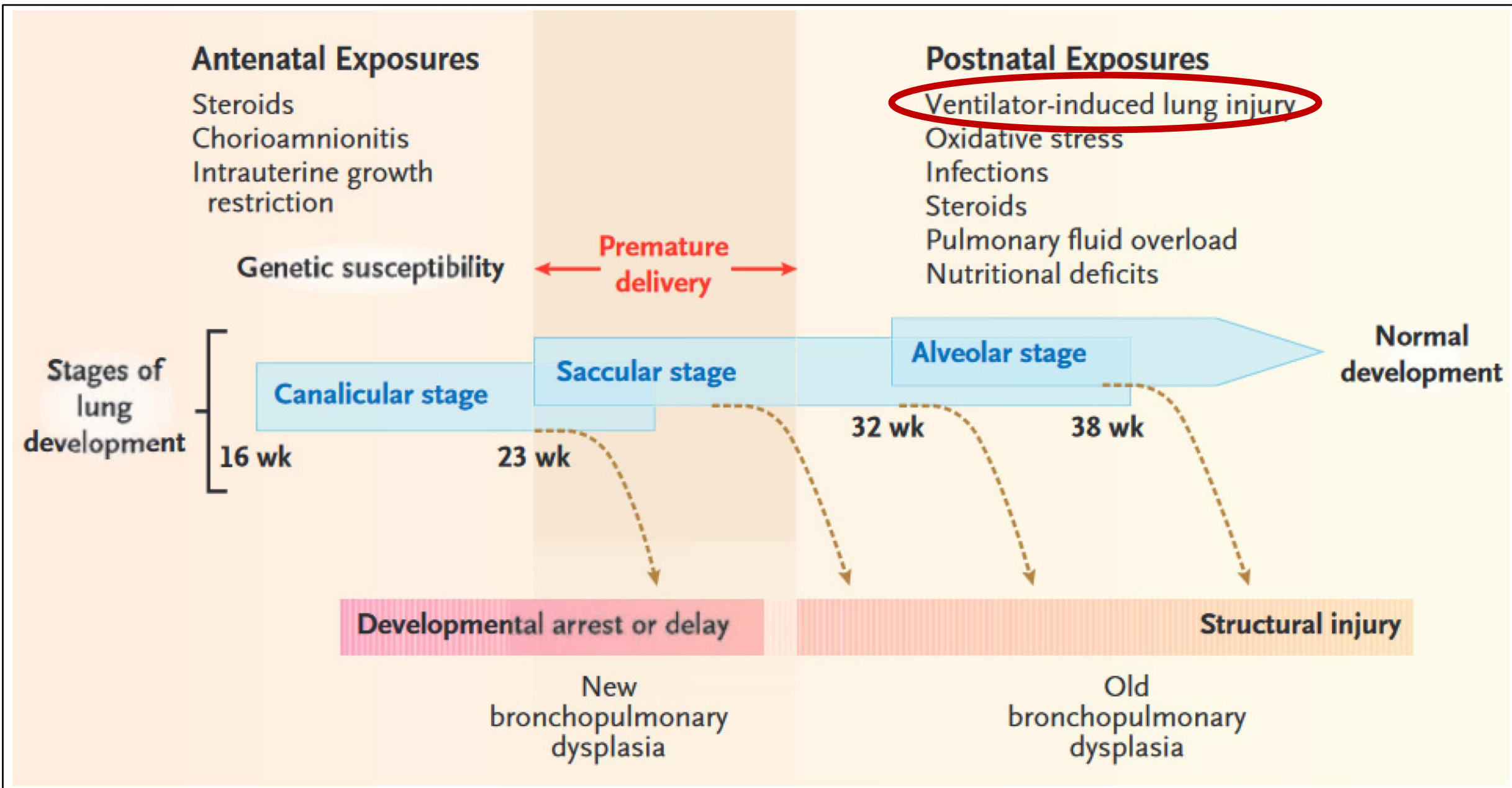
# Prevention of BPD Requires:

**Attitude**

**Knowledge**

**Implementation**

Knowledge



# Ventilator-Induced Lung Injury - Mechanisms

**Volutrauma**

**Atelectrauma**

**Biotrauma**

**Barotrauma**

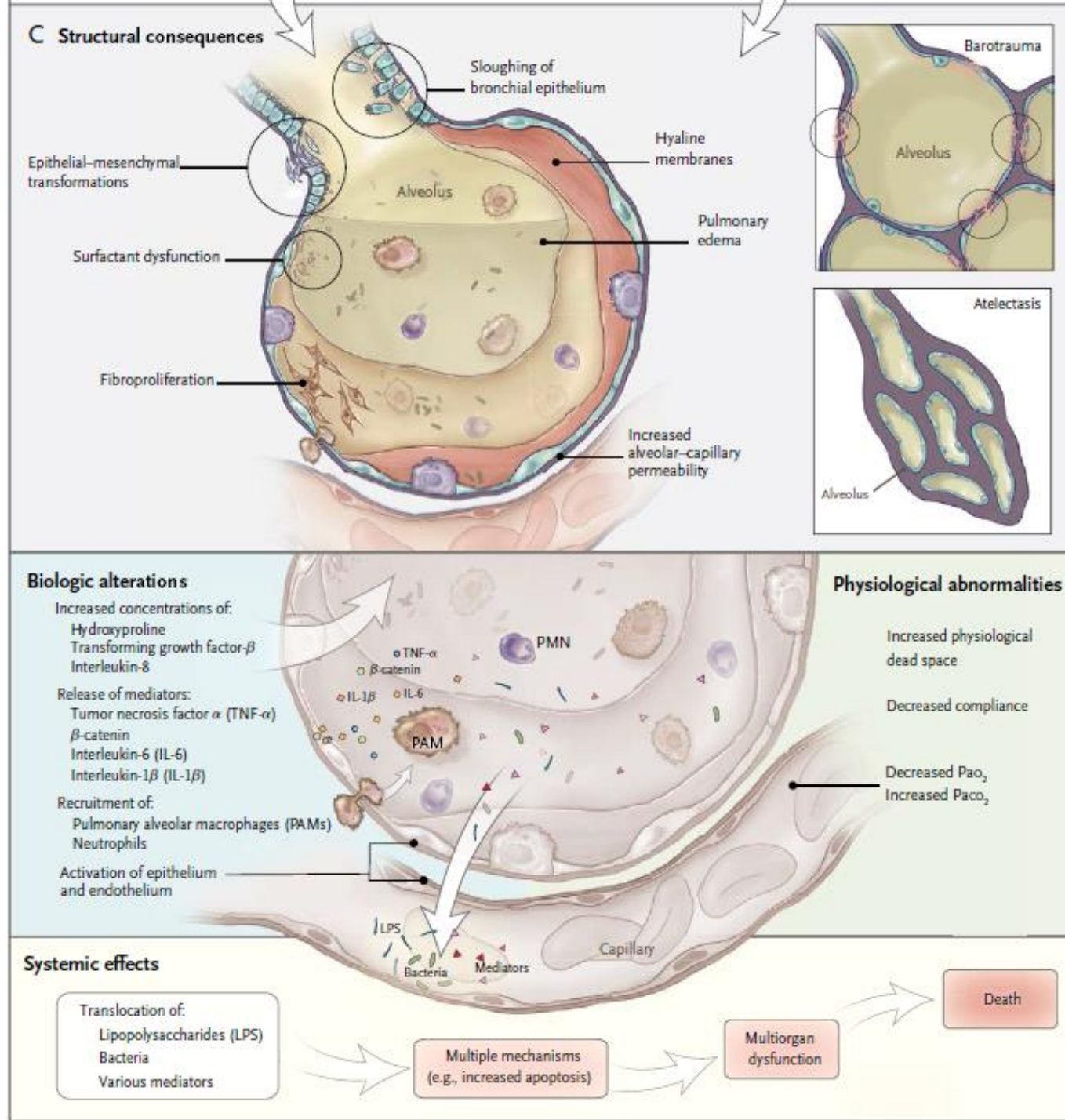


**Oxitrauma**

**Rheotrauma**

**Ergotrauma**

# VILI



Slutsky and Ranieri.  
NEJM 2013;369:2126-36

# Evidence Summary

(Interventions tested in RCTs, with evidence of effect only, variable certainty)

Intervention	Outcome	Relative Risk Reduction (%)	Absolute Risk Reduction (%)
nCPAP vs mech ventilation	Death or BPD	9	4
Volume targeted vs pressure limited ventilation	Death or BPD	27	12
	BPD in survivors	32	11
Elective HFOV vs conventional ventilation	BPD in survivors	14	5
	Death or BPD	10	5
Surfactant $\leq$ 2hrs of age vs $>$ 2hrs of age+MV	BPD	31	3
	Death or BPD	17	6
LISA vs INSURE	BPD in survivors	43	8
	Death or BPD	45	11

BPD = Oxygen at 36 weeks PMA or at EDD

Cochrane reviews; Schmolzer et al 2013, Aldana-Aguirre et al, 2017



# Evidence Summary

(Interventions tested in RCTs, with evidence of effect only, variable quality)

Intervention	Outcome	Relative Risk Reduction (%)	Absolute Risk Reduction (%)
Caffeine	BPD in survivors	22	11
Vitamin A	BPD in survivors	13	7
	Death or BPD	8	5
Vitamin D	BPD	64	
Corticosteroids	See later slides		

# NeOProM – Secondary Outcomes

	Lower SpO2 Target (%)	Higher SpO2 Target (%)	Risk Difference (%)	Relative Risk
Death before 36 wks PMA	17	14	2.5	1.18
Death before hospital DC	19	16	2.6	1.17
Severe NEC	9	7	2.3	1.33
Retinopathy of prematurity*	11	15	- 4	0.74
Suppl O2 @ 36 wks PMA	25	30	-5.6	0.81

\*Treated retinopathy of prematurity before corrected age of 18-24 mo

Oxygen

With

Love



Seymour  
("see-more")

# Non-respiratory Interventions that may Prevent BPD

- Prevention of Infection<sup>1</sup>
- Breast milk usage<sup>2,3,4,5</sup>

1. Lapcharoensap et al. J Pediatr 2017; 180:105-109.

2. Villamor-Martinez E. et al Front. Pediatr 2019; 7:224.

3. Villamor-Martinez E. et al. Nutrients 2018, 10, 238

4. Huang J, et al. Arch Dis Child Fetal Neonatal Ed 2019;104:F128–F136

5. Patel et al Arch Dis Child Fetal Ed. 2017 May ; 102: F256–F261

# No reduction in BPD Demonstrated (Other Outcomes may Improve)

- Antenatal corticosteroids
- Inhaled nitric oxide<sup>1</sup>
- Sustained inflation<sup>3</sup>
- Different supplemental FiO<sub>2</sub> levels during resuscitation
- Prophylactic PDA closure
- Azithromycin<sup>2</sup>
- Indomethacin
- Bronchodilators
- Diuretics
- Vitamin E

1. Barrington et al. Cochrane review 2017

2. Lowe et al. Lancet Respir Med 2024

3. Kirpalani et al. JAMA 2019

# Harm > Benefit

- Early (< 7 days dexamethasone)<sup>1</sup>
- Inhaled budesonide<sup>2,3</sup>

1. Doyle et al. Cochrane review 2021
2. Van de loo et al. Cochrane review 2024
3. Bassler et al, NEJM 2018

# Jury Still Out

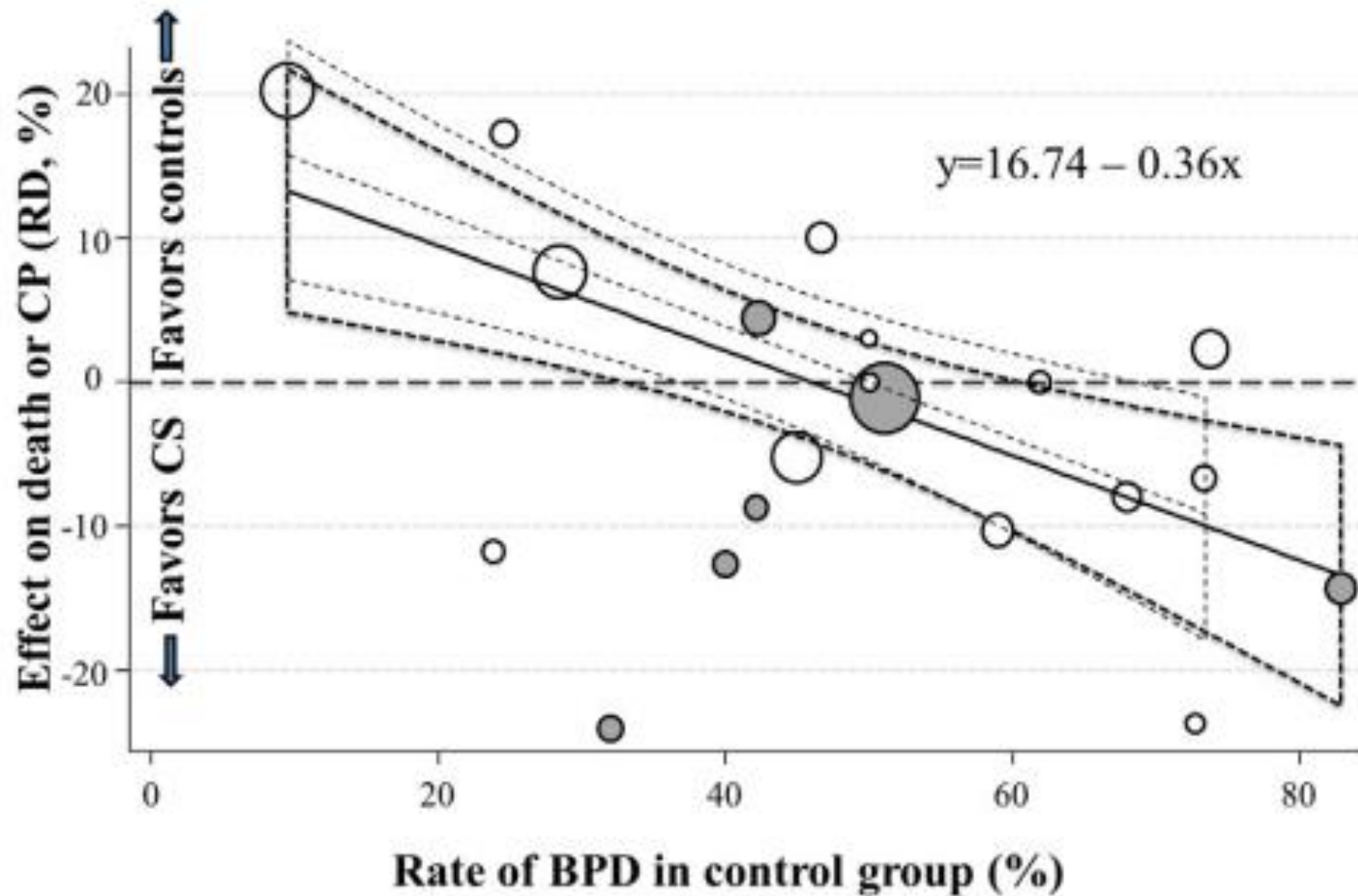
- Intratracheal budesonide with surfactant<sup>1</sup>
- Early (prophylactic hydrocortisone)<sup>2</sup>

1. Van de loo et al. Cochrane review 2024
2. Baud et al, 2016; Shaffer et al, 2019

# Postnatal Corticosteroids

	< 7 days	≥ 7 days
Dexamethasone	Increases risk of death or CP, CP among survivors, and major neurosensory disability	DART regimen widely used but needs more study
Hydrocortisone	< 48 hrs (PREMILOC regimen) Improved survival without BPD but potential risks of infection, GI perforation (in combination with NSAIDs), IVH (in babies with high baseline cortisol)	No benefit (2 large trials)





A firefighter wearing a dark jacket and a yellow and black glove is using a red fire extinguisher to spray a large fire. The fire is bright orange and yellow, with a thick plume of white smoke rising from it. The firefighter is positioned on the left side of the frame, and the fire is on the right. The background is dark and out of focus.

## Bronchopulmonary Dysplasia

Postnatal  
Corticosteroids

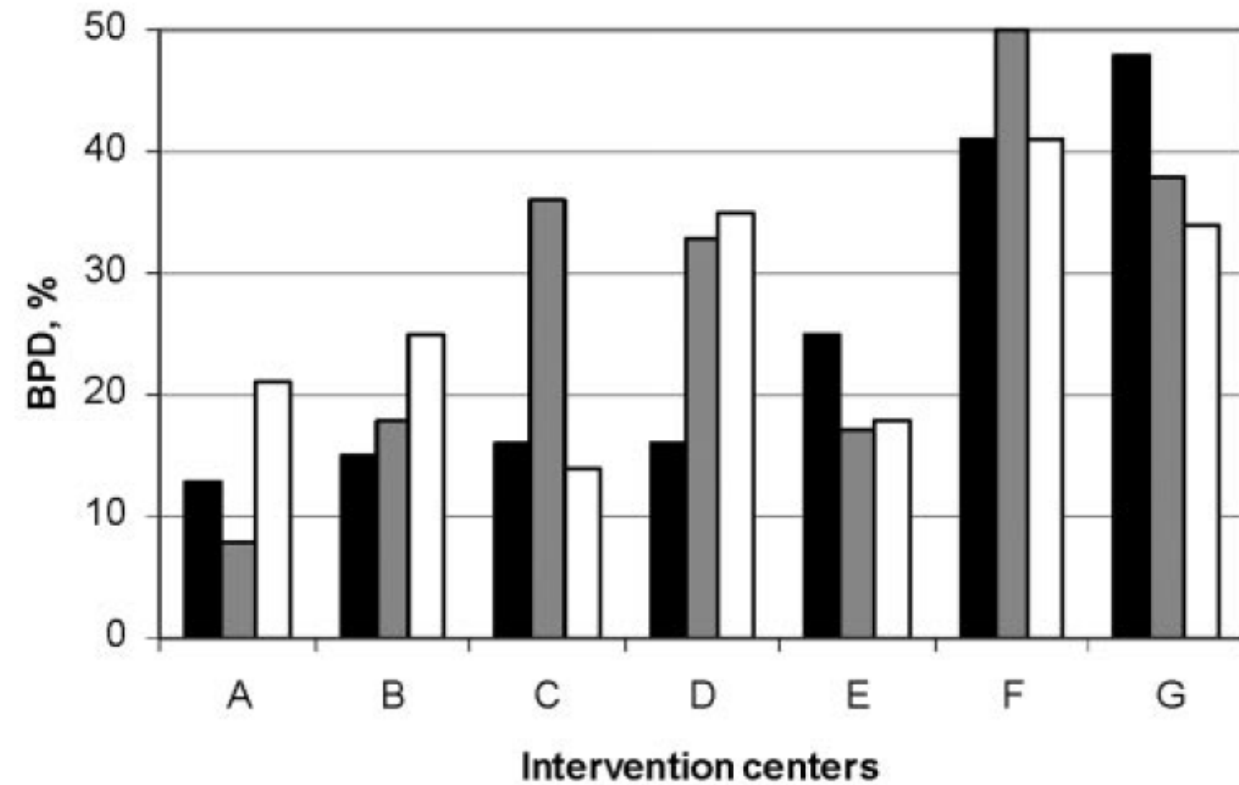
# Implementation

(Translation into Practice, QI, health-care delivery)

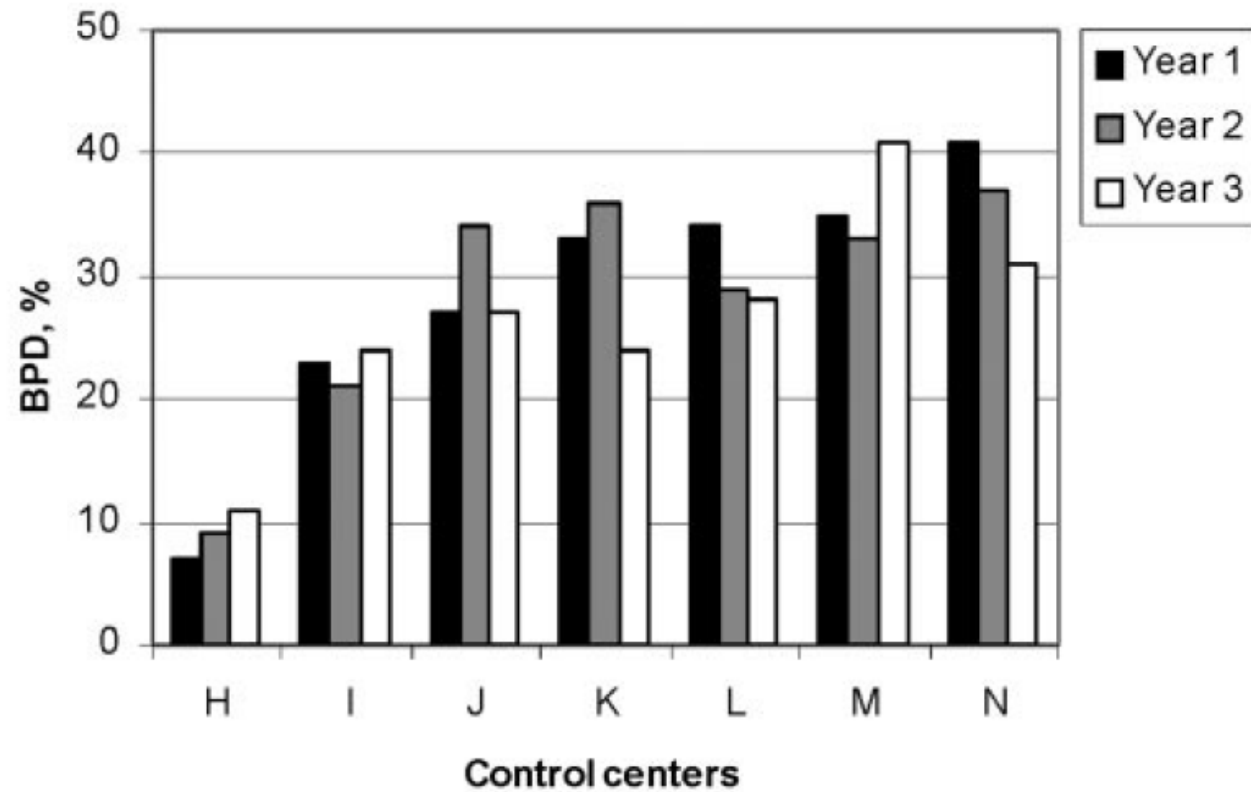
# QI Projects and BPD

- Projects primarily targeting BPD or lung injury
- Golden hour projects
- Variable results

# NRN Cluster RCT of Benchmarking & Multi-modal QI



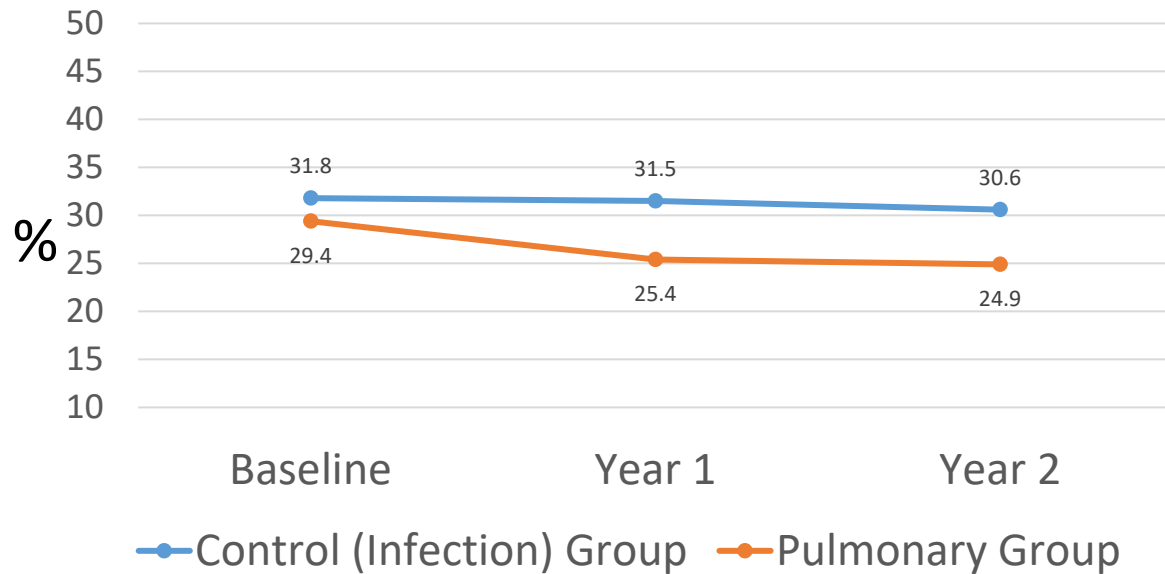
Survival free of BPD 63.3 → 62.2%



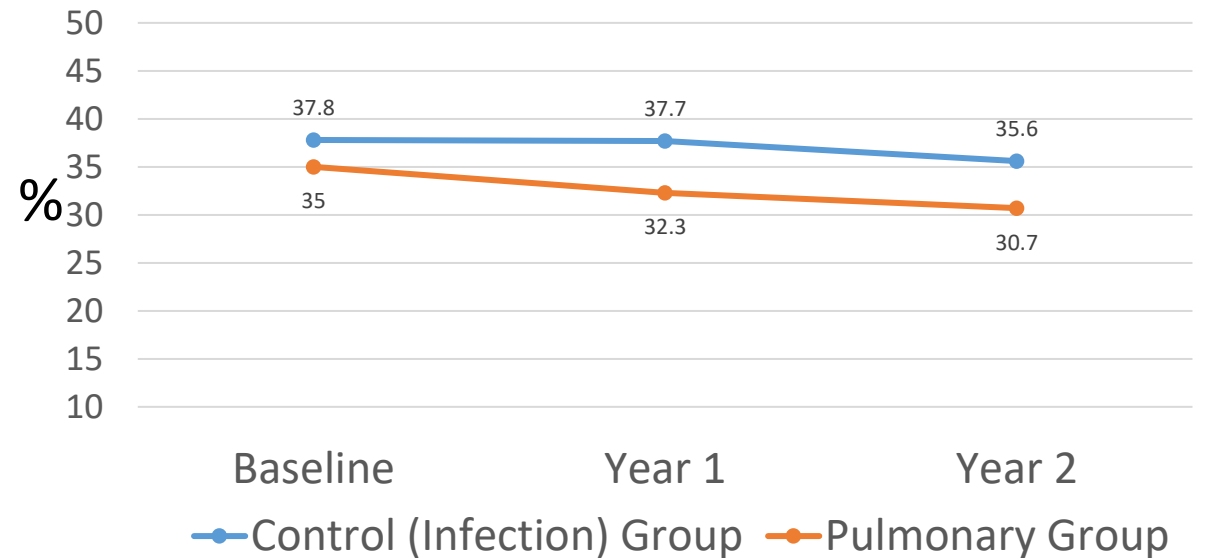
Survival free of BPD 62.7 → 62.8%

# EPIQ Cluster RCT (Canadian Neonatal Network)

## BPD

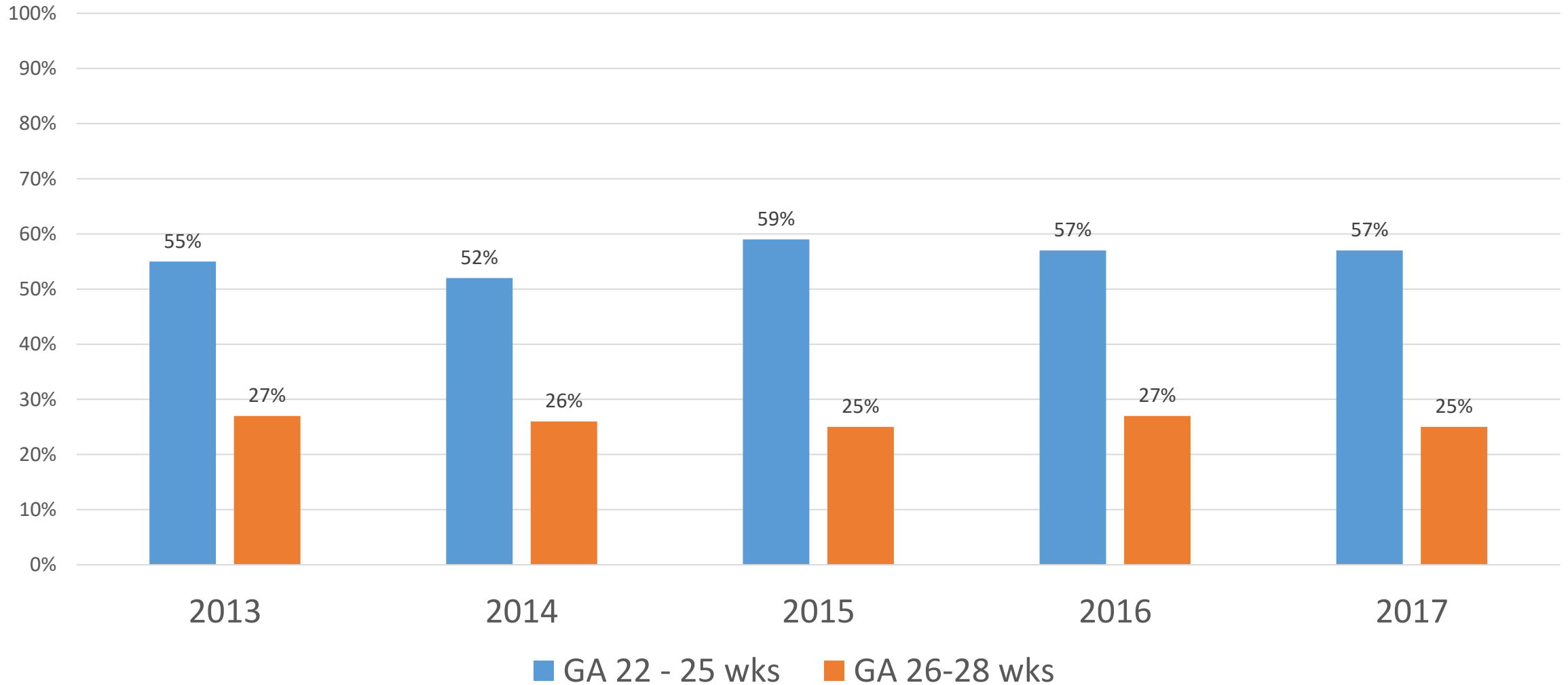


## BPD or Death



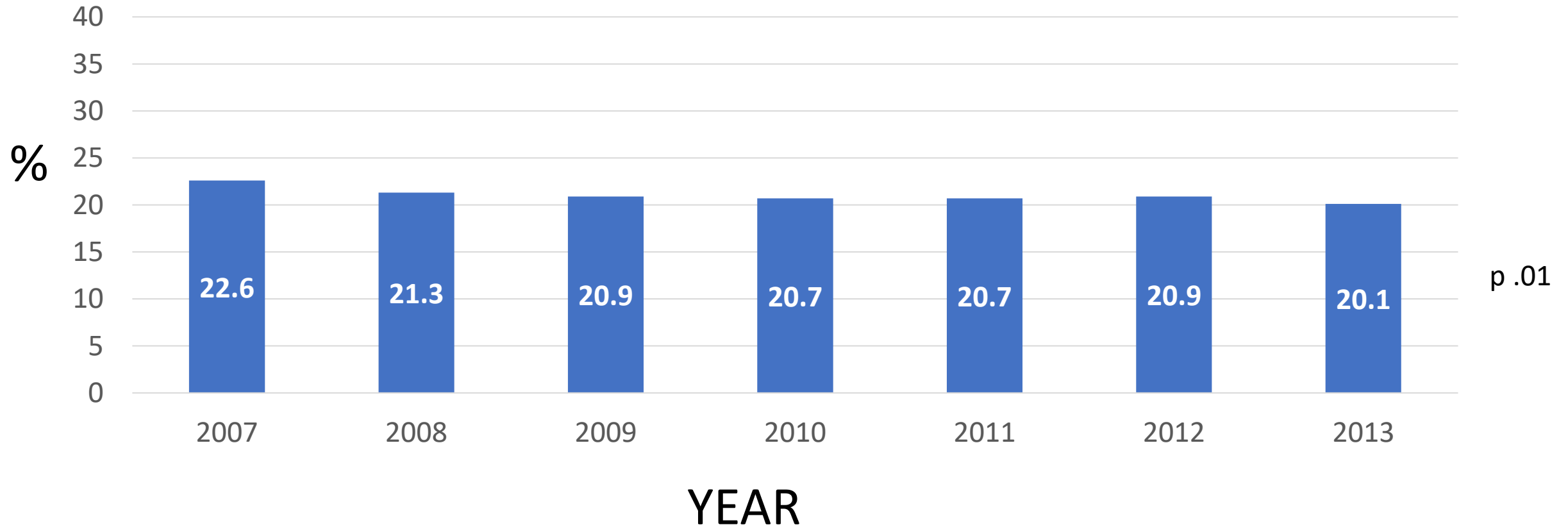
The difference in incidence trends (slopes of trend lines) in the infection and pulmonary groups was  $-0.0006$  (95% CI  $-0.0011$  to  $-0.0001$ ) for bronchopulmonary dysplasia

# Evidence-based Practice for Improving Quality - 3



p = 0.65 and 0.2 respectively

# The 100,000 Babies Campaign: Chronic Lung Disease in Survivors



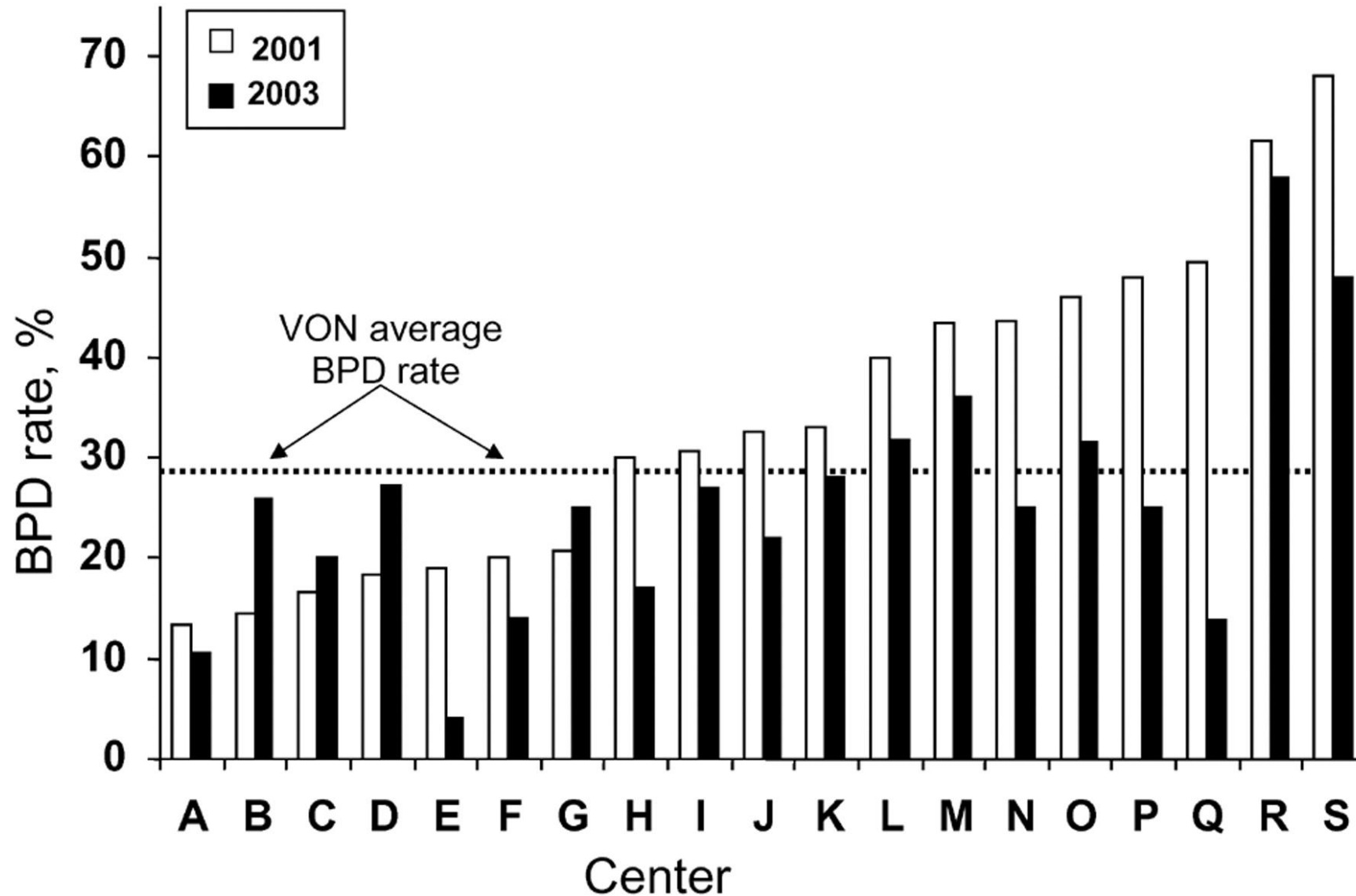
CLD = Alive on > room air at 36 wk PMA

Ellsbury et al, Pediatrics. 2016;137:e20150389



# VON: Breathsavers NICQ Project

## BPD Before and After Implementing PBPs



# VON: Reducing Lung Injury (ReLI) Group

## Results of 9-year Quality Improvement Collaborative Participation by 8 NICUs

**TABLE 6** Changes in Outcome and Treatment According to Birth Weight Group

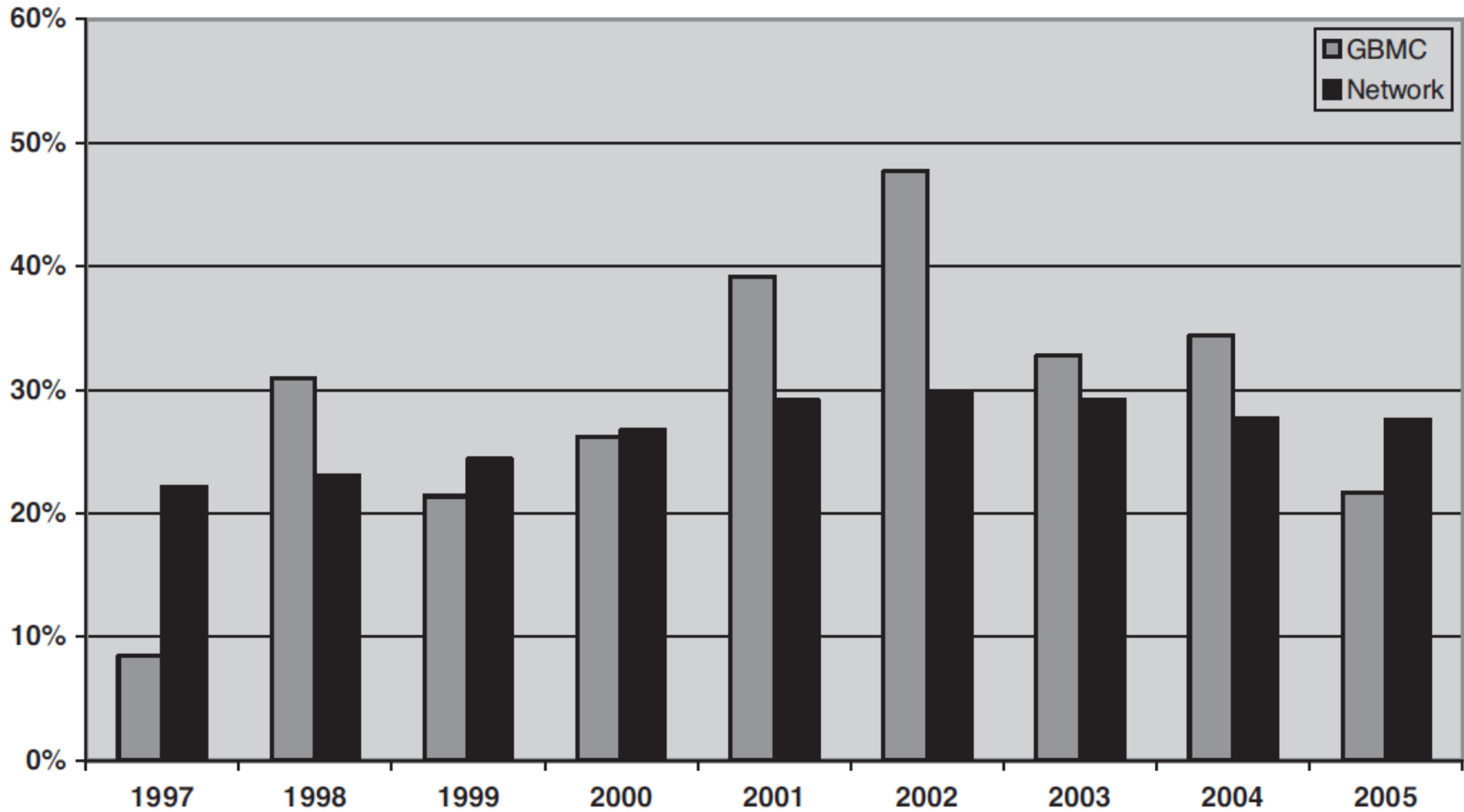
Outcome/Treatment	BW 501–1000 g					BW 1001–1500 g				
	1998 (N = 557), % <sup>b</sup>	2001 (N = 599), % <sup>b</sup>	2006 (N = 595), % <sup>b</sup>	aOR (95% CI) <sup>a</sup>		1998 (N = 709), % <sup>b</sup>	2001 (N = 761), % <sup>b</sup>	2006 (N = 844), % <sup>b</sup>	aOR (95% CI) <sup>a</sup>	
				1998 vs 2001	1998 vs 2006				1998 vs 2001	1998 vs 2006
BPD-free survival	47	39	37	0.7 (0.5–0.9) <sup>c</sup>	0.6 (0.5–0.8) <sup>d</sup>	84	86	86	1.1 (0.8–1.6)	1.3 (1.0–1.9)
Survival	83	81	85	0.8 (0.6–1.2)	1.3 (0.9–2.0)	96	97	98	1.4 (0.7–2.8)	2.2 (1.1–4.7) <sup>c</sup>
BPD	44	52	57	1.5 (1.1–2.1) <sup>d</sup>	1.8 (1.3–2.4) <sup>d</sup>	13	12	12	0.9 (0.6–1.3)	0.8 (0.6–1.2)
DR intubation	92	79	82	0.1 (0.09–0.2) <sup>d</sup>	0.2 (0.09–0.3) <sup>d</sup>	53	37	31	0.4 (0.3–0.5) <sup>d</sup>	0.3 (0.2–0.3) <sup>d</sup>
Any surfactant	89	85	90	0.4 (0.3–0.7) <sup>d</sup>	0.8 (0.5–1.3)	51	46	49	0.7 (0.6–1.0) <sup>c</sup>	0.8 (0.6–1.0)
Surfactant at <30 min	61	85	92	4.7 (3.2–6.9) <sup>d</sup>	10.3 (6.6–16.1) <sup>d</sup>	46	62	68	2.3 (1.5–3.4) <sup>d</sup>	3.4 (2.3–5.1) <sup>d</sup>
Conventional ventilation	92	84	87	0.3 (0.2–0.4) <sup>d</sup>	0.3 (0.2–0.5) <sup>d</sup>	62	47	45	0.4 (0.3–0.5) <sup>d</sup>	0.3 (0.2–0.4) <sup>d</sup>
High-frequency ventilation	60	47	53	0.4 (0.3–0.6) <sup>d</sup>	0.6 (0.4–0.8) <sup>d</sup>	14	10	10	0.8 (0.5–1.1)	0.7 (0.5–1.0)
NCPAP at any time	68	81	85	2.3 (1.7–3.2) <sup>d</sup>	3.4 (2.4–4.7) <sup>d</sup>	49	65	73	2.5 (2.0–3.2) <sup>d</sup>	3.5 (2.7–4.4) <sup>d</sup>
Steroids for BPD	63	27	21	0.1 (0.09–0.2) <sup>d</sup>	0.1 (0.1–0.1) <sup>d</sup>	14	3	2	0.2 (0.1–0.3) <sup>d</sup>	0.07 (0.0–0.1) <sup>d</sup>

<sup>a</sup> ORs are adjusted for birth weight percentile category, gestational age group, prenatal care (yes/no), antenatal steroids, gender, black maternal race, outborn birth location, vaginal delivery, multiple birth, Apgar score of <4 at 1 min, early-onset bacterial sepsis, and birth defect.

<sup>b</sup> Unadjusted.

<sup>c</sup>  $P < .05$ .

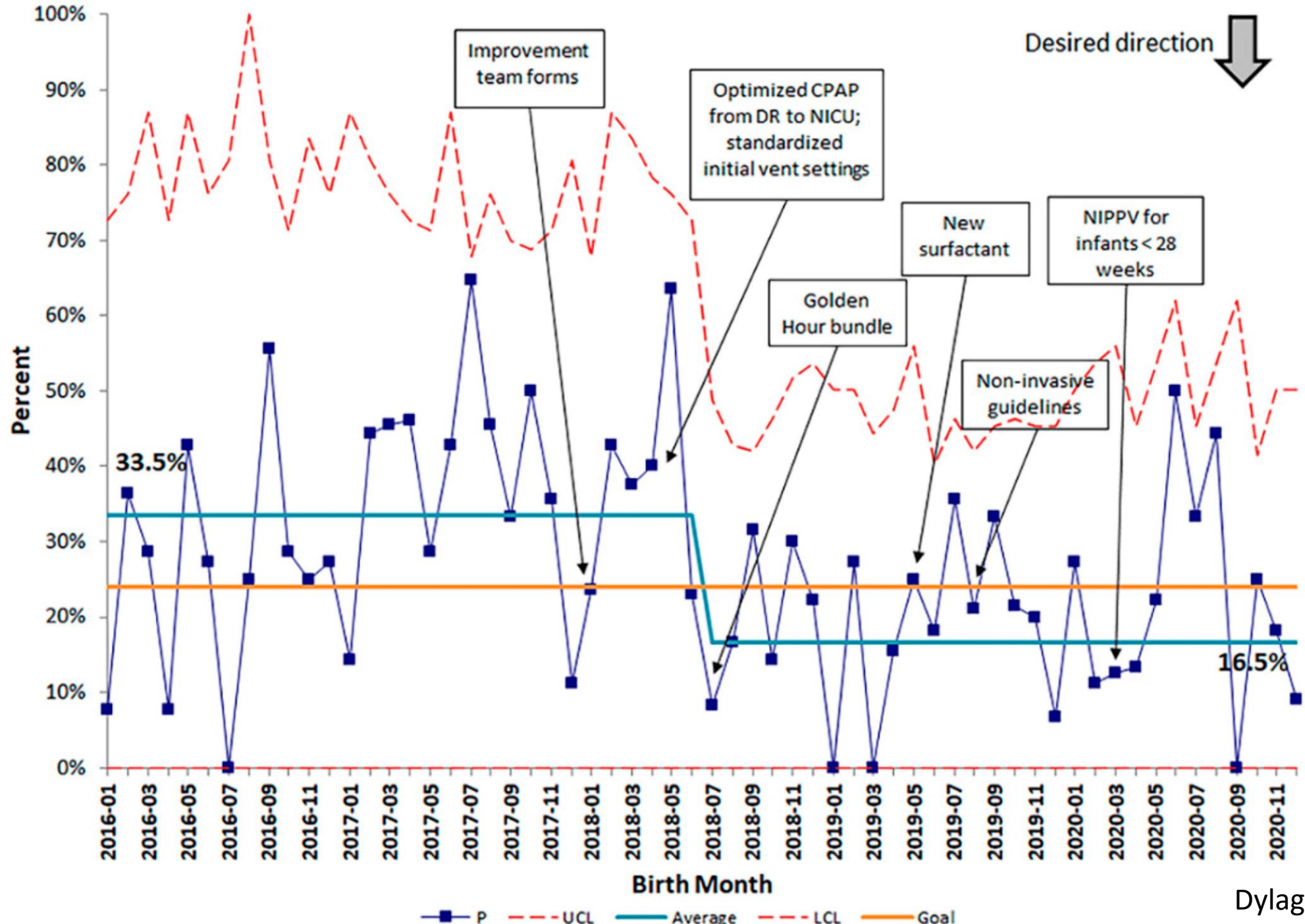
<sup>d</sup>  $P < .01$ .



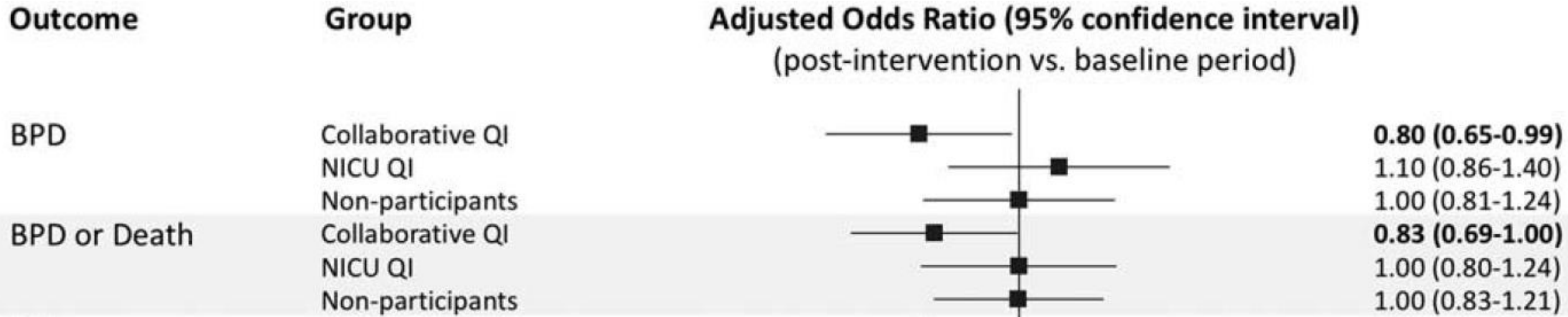
# Systematic Review: QI to Reduce BPD

- Publications describing QI projects to reduce BPD, n = 34
- Published between 2001 – 2020
- Interventions: Delivery room-based interventions; surfactant delivery, increased and optimized non-invasive ventilation; approach to mechanical ventilation; avoidance of hyperoxia
- Single center reports – BPD ↓ reported in 15 / 22
- QI collaboratives - BPD ↓ reported in 5 / 7

Healy et al 2021

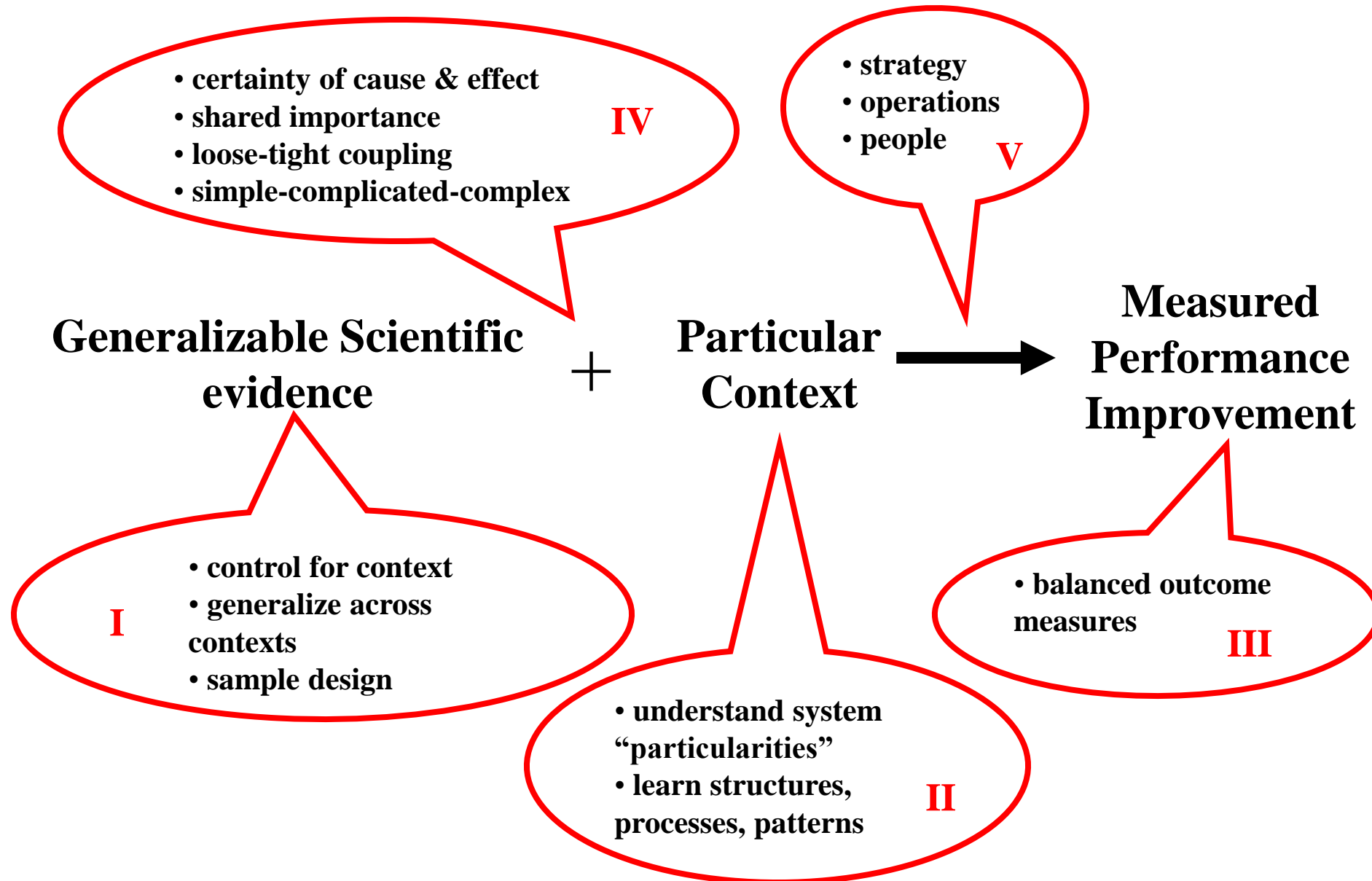


# Golden Hour Projects: CPQCC



Why Variable Results?

# Linking Evidence to Improvement





# Some of the PBPs Used in BPD QI Efforts

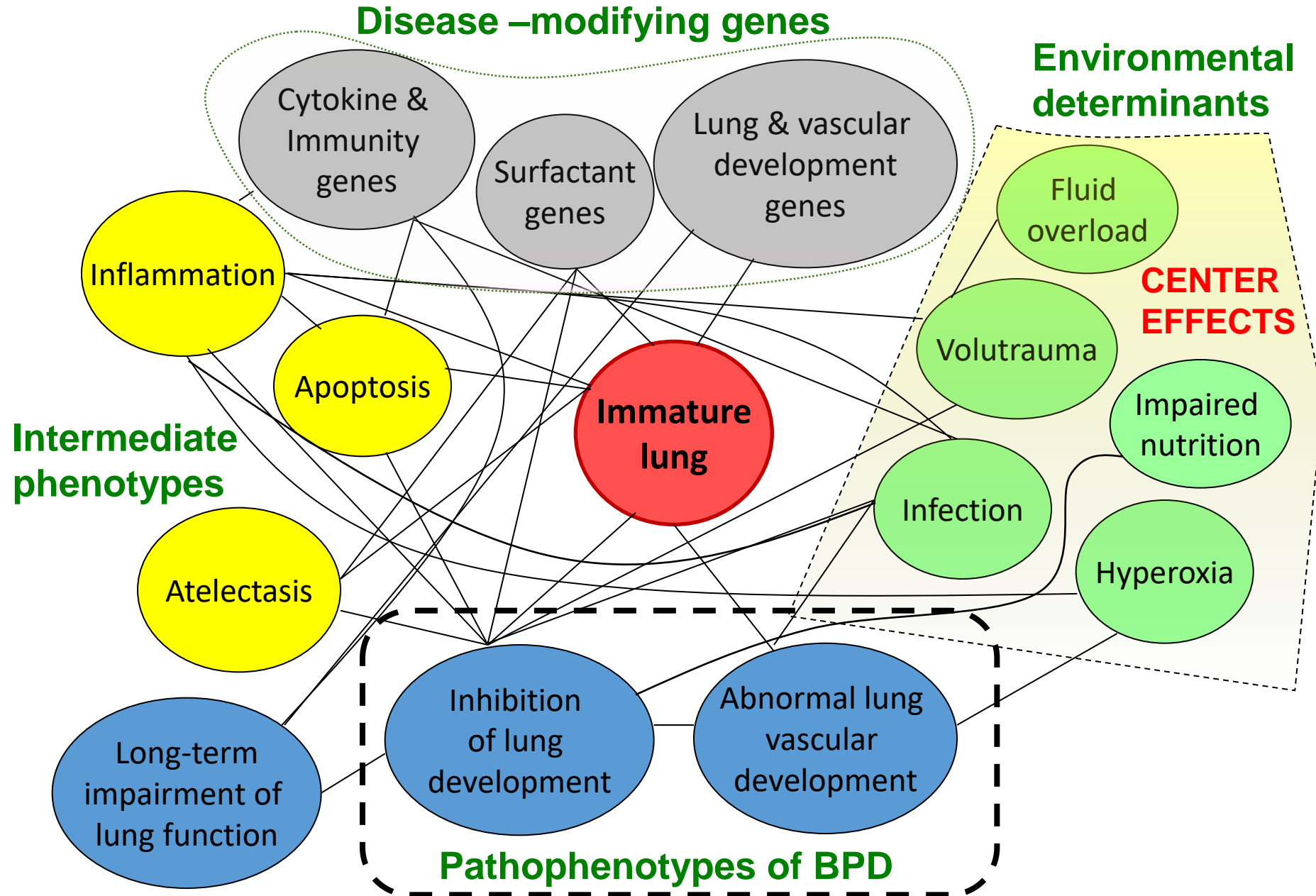
(In various combinations, often by center's choice)

- Antenatal steroids
- Surfactant (including prophylactic)
- CPAP / avoidance of intubation
- T-piece resuscitator
- INSURE
- Volume ventilation
- Early extubation
- NIPPV
- Oxygen saturation targeting
- Permissive hypercapnia
- Lower oxygen saturation goals
- Fluid restriction
- Vitamin A
- Caffeine
- Aggressive PDA management
- Non-routine analgesics/sedatives

# BPD

- Not one disease
- Heterogeneity in the clinical phenotype, genetic basis, and pathology
- “All normal lungs are similar; every abnormal lung is abnormal in its own way”
- Our current state of knowledge similar to that regarding sepsis in 1930s, or leukemias in 1950s

# BPD disease network

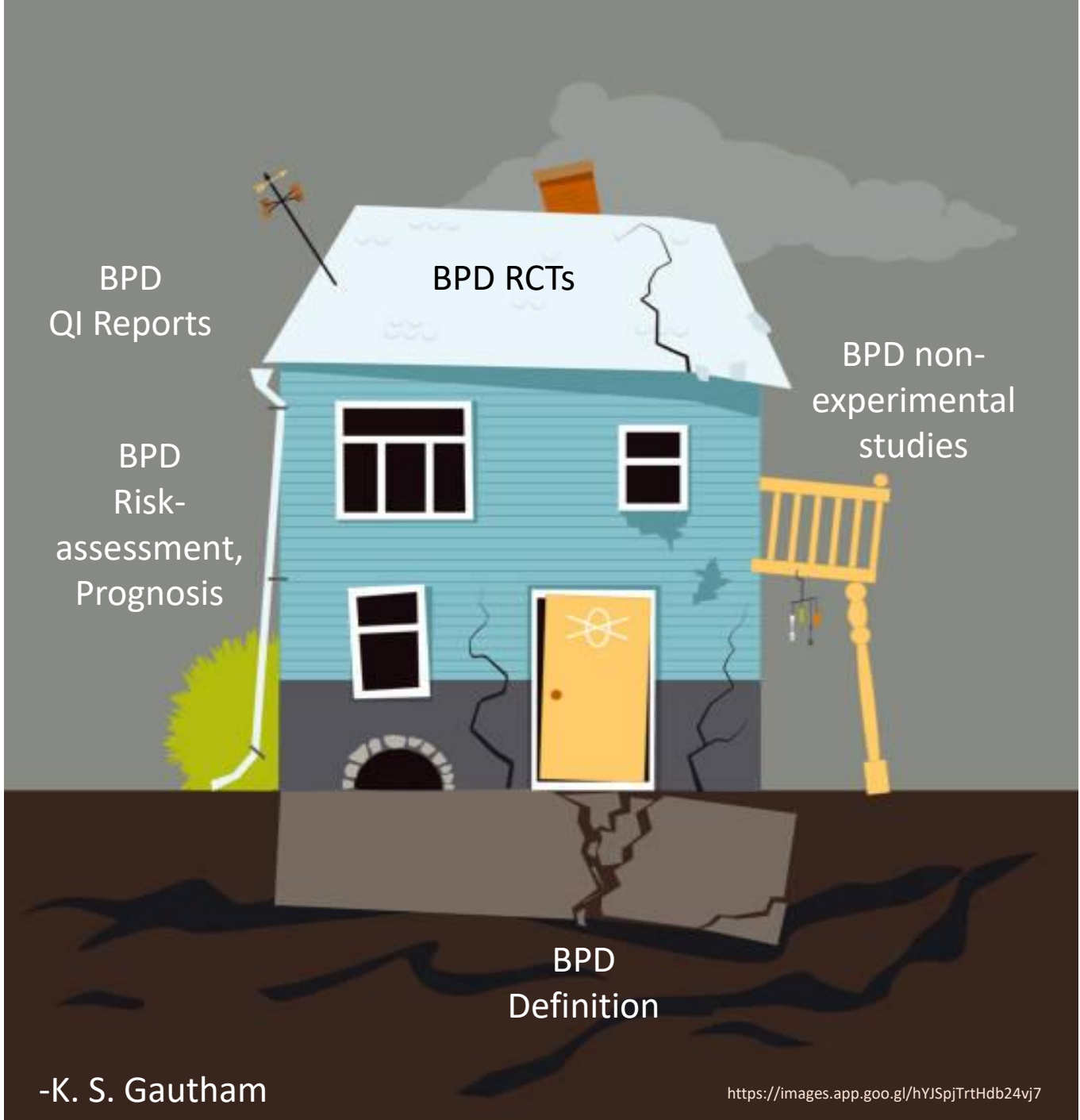


# Terminology & Definitions

- Bronchopulmonary dysplasia
  - Chronic lung disease
- Various definitions
- 28 consecutive days of oxygen
  - Oxygen on day 28
  - Oxygen at 36 weeks PMA
  - Respiratory support @ 36 wks PMA
  - Oxygen challenge test
  - Radiographic findings

# What Outcome to Target?

- CLD
- BPD
- Severity of BPD
- Death or BPD
- Sub-type of BPD (several phenotypes)
- Compliance with unit guidelines / best practices
- Different goals for different GA categories
- Discharge on oxygen
- Tracheostomy
- Ventilator days



BPD  
QI Reports

BPD RCTs

BPD non-  
experimental  
studies

BPD  
Risk-  
assessment,  
Prognosis

BPD  
Definition

Attitude (and belief)

# Two Conceptual Models for Nosocomial Sepsis

	ENTITLEMENT	PREVENTION
Causality	Unavoidable – inherent risk from poor immune function and necessary invasive care	Preventable in most instances
Focus of care team	Early detection	Prevention
Why did it happen?	Chance or unavoidable	Breakdown in ideal care
Responsibility	Baby's vulnerability	Care team
Motivation for improvement	Fatalistic, inevitable	Challenge to continually improve



# Central Line–Associated Bloodstream Infections in Neonatal Intensive Care: Changing the Mental Model from Inevitability to Preventability

Gautham K. Suresh, M.D., D.M., M.S.<sup>1</sup> William H. Edwards, M.D.<sup>1</sup>

<sup>1</sup> Department of Pediatrics, Dartmouth Medical School, Lebanon, New Hampshire

Am J Perinatol 2012;29:57–64.

Address for correspondence and reprint requests Gautham K. Suresh, M.D., D.M., M.S., Department of Pediatrics, Rubin 529, Dartmouth-Hitchcock Medical Center, One Medical Center Drive, Lebanon, NH 03756 (e-mail: gautham.suresh@hitchcock.org).

## Abstract

Previously considered unavoidable complications of hospital care (reflecting an “entitlement” mental model), health care–associated infections are now considered as medical errors and cause significant preventable morbidity and mortality in neonates. Prevention of such infections, particularly central line–associated bloodstream infections (CLABSI), should be an important patient safety priority for all neonatal intensive care units (NICUs). An important first step is to promote a mental model of CLABSIs as preventable complications of care. Other general strategies are (1) promoting an organizational culture of safety and empowerment of staff; (2) hand hygiene; (3) avoiding overcrowding and understaffing; (4) using breast milk for enteral feedings; and (5) involving families in infection prevention efforts. Specific strategies to prevent

## Keywords

- ▶ health care–associated infection
- ▶ nosocomial infection

# Who is the 'Ventilator'?

The machine



The clinician  
using the  
machine



Both are important in the causation  
and prevention of BPD

# Physician-induced Lung Injury

- Term used by Villar 2005 in relation to ARDS
- Preventable lung injury not avoided due to lack of knowledge, not following evidence-based practices, omissions, errors
- ‘Modifiable risk factor’ contributing to BPD
- Emphasizes preventability, accountability

# Human Fallibility / Failure

- Necessary fallibility (things beyond our capacity)
- Unnecessary fallibility
  - Ignorance (knowledge not yet present)
  - Ineptitude (fail to apply knowledge correctly)

# 'Respiratory Ineptitude'

- Manual PPV / Hand-bagging

*“There is perhaps nothing more dangerous for the preterm lung than an anxious physician with an endotracheal tube and a bag.”<sup>1</sup>*

- Trying to assess lung compliance by bagging – ‘educated hand’ myth<sup>2,3</sup>

1. Jobe AH. J Pediatr. 2005 Sep;147:284-6
2. Bowman et al. J Pediatr. 2012 Mar;160:372-376
3. Kattwinkel et al. Pediatrics. 2009 Mar;123:e465-70

# 'Respiratory Ineptitude'

- 'Road trips' to OR, radiology, IR & from DR
- Delaying extubation needlessly
- Wrong weight entered into the ventilator  
(Tidal volume per kg erroneous)
- Ventilation prior to and during transport

# 'Respiratory Ineptitude'

- Inconsistency of care
  - 'Ventilators' have different styles based on training and experience
- Lack of vigilance and monitoring
  - Oxygen saturation, tidal volume, PIP and PEEP, bedside pulmonary graphics, blood gases, transcutaneous gases

# LUNG INJURY



- Survival
- Lung health
- Brain health

**LUNG INFLATION**  
Gas exchange



# What Causes Ineptitude?

- Focus on the visible rather than invisible
- Focus on short-term and ignoring long-term ('short-termism')
- Lack of belief in preventability and one's own contribution to such preventability
- Unit culture and group beliefs – Plato's cave

# Conclusions

- A portion of BPD in your unit is preventable
- Prevention requires a belief in preventability + implementation of practices supported by high-quality evidence + vigilance and meticulous monitoring of respiratory support and status
- Monitor multiple indicators of lung health, not just BPD Yes/No

# The Amazing Preterm Lung

- The very preterm lung is easily injured even with gentle ventilation
- Injury can be minimized with ACS, surfactant, CPAP, limiting oxygen, non-invasive ventilation
- Lung can function, ‘heal’, grow in spite of injury, and avoid fibrosis
- Developmental and repair programs can over-ride ongoing injury to permit relatively normal lung structure and function by midchildhood
- *“The neonatal community tends to focus on the most severe cases with injured lungs and poor neurodevelopmental outcomes. It is worth celebrating the remarkable lungs for the majority of preterm infants.”*

Thank You!