SAP

SOCIEDAD ARGENTINA DE PEDIATRÍA

Bronchopulmonary Dysplasia: Evidence for Best Practice

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Bronchopulmonary Dysplasia: Evidence for Best Practice

Disclosure

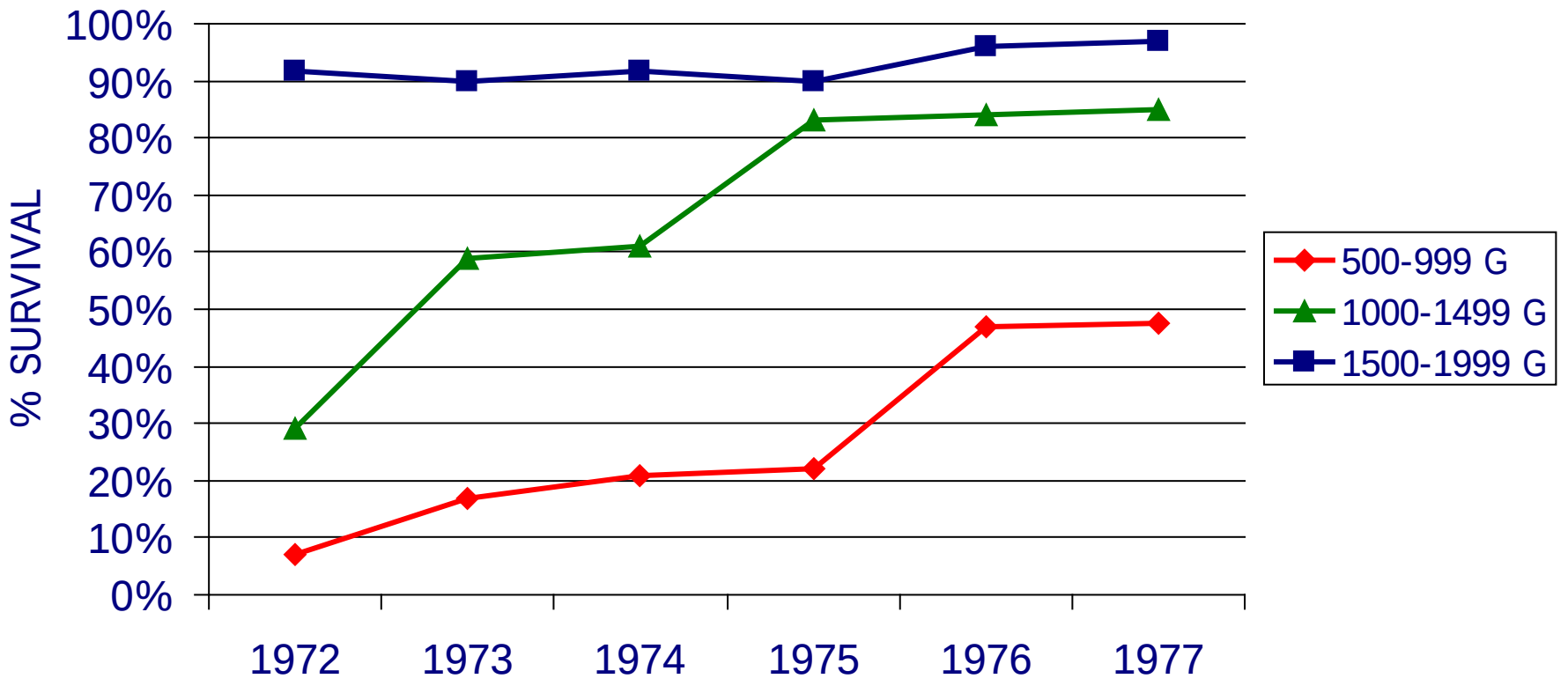
Dr. Soll is President of
The Vermont Oxford Network and
Coordinating Editor of Cochrane Neonatal

No other relevant financial issues to disclose.

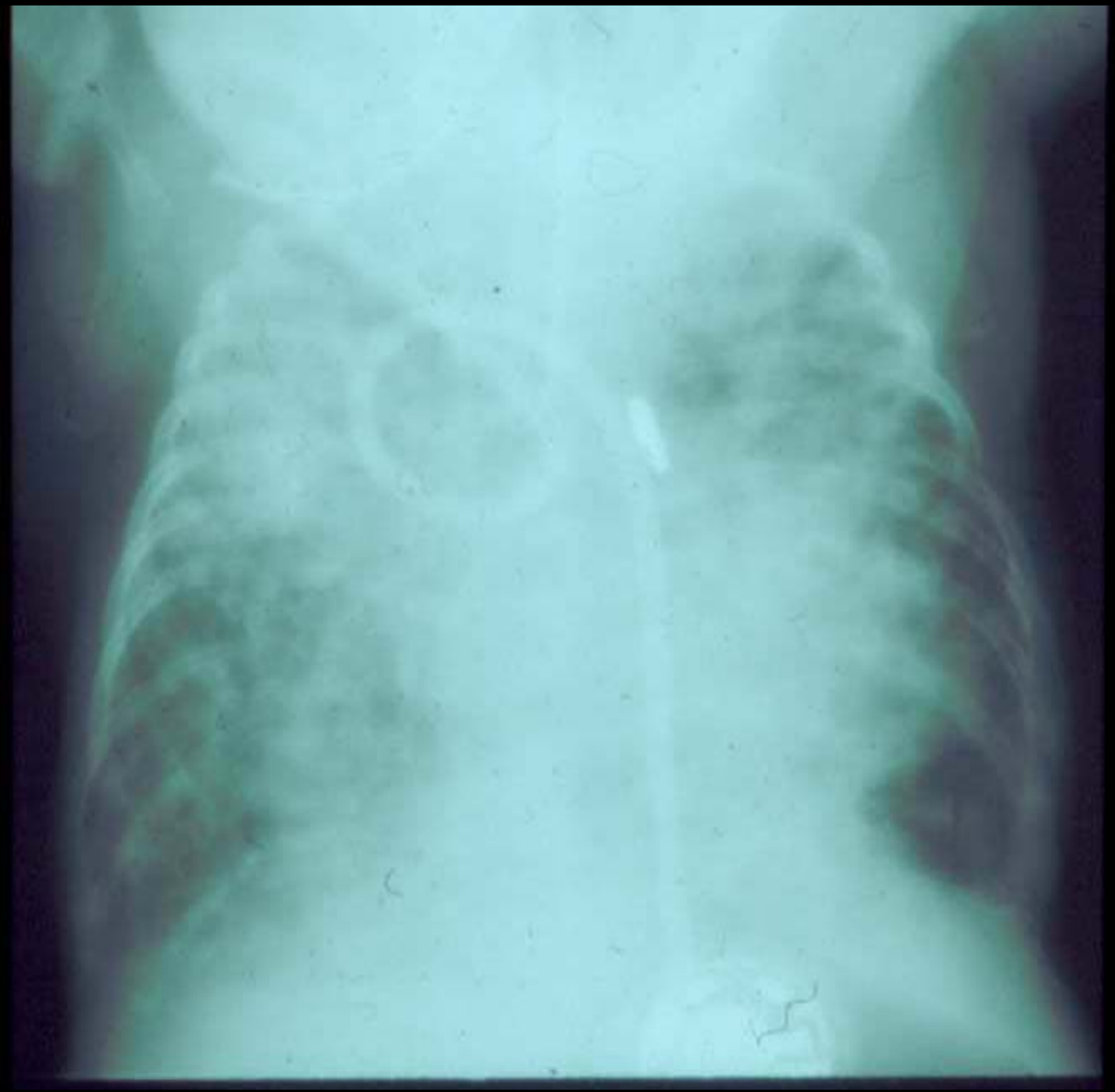
Bronchopulmonary Dysplasia: Evidence for Best Practice

- Incidence and prevalence of Bronchopulmonary Dysplasia
- Associations, risk factors, and protective factors
- Bronchopulmonary Dysplasia definitions
- Evidence based practices for:
  - Prevention of Bronchopulmonary Dysplasia
  - Treatment of Bronchopulmonary Dysplasia

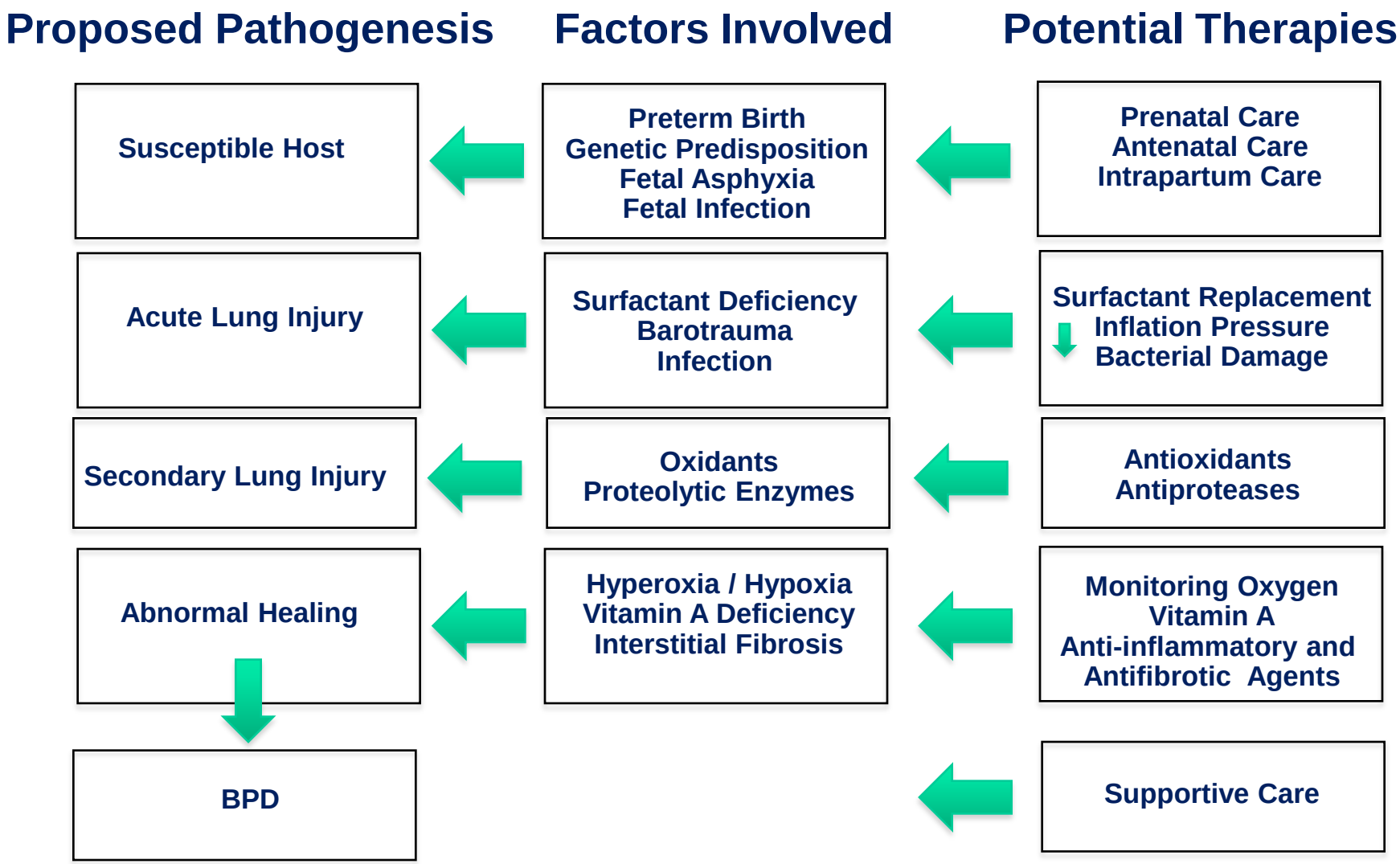
Improved survival with the introduction of mechanical ventilation in the 1970's



Wung JT and coworkers. J Pediatrics 1979; 95: 846



Bronchopulmonary Dysplasia: proposed pathogenesis, contributing factors and potential treatments

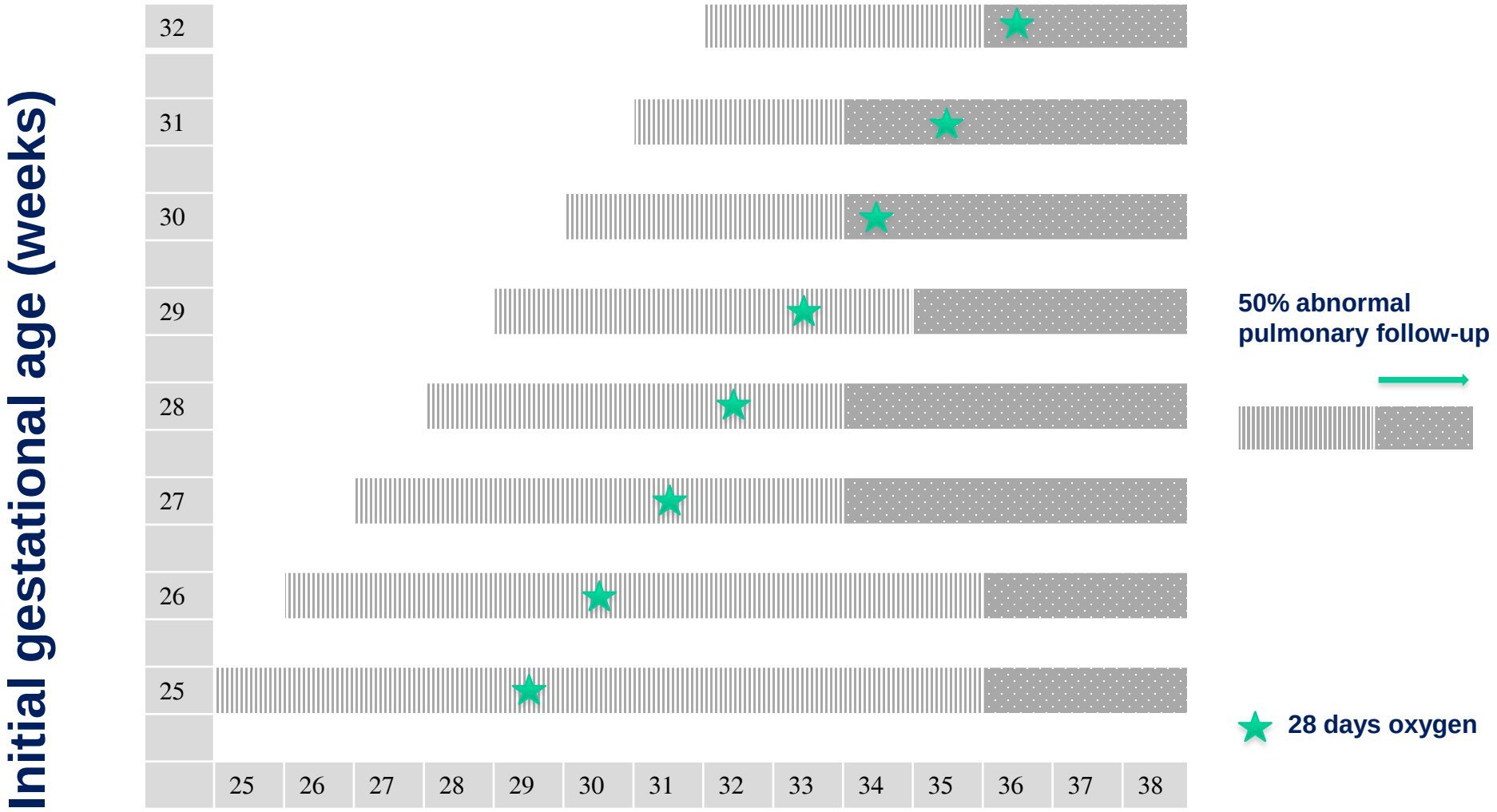


What do we mean when we say “Bronchopulmonary Dysplasia”?

Original definition:

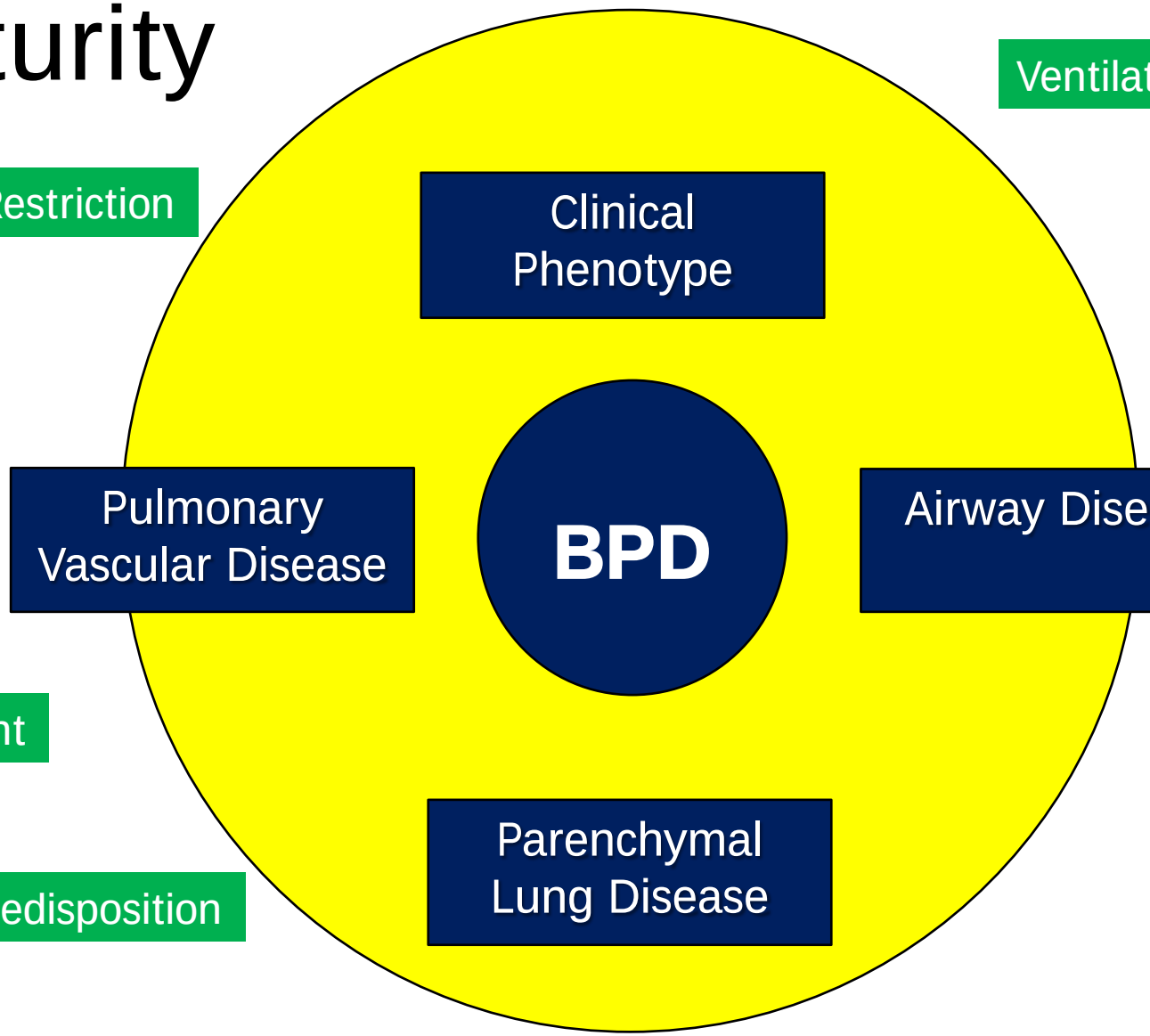
- On assisted ventilation at some time during first 3 days of life
- Requiring supplemental oxygen at day 28 to 30
- Radiographic features consistent with bronchopulmonary dysplasia

Evolving definitions: Why 36 weeks' postmenstrual age?



Shennan 1988

Prematurity



Intrauterine Growth Restriction

Antenatal Steroids

Nutritional Impairment

Genetic/Epigenetic Predisposition

Ventilator Induced Lung Injury

Postnatal Infection

Oxygen Toxicity

Patent Ductus Arteriosus

Higgins RD, Jobe AH, Koso-Thomas M, et al. Bronchopulmonary Dysplasia: Executive Summary of a Workshop. J Pediatr 2018; 197:300.

Newer Definitions: Bronchopulmonary Dysplasia

Severity – Based Diagnostic Criteria for BPD
For infants at 36 weeks PMA or discharge

Received oxygen for at least 28 days and at 36 week's postmenstrual age has:

Mild BPD:	in room air
Moderate BPD:	$FiO_2 < 0.3$
Severe BPD:	$FiO_2 \geq 0.3$ and/or PPV or CPAP

Ehrenkranz 2005

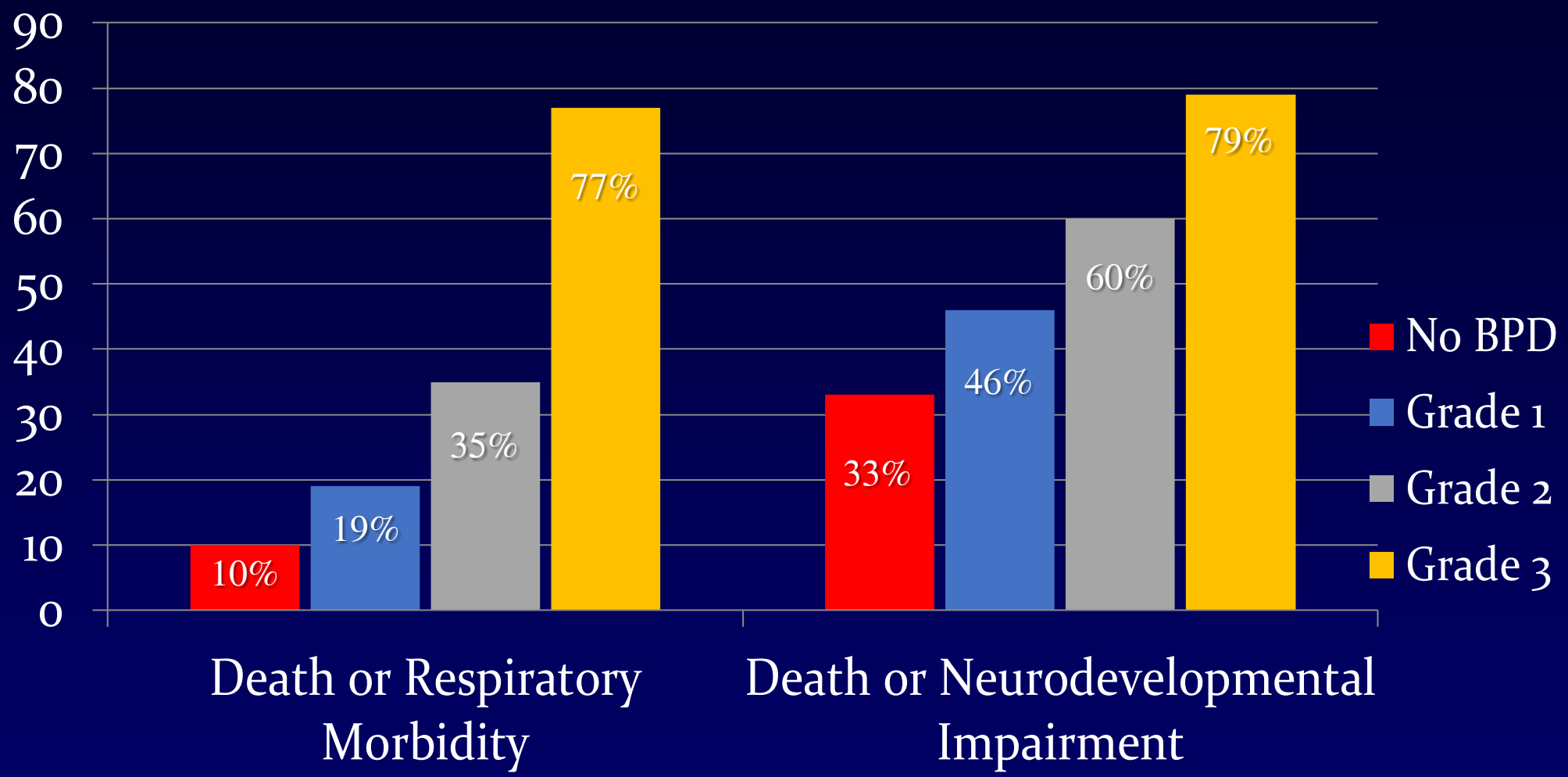
Suggested refinements to the definition of Bronchopulmonary Dysplasia

A preterm infant (< 32 weeks' gestational age) with BPD has persistent parenchymal lung disease, radiographic confirmation of parenchymal lung disease, and at 36 weeks' postmenstrual age requires one of the following FiO2 ranges/oxygen levels/O2 concentrations for ≥ 3 consecutive days to maintain arterial oxygen saturation in the 90% to 95% range

Grade	Invasive IPPV	NCPAP, NIPPV Nasal cannula > 3 L/min	Nasal cannula 1 to 3 L/min	Hood Oxygen	Nasal cannula < 1 L/min
Grade I	n/a	0.21	0.22 to 0.29	0.22 to 0.29	0.22 to 0.70
Grade II	0.21	0.22 to 0.29	≥ 0.30	≥ 0.30	> 0.70
Grade III	> 0.21	≥ 0.30			
Grade III (A)	Early death (between 14 days postnatal age and 36 weeks) owing to persistent parenchymal lung disease and respiratory failure that cannot be attributable to other neonatal morbidities				

Higgins and colleagues. Bronchopulmonary Dysplasia: Executive Summary of a Workshop. J Pediatr 2018; 197:300.

BPD Severity and Outcome



Jensen EA and colleagues. The Diagnosis of Bronchopulmonary Dysplasia in Very Preterm Infants: An Evidence-Based Approach. Am J Respir Crit Care Med. 2019 Apr 17. doi: 10.1164/rccm.201812-2348OC.

JAMA Pediatrics

Revisiting the Definition of Bronchopulmonary Dysplasia: Effect of Changing Panoply of Respiratory Support for Preterm Neonates

Tetsuya Isayama, MD; Shoo K. Lee, MBBS, PhD; Junmin Yang, MSc; David Lee, MD; Sibasis Daspal, MD; Michael Dunn, MD; Prakesh S. Shah, MD, MSc; for the Canadian Neonatal Network and Canadian Neonatal Follow-Up Network Investigators

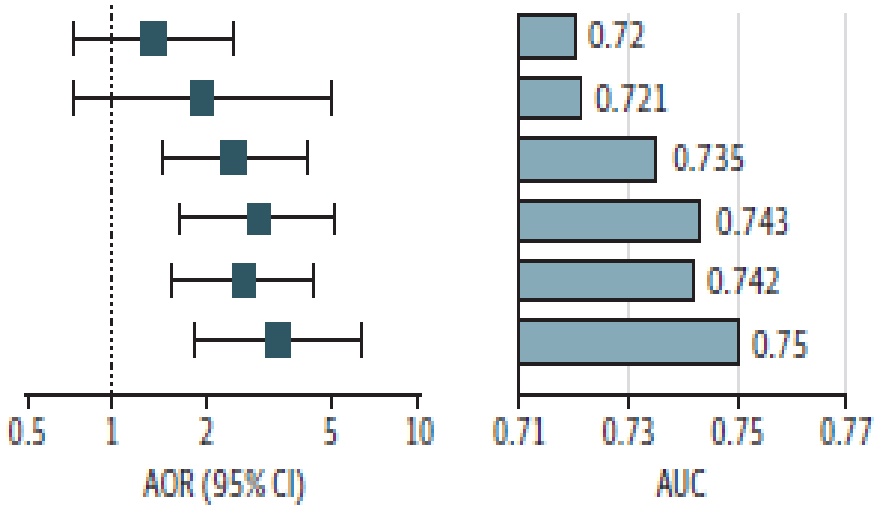
JAMA Pediatrics 2017 doi:10.1001/jamapediatrics.2016.4141

JAMA Pediatrics

Association of 6 Traditional Bronchopulmonary Dysplasia (BPD) Definitions With Adverse Outcomes at 18 to 21 Months of Age

A Serious respiratory morbidity

Traditional BPD Definitions	Adverse Outcome In BPD (+) Infants	Adverse Outcome In BPD (−) Infants	AOR (95% CI)[a]
Oxygen, 28 d	71/893 (8.0)	17/513 (3.3)	1.3 (0.7-2.4)
Oxygen/RS, 28 d	81/1123 (7.2)	7/283 (2.5)	1.9 (0.7-5.0)
Oxygen, 28 d and Oxygen/RS 36 wk PMA	62/579 (10.7)	26/827 (3.1)	2.4 (1.4-4.2)
Oxygen/RS, 28 d and 36 wk PMA	66/620 (10.7)	22/786 (2.8)	2.9 (1.6-5.2)
Oxygen, 36 wk PMA	61/548 (11.1)	27/858 (3.2)	2.6 (1.5-4.4)
Oxygen/RS 36 wk PMA	69/652 (10.6)	19/754 (2.5)	3.4 (1.8-6.3)



Definitions using oxygen requirement alone as the criterion at various postmenstrual ages were less predictive compared with those using the criterion of oxygen/respiratory support (RS) (receiving supplemental oxygen and/or positive-pressure RS)

Among those, oxygen/RS at 36 weeks had the highest AOR and area under the curve (AUC) for all outcomes.

Bronchopulmonary Dysplasia: Evidence for Best Practice

Why do I care about Bronchopulmonary Dysplasia?

Why do I care about Bronchopulmonary Dysplasia?

Impact on Pulmonary Outcomes

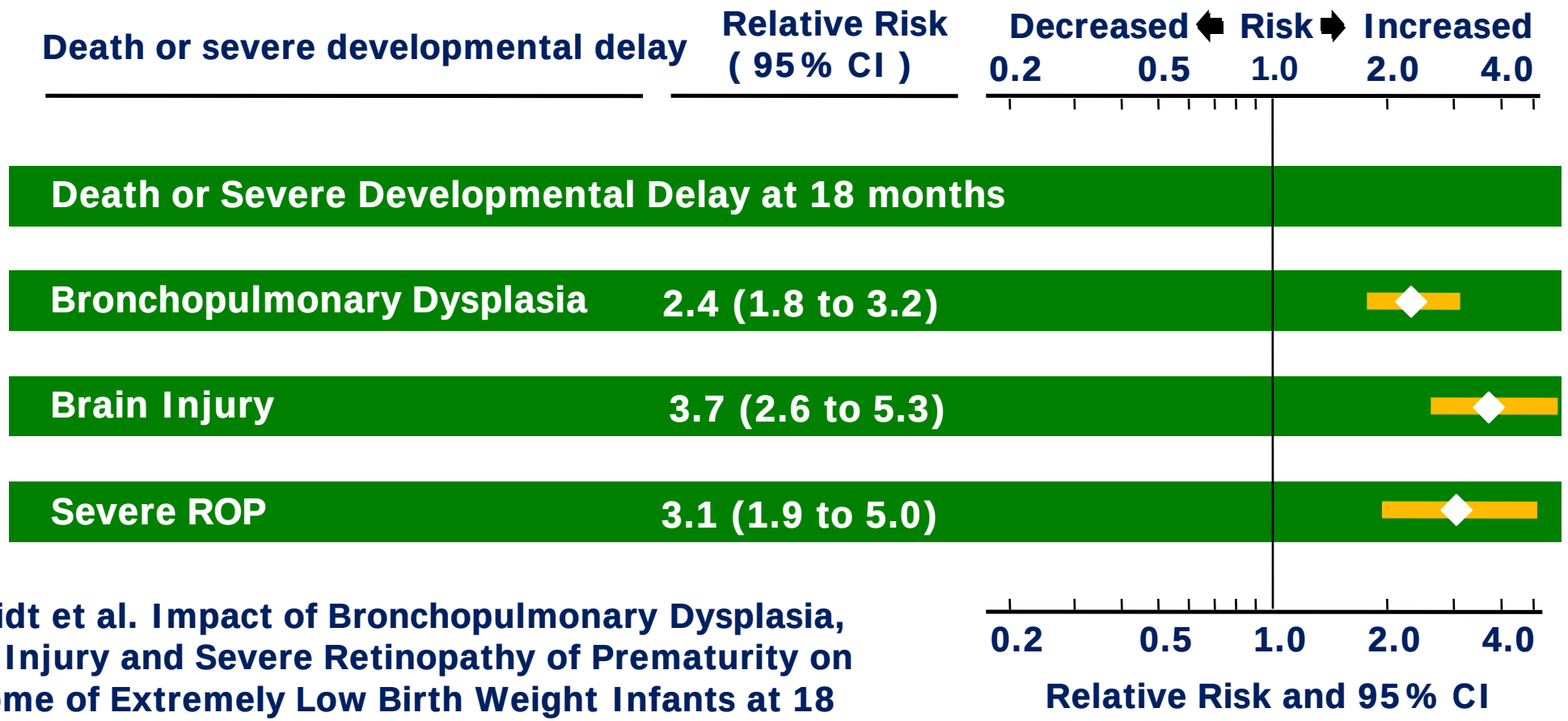
In the first 2 years of life
- Re-hospitalization for respiratory illness

After 4 to 5 years of life
- Asthma
- Chronic respiratory symptoms

In adolescence
- Abnormal pulmonary function

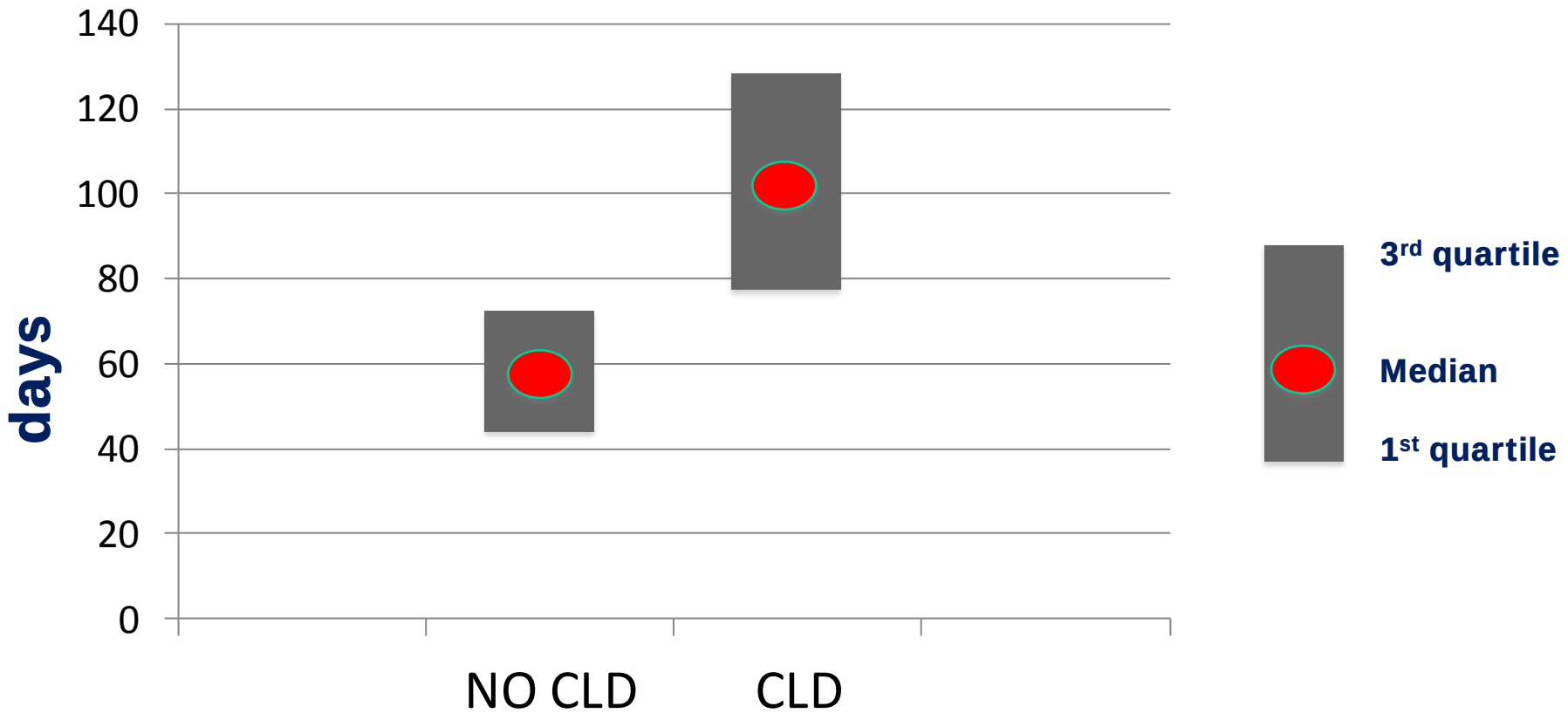
Impact of Bronchopulmonary Dysplasia on Death or Severe Neurodevelopmental Delay

SCHMIDT AND COWORKERS 2003



Schmidt et al. Impact of Bronchopulmonary Dysplasia, Brain Injury and Severe Retinopathy of Prematurity on Outcome of Extremely Low Birth Weight Infants at 18 Months. Jama 2003

Chronic Lung Disease and Length of Stay



VON VLBW Database 2013

THERAPY FOR BPD: EVIDENCE BASED?

Bronchopulmonary Dysplasia: Evidence for Best Practice

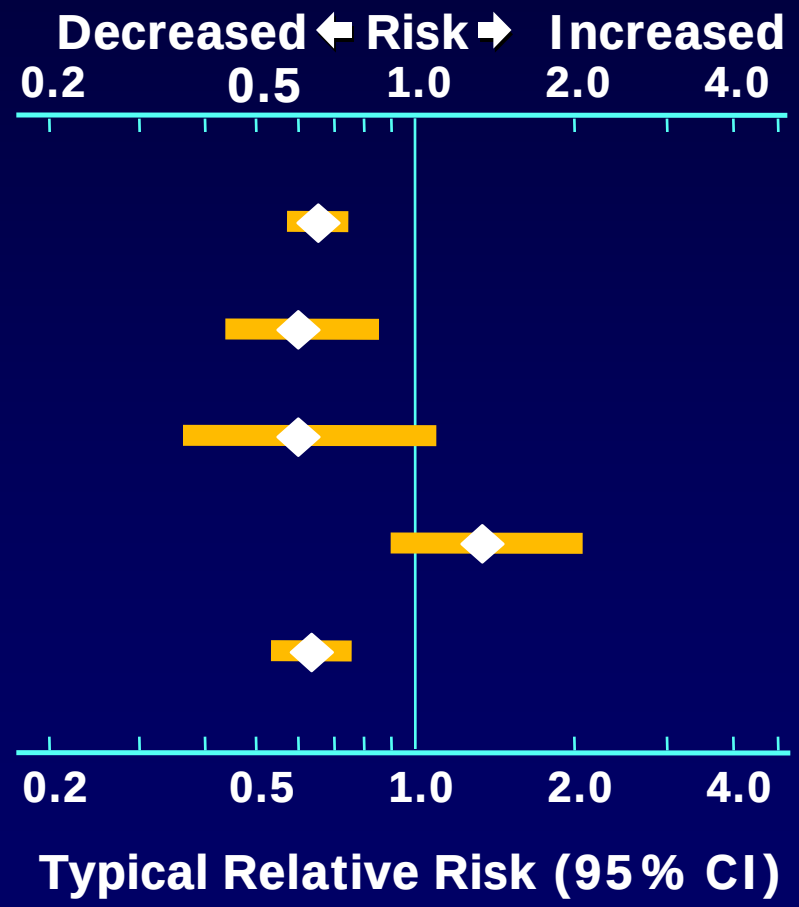
What can we do prior to delivery to prevent BPD?

- Prevention of Preterm Birth
- Antenatal Corticosteroids

PROPHYLACTIC CORTICOSTEROIDS PRIOR TO PRETERM BIRTH

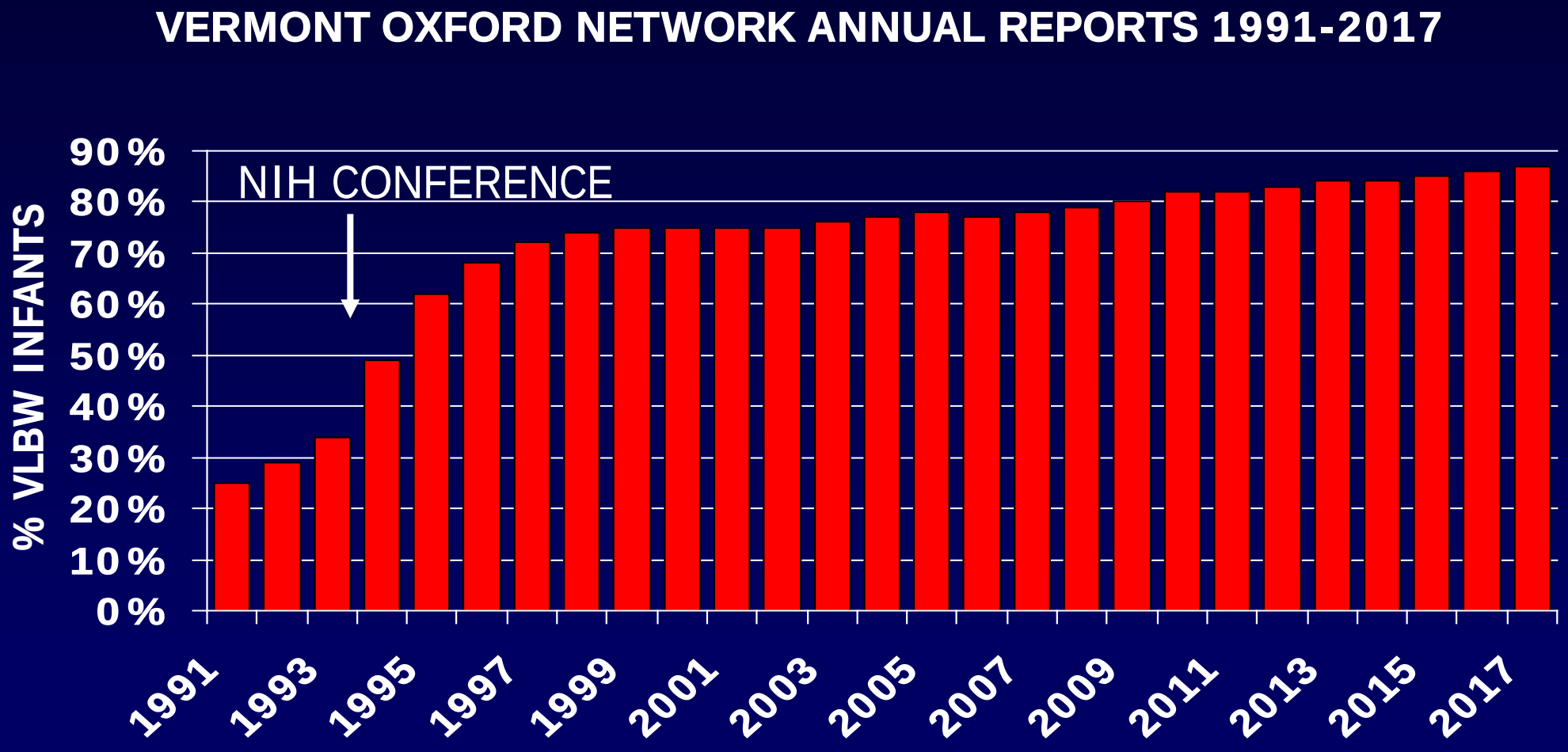
OVERVIEW OF 18 RANDOMIZED CONTROLLED TRIALS

Outcome (# of trials)	Typical Relative Risk (95% CI)
RDS (14)	0.64 (0.56, 0.72)
Periventricular hemorrhage (4)	0.57 (0.41, 0.78)
Necrotizing enterocolitis (4)	0.60 (0.33, 1.09)
Bronchopulmonary dysplasia (3)	1.38 (0.90, 2.11)
Neonatal death (13)	0.63 (0.51, 0.77)



Crowley (1992)

Antenatal Corticosteroids



Bronchopulmonary Dysplasia: Evidence for Best Practice

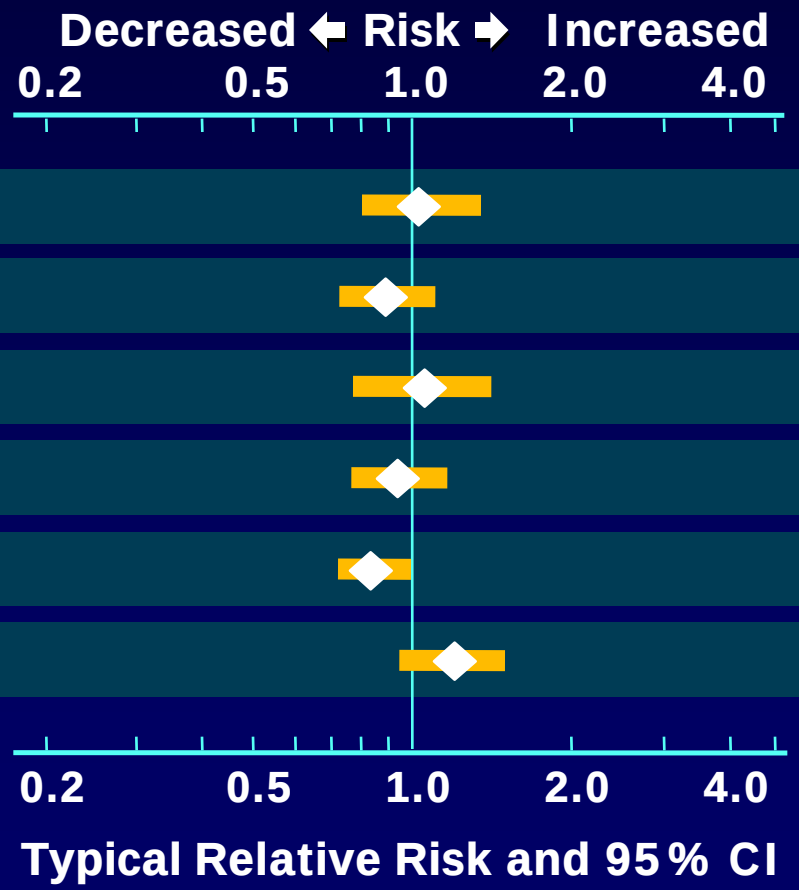
Can we prevent bronchopulmonary dysplasia with newer techniques of respiratory support?

With newer forms of conventional mechanical ventilation?
With High Frequency Oscillation (HFOV)?
With less invasive forms of respiratory support like nasal CPAP?

PATIENT TRIGGERED VENTILATION

OVERVIEW OF 9 RANDOMIZED CONTROLLED TRIALS

Outcome (number of studies)	Typical Risk Difference (95% CI)
AIRLEAK (6)	0.00 (-0.03, 0.03)
PATENT DUCTUS ARTERIOSUS (5)	-0.04 (-0.09, 0.02)
SEVERE IVH (5)	0.00 (-0.02, 0.03)
O2 at 28 DAYS (4)	-0.03 (-0.09, 0.03)
O2 at 36 WEEKS PCA (3)	-0.04 (-0.09, 0.00)
MORTALITY (4)	0.02 (-0.01, 0.06)

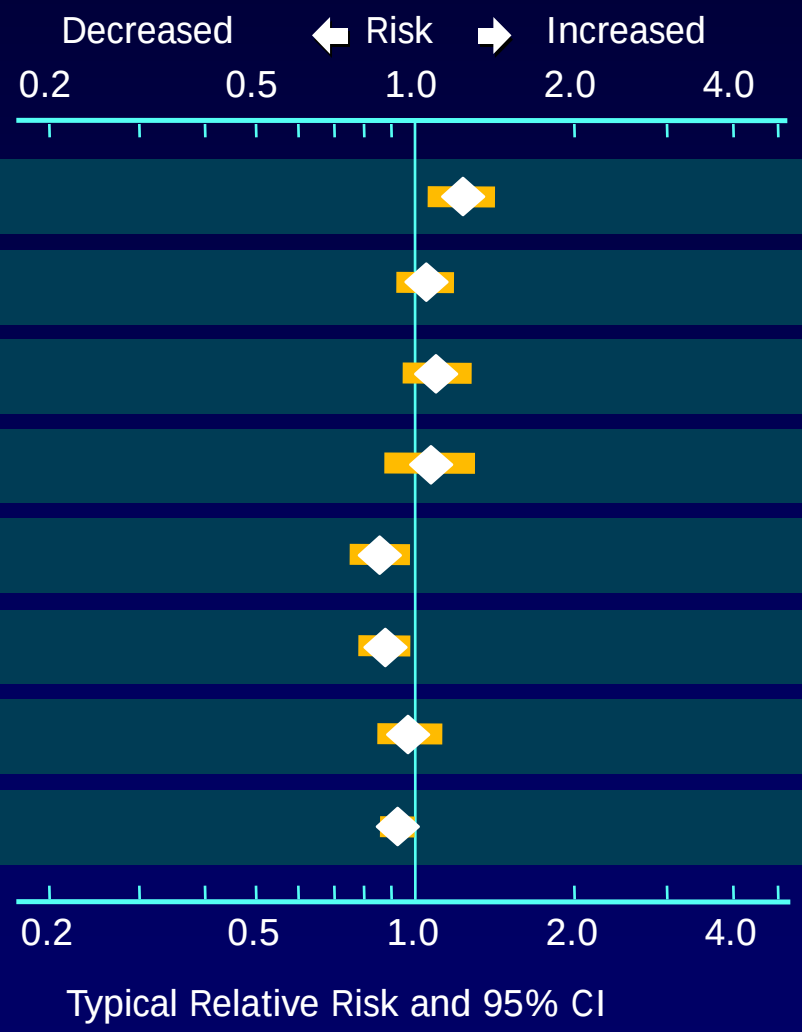


Modified from Greenough 2000

Elective High Frequency Oscillatory Ventilation

META-ANALYSIS OF 19 RANDOMIZED CONTROLLED TRIALS

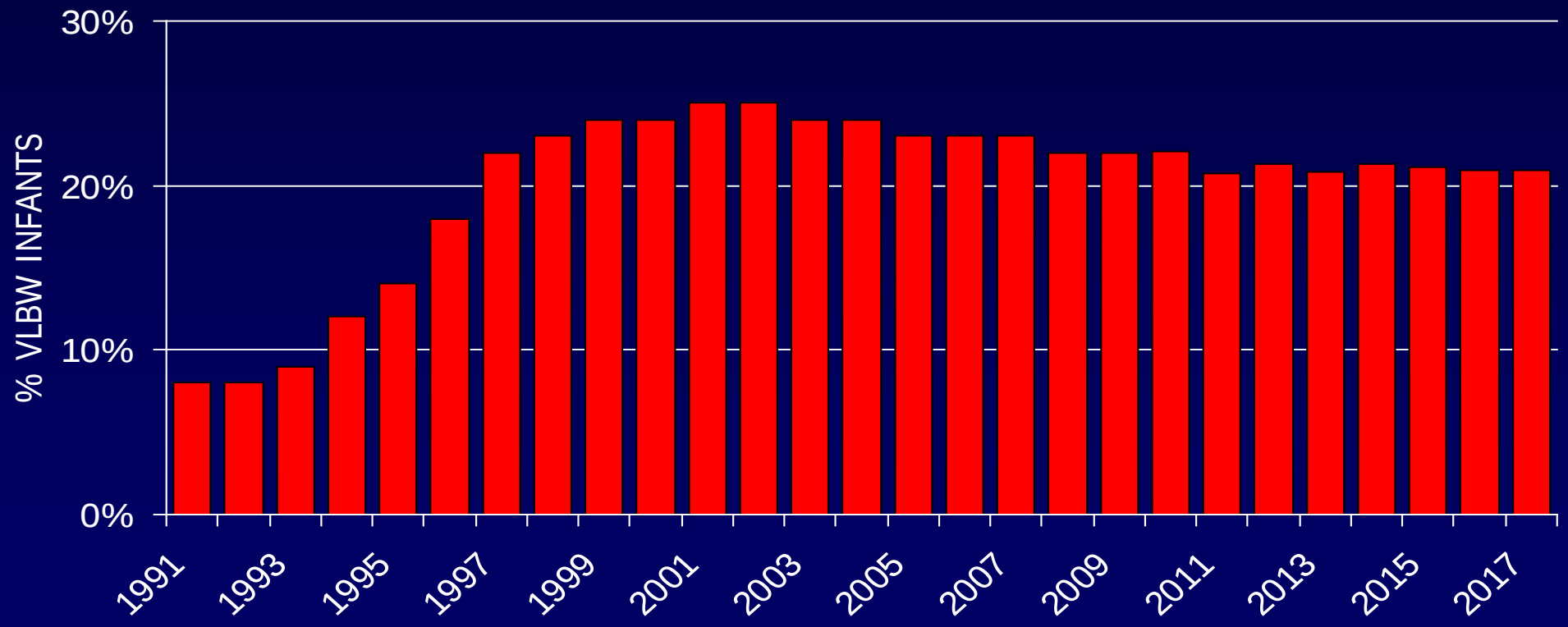
OUTCOME (STUDIES)	Typical Risk Difference (95% CI)
PULMONARY AIRLEAK (13)	0.04 (0.01, 0.07)
IVH (12)	0.02 (-0.02, 0.05)
SEVERE IVH (18)	0.01 (-0.01, 0.04)
PVL (17)	0.00 (-0.01, 0.02)
SEVERE RETINOPATHY (12)	-0.04 (-0.07, -0.01)
CHRONIC LUNG DISEASE (17)	-0.05 (-0.08, -0.02)
DEATH (17)	-0.01 (-0.03, 0.02)
CLD/DEATH @ 36 WKS PMA (17)	-0.05 (-0.08, -0.01)



Cools 2015

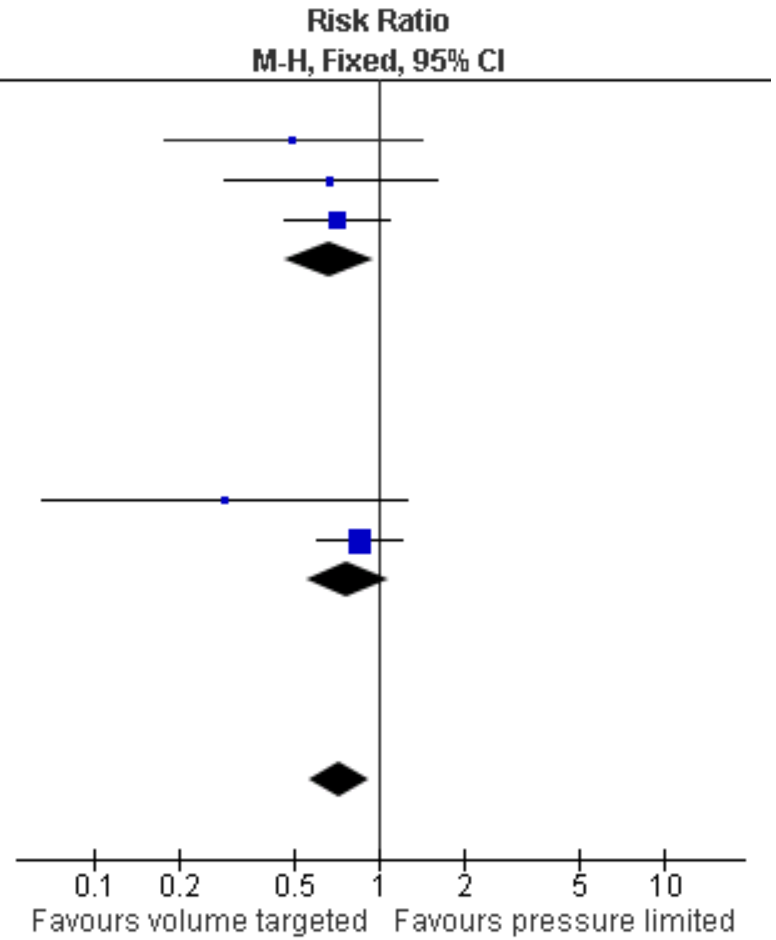
High Frequency Ventilation

VERMONT OXFORD NETWORK ANNUAL REPORTS 1991-2017



Volume Targeted Ventilation vs. Pressure Limited Ventilation Effect on BPD or Death

Study or Subgroup	Volume targeted Events	Total	Pressure limited Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
1.3.1 Strict Studies							
Keszler 2004a	3	9	6	9	6.3%	0.50 [0.18, 1.40]	2004
Lista 2004	7	30	8	23	9.5%	0.67 [0.28, 1.58]	2004
Singh 2006	21	57	27	52	29.7%	0.71 [0.46, 1.09]	2006
Subtotal (95% CI)		**96**		**84**	**45.5%**	**0.67 [0.47, 0.96]**	
Total events	31		41				
Heterogeneity: Chi² = 0.38, df = 2 (P = 0.83); I² = 0%							
Test for overall effect: Z = 2.16 (P = 0.03)							
1.3.2 Hybrid Studies							
Sinha 1997	2	25	7	25	7.4%	0.29 [0.07, 1.24]	1997
D'Angio 2005	38	104	45	105	47.1%	0.85 [0.61, 1.19]	2005
Subtotal (95% CI)		**129**		**130**	**54.5%**	**0.78 [0.56, 1.08]**	
Total events	40		52				
Heterogeneity: Chi² = 2.08, df = 1 (P = 0.15); I² = 52%							
Test for overall effect: Z = 1.52 (P = 0.13)							
Total (95% CI)		**225**		**214**	**100.0%**	**0.73 [0.57, 0.93]**	
Total events	71		93				
Heterogeneity: Chi² = 2.96, df = 4 (P = 0.57); I² = 0%							
Test for overall effect: Z = 2.56 (P = 0.01)							
Test for subgroup differences: Not applicable							



Typical relative risk 0.73, 95% CI 0.57 to 0.93

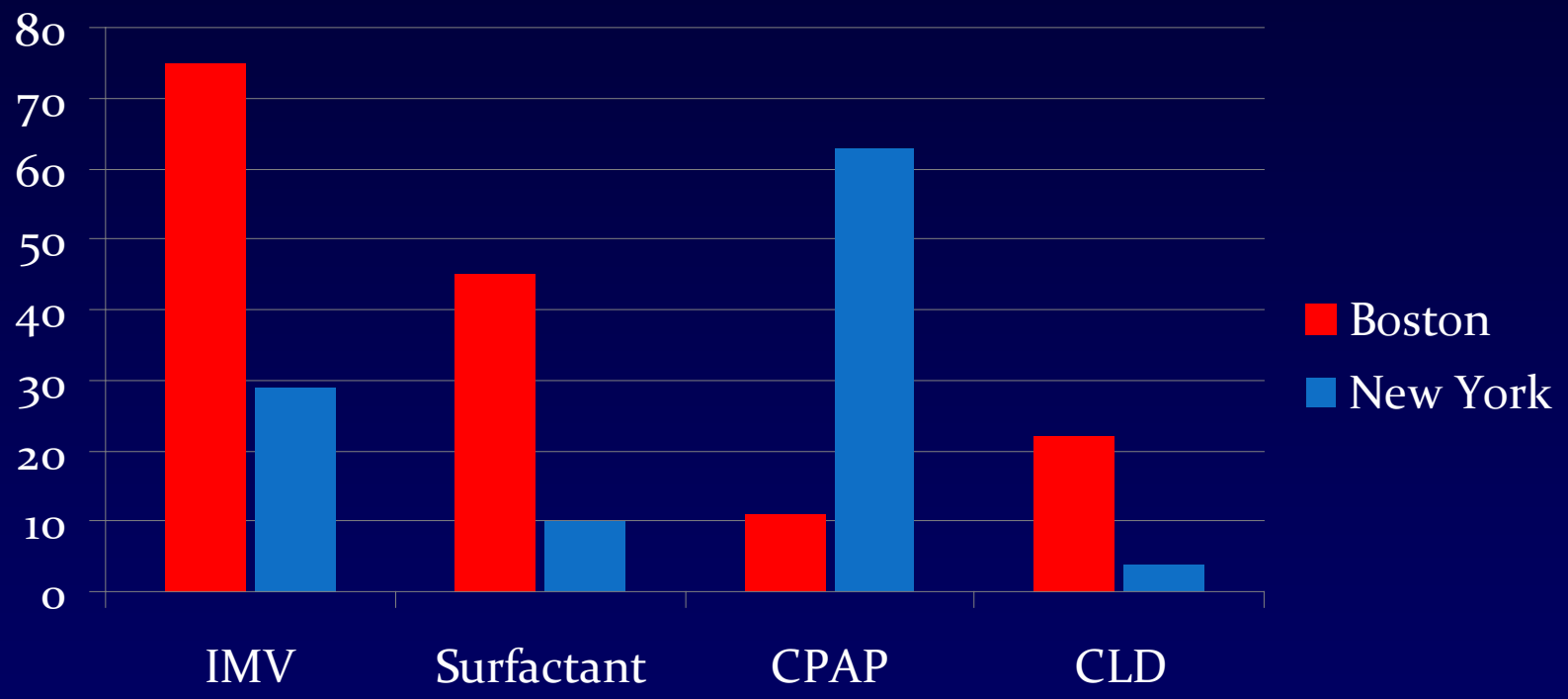
Wheeler 2010

What about CPAP?

% survivors at 28 days

% survivors in O2 at 28 days

Do Clinical Markers of Barotrauma and Oxygen Toxicity Explain Interhospital Variation in Rates of CLD?

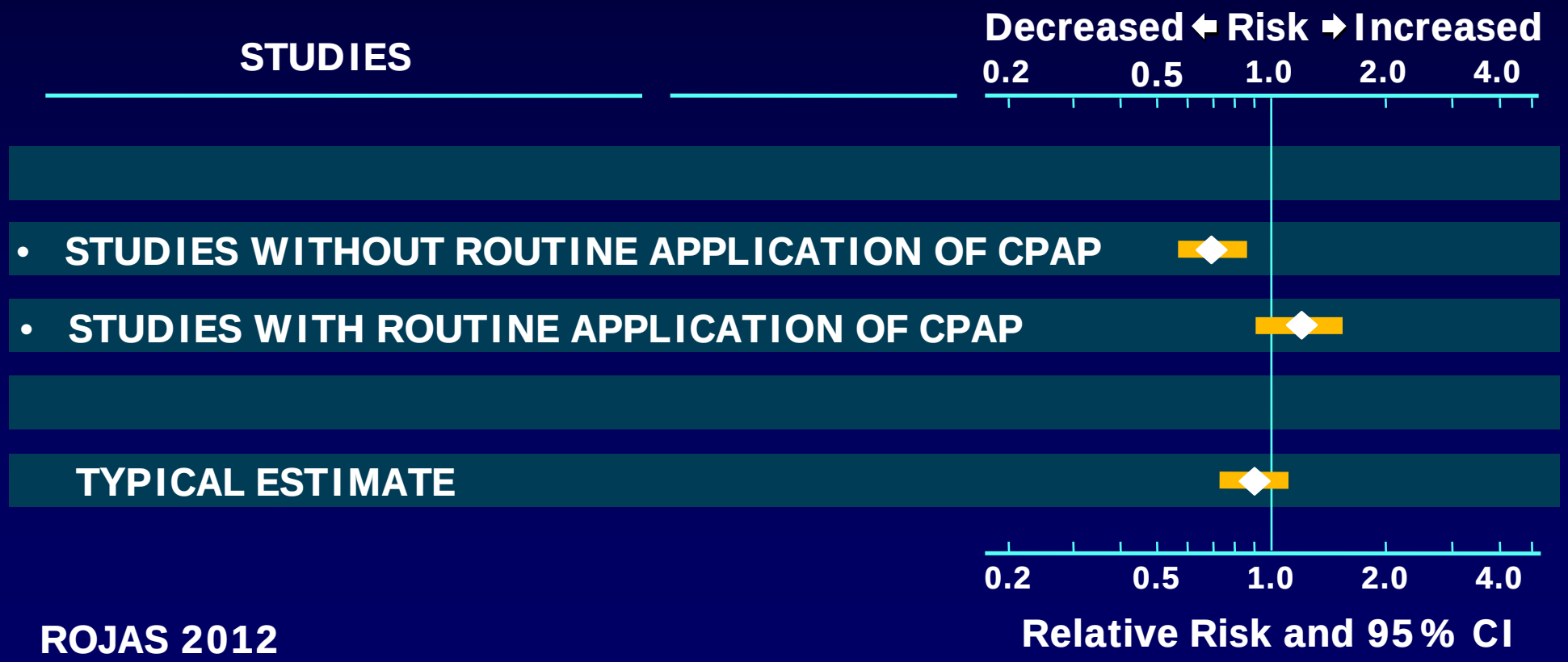


Conclusion: NICU-specific risk of CLD was predominantly associated with the decision to use mechanical ventilation

Van Marter. Pediatrics 2000

Prophylactic Surfactant Administration vs. Selective Treatment of RDS

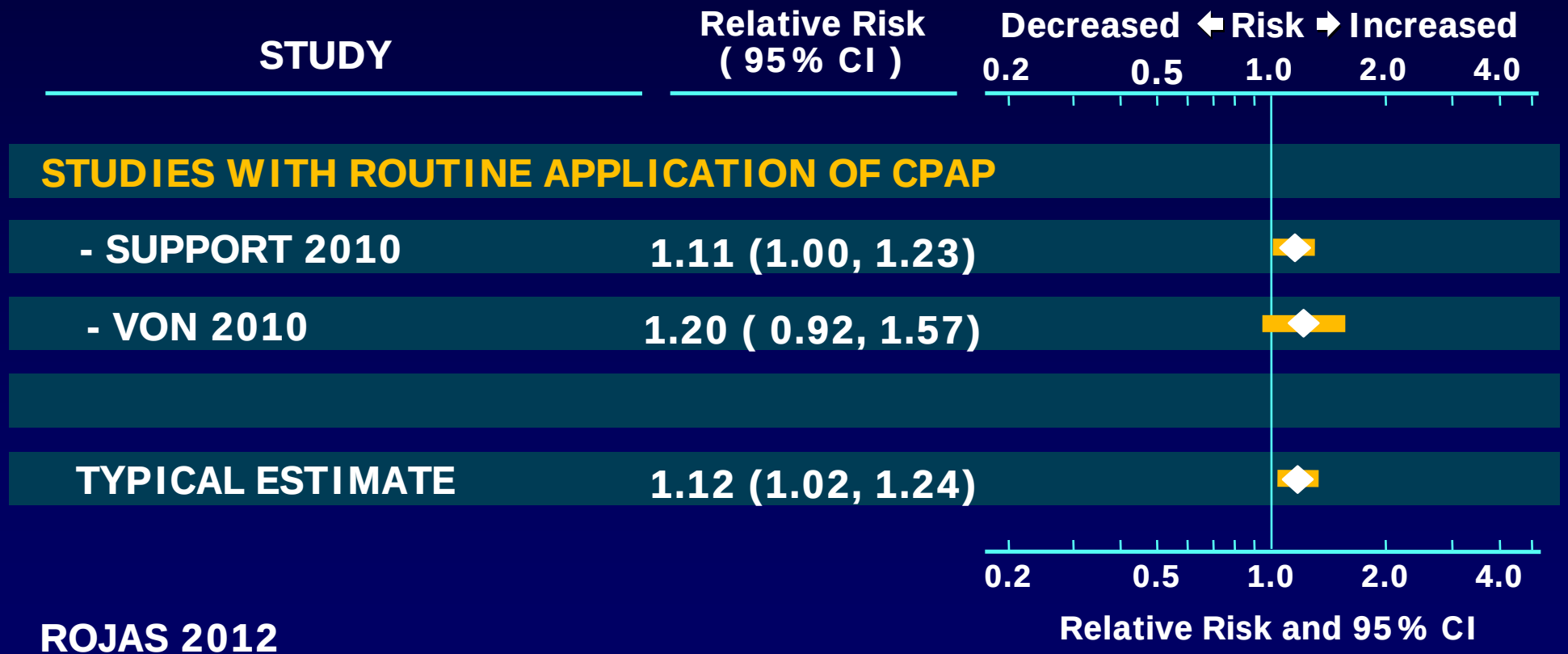
Neonatal Mortality



ROJAS 2012

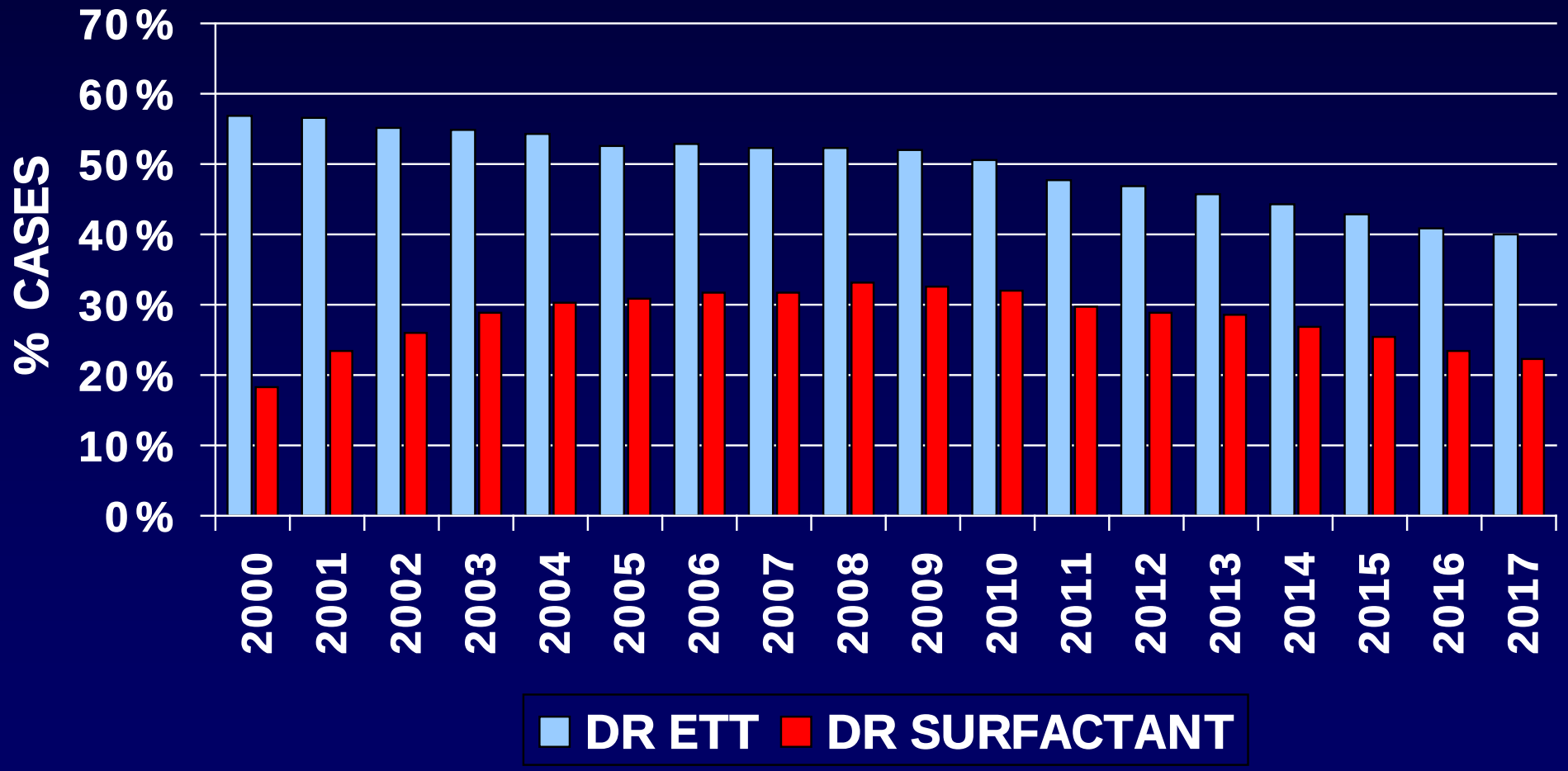
Prophylactic Surfactant Administration vs. Selective Treatment of RDS

Death or BPD at 36 weeks' postmenstrual age

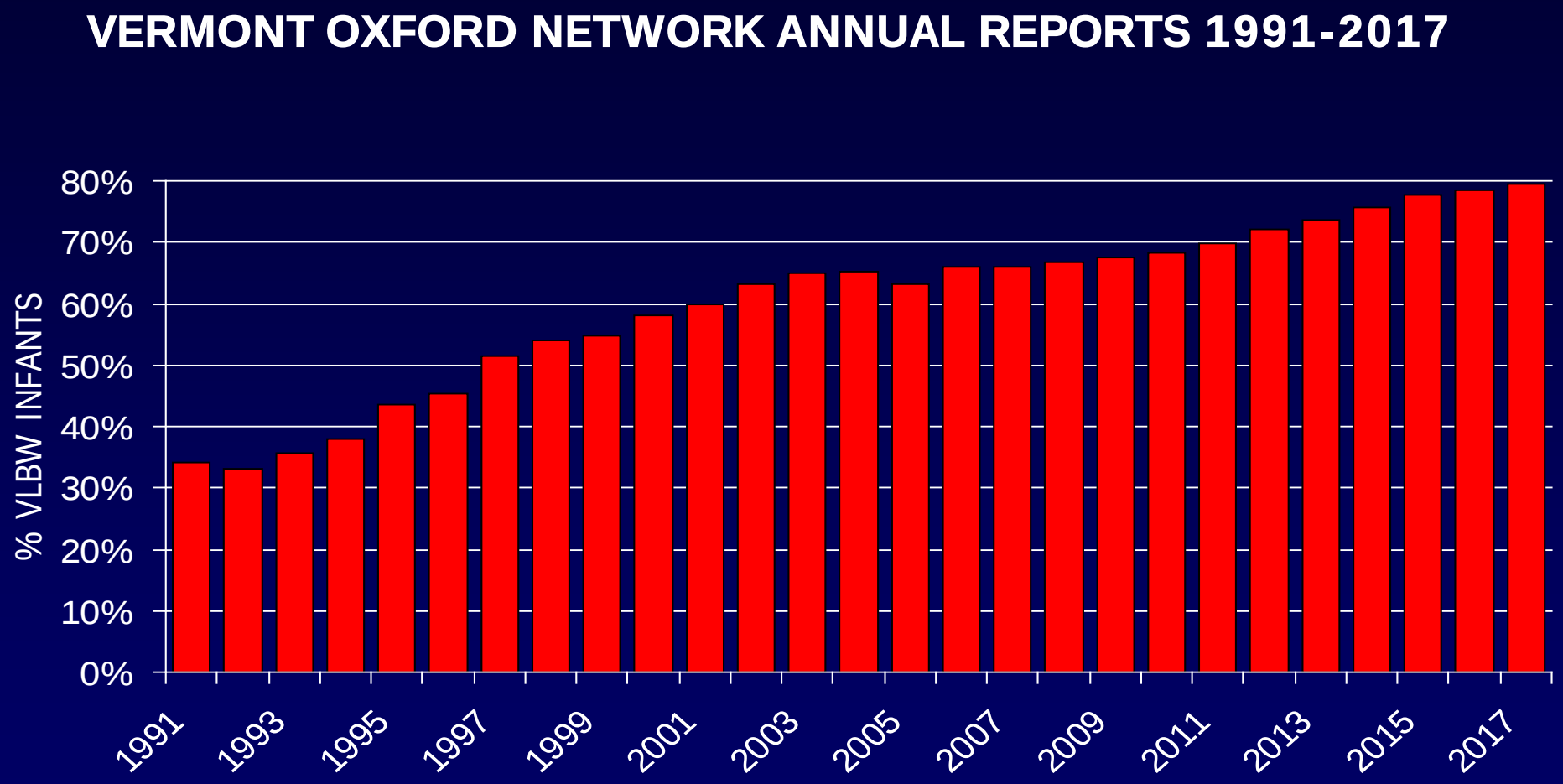


ROJAS 2012

DELIVERY ROOM PRACTICES IN VLBW INFANTS



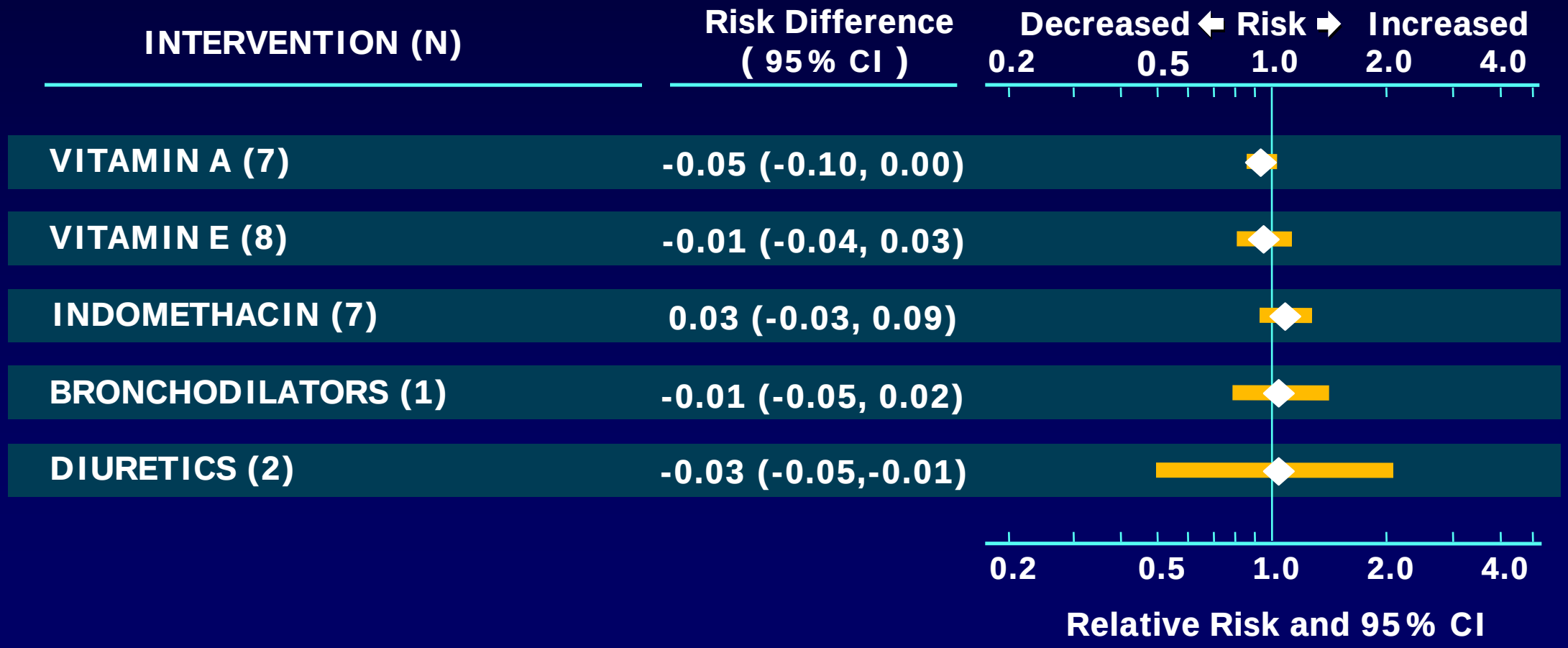
Any Nasal Continuous Positive Airway Pressure



Can we prevent or treat bronchopulmonary dysplasia with specific pharmacologic interventions?

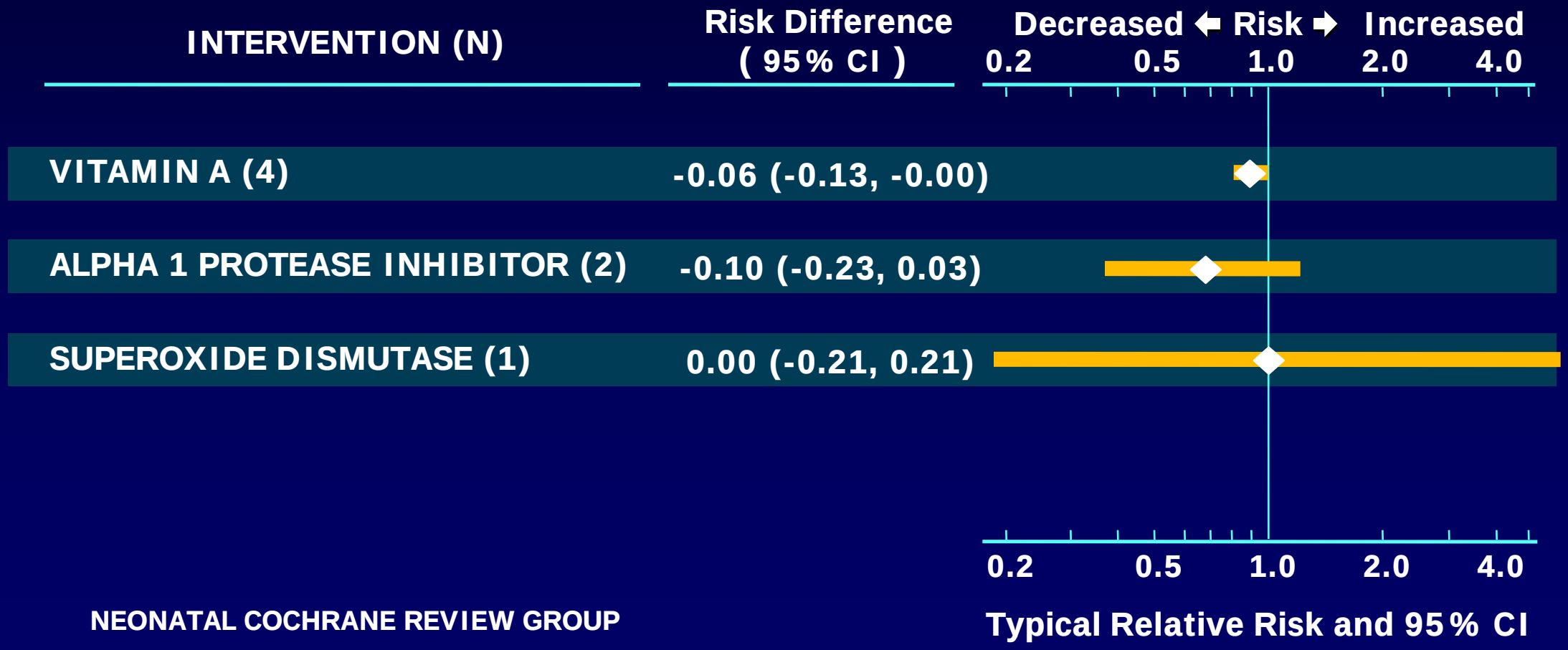
PHARMACOLOGIC INTERVENTIONS AND BRONCHOPULMONARY DYSPLASIA: EVIDENCE FROM RANDOMIZED CONTROLLED TRIALS

EFFECT ON BRONCHOPULMONARY DYSPLASIA (STATUS AT 28 DAYS)



PHARMACOLOGIC INTERVENTIONS AND CHRONIC LUNG DISEASE: EVIDENCE FROM RANDOMIZED CONTROLLED TRIALS

EFFECT ON CHRONIC LUNG DISEASE AT 36 WEEKS POSTMENSTRUAL AGE



NEONATAL COCHRANE REVIEW GROUP

The NEW ENGLAND JOURNAL of MEDICINE

Caffeine Therapy for Apnea of Prematurity

Barbara Schmidt, M.D., Robin S. Roberts, M.Sc., Peter Davis, M.D.,
Lex W. Doyle, M.D., Keith J. Barrington, M.D., Arne Ohlsson, M.D.,
Alfonso Solimano, M.D., and Win Tin, M.D. for the Caffeine for Apnea of Prematurity Trial Group

N Engl J Med 2006; 354:2112-2121May 18, 2006DOI: 10.1056/NEJMoa054065

Caffeine

The CAP Trial: Schmidt and coworkers

Outcome	Caffeine	Control	Adjusted OR (95% CI)
Initial Report			
BPD	36.3%	46.9%	0.64 (0.52 to 0.78)
Death	5.2%	5.5%	0.96 (0.64 to 1.44)
2 Year Report			
CP	4.4%	7.3%	0.59 (0.39 to 0.89)
Death or Disability	40.2%	46.2%	0.79 (0.65 to 0.92)
5 Year Report			
Death or Disability	21.1%	24.8%	0.86 (0.67 to 1.09)

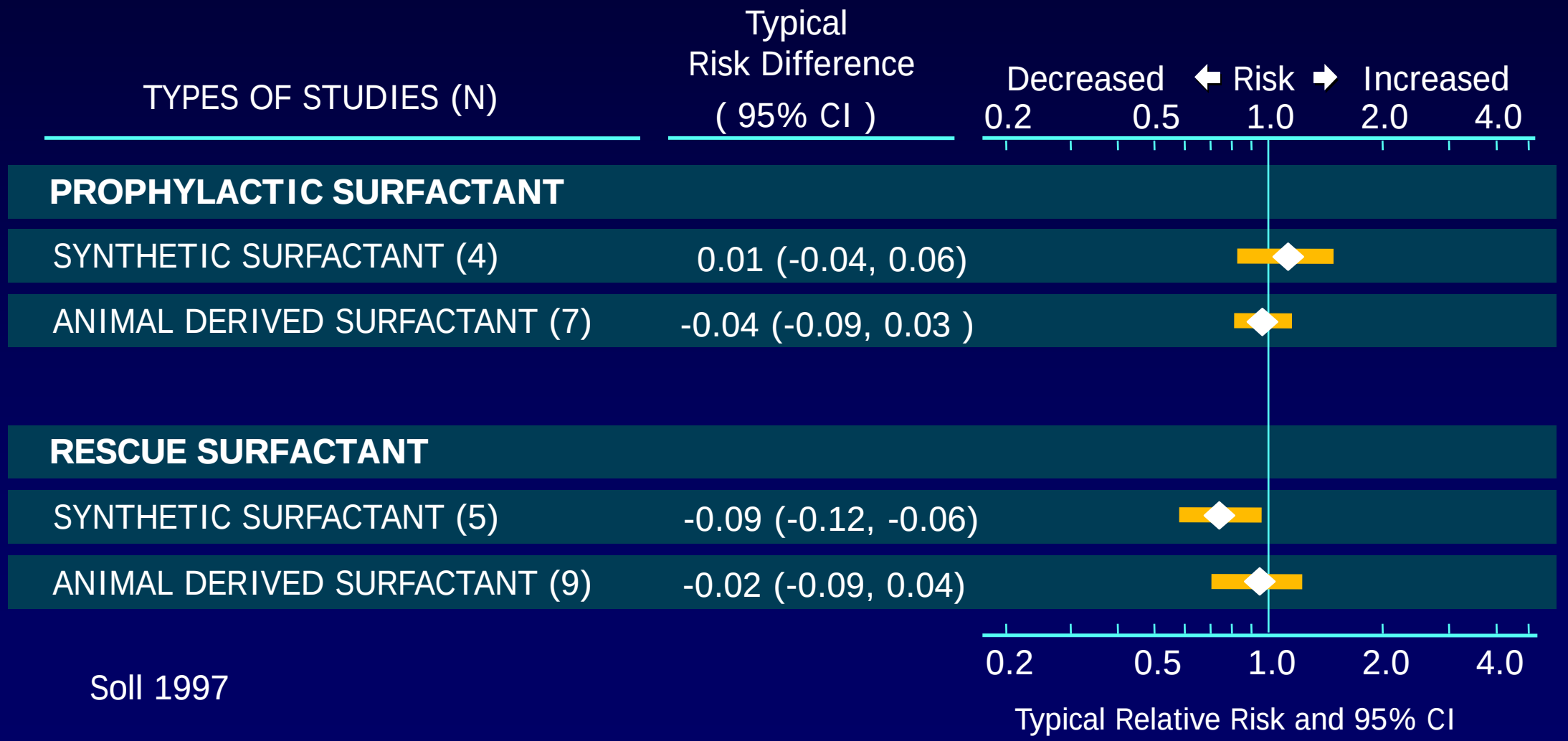
Caffeine: Who should I treat?

Effect on Bronchopulmonary Dysplasia

Indication	Caffeine	Control	Odds ratio (95% CI)
Apnea treatment	107/413	141/392	0.62 [0.46, 0.84]
Apnea prophylaxis	84/226	94/211	0.74 [0.50, 1.08]
Pre-extubation	158/322	212/350	0.63 [0.46, 0.85]
Overall			0.65 [0.54, 0.78]

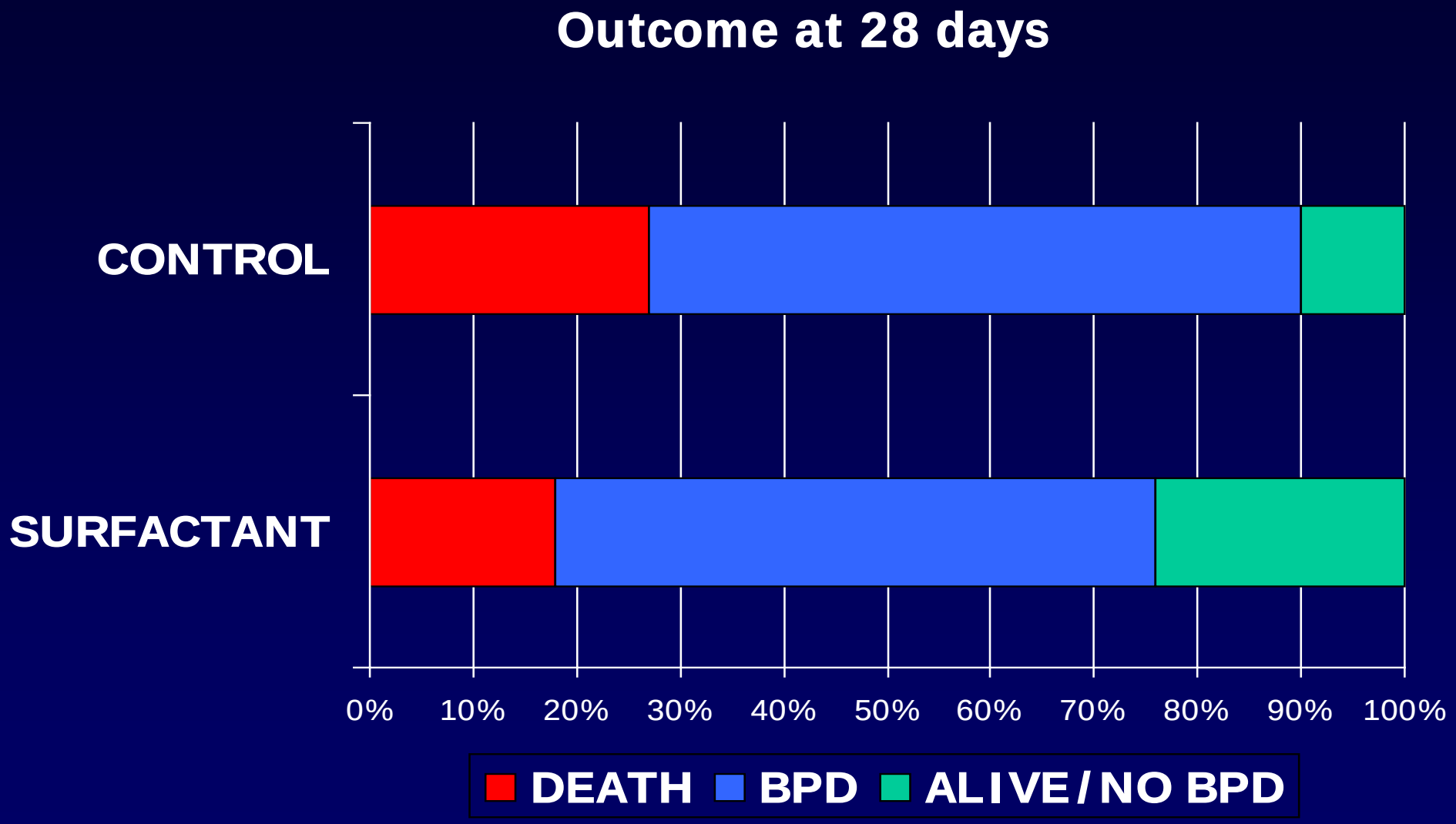
SURFACTANT THERAPY:
EVIDENCE FROM RANDOMIZED CONTROLLED TRIALS

EFFECT ON BRONCHOPULMONARY DYSPLASIA



Soll 1997

Surfactant therapy and bronchopulmonary dysplasia

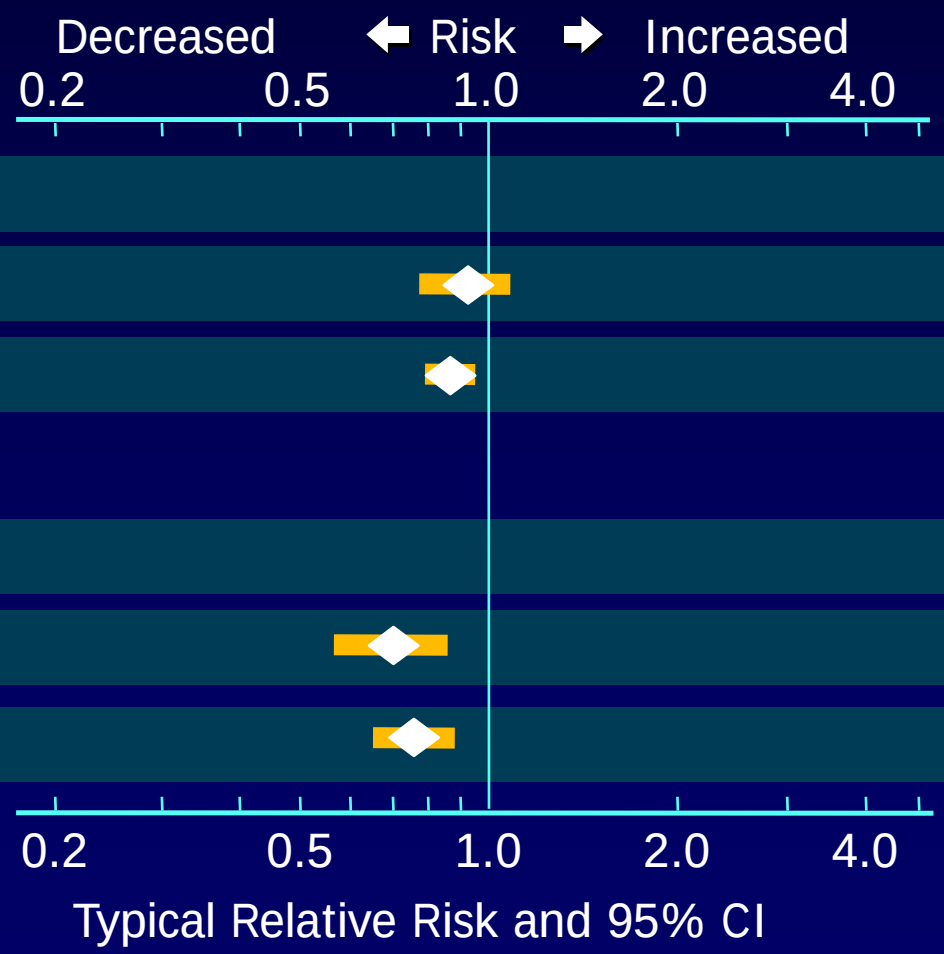


Liechty EA. Pediatrics 1991

SURFACTANT THERAPY:
EVIDENCE FROM RANDOMIZED CONTROLLED TRIALS

EFFECT ON BRONCHOPULMONARY DYSPLASIA OR DEATH

TYPES OF STUDIES (N)	Typical Risk Difference (95% CI)
PROPHYLACTIC SURFACTANT	
SYNTHETIC SURFACTANT (4)	-0.04 (-0.10, 0.01)
ANIMAL DERIVED SURFACTANT (7)	-0.10 (-0.16, -0.04)
RESCUE SURFACTANT	
SYNTHETIC SURFACTANT (4)	-0.08 (-0.11, -0.05)
ANIMAL DERIVED SURFACTANT (10)	-0.14 (-0.21, -0.07)



From the Cochrane Library

Neonatology

Novel Surfactant Application Techniques: Will they change outcome?

Whittney D. Barkhuff, MD, Roger F. Soll, MD

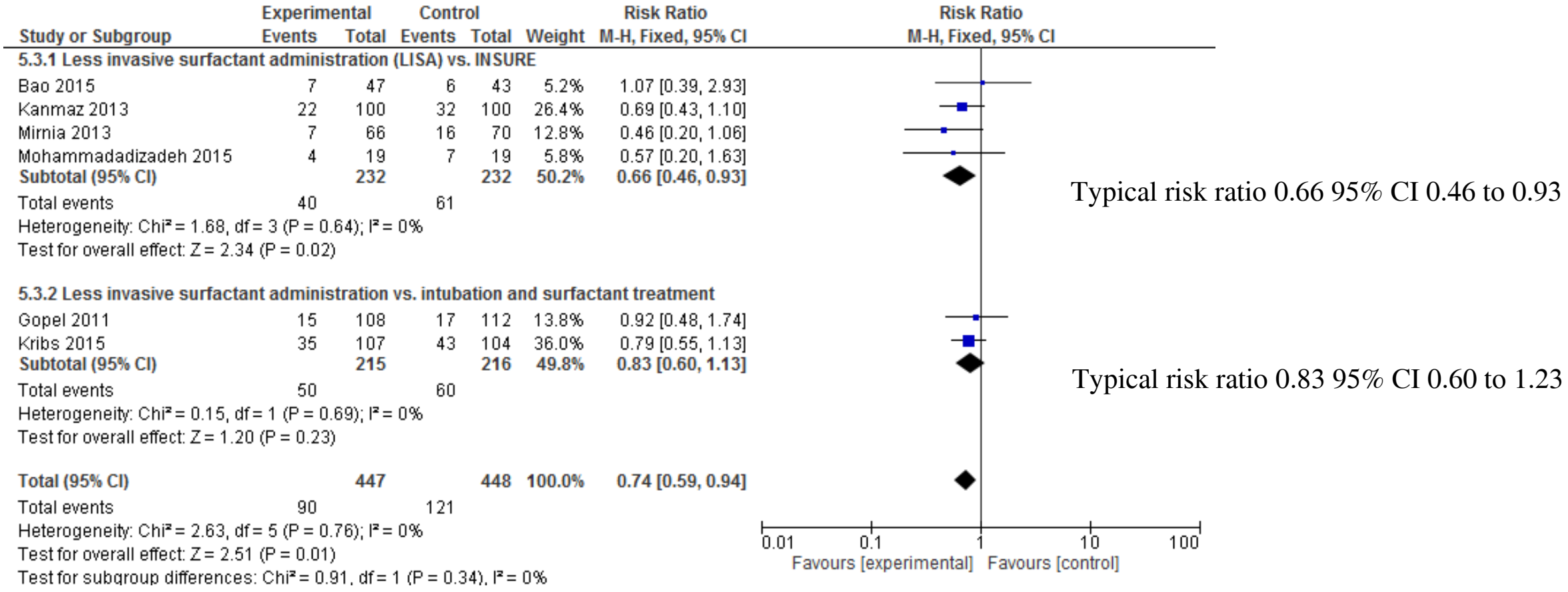
Thin Catheter Administration

InSurE

Selective Surfactant Administration

Thin Catheter Administration

Less Invasive Surfactant Administration
Effect on Bronchopulmonary Dysplasia or Death



Typical risk ratio 0.66 95% CI 0.46 to 0.93

Typical risk ratio 0.83 95% CI 0.60 to 1.23

Typical risk ratio 0.74 95% CI 0.59 to 0.94; Typical risk difference -0.07 95% CI -0.12 to -0.02

Postnatal Steroid Therapy: Systematic Overview

Cochrane Neonatal

<u>Early Steroid Treatment:</u>

- before or at 7 Days
- studies 30
- enrolled infants 3750

<u>Late Steroid Treatment:</u>

- after 7 Days
- studies 21
- enrolled infants 1424

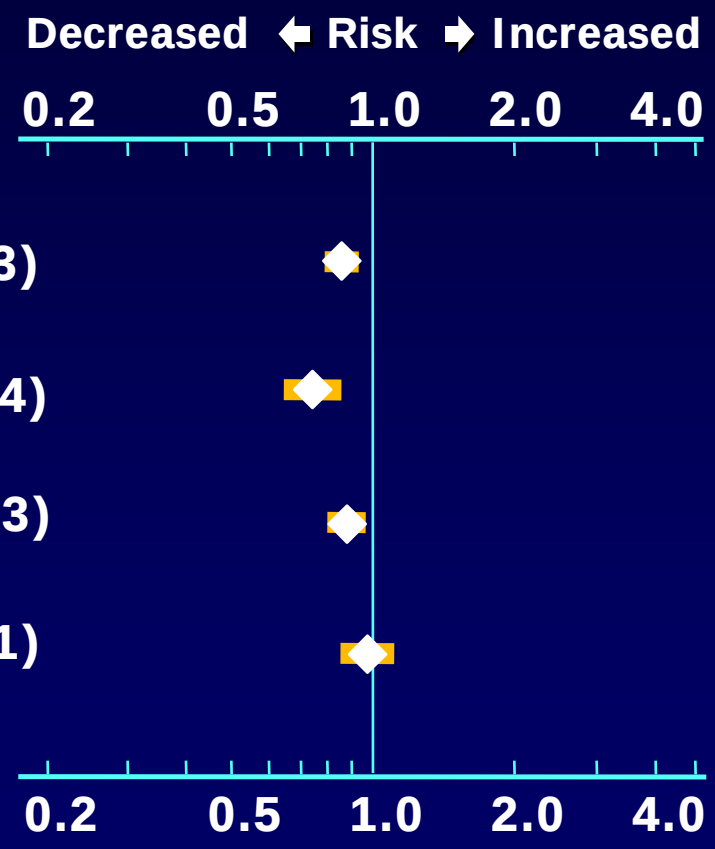
Doyle LW, Ehrenkranz RA, Halliday HL. Early (< 8 days) postnatal corticosteroids for preventing chronic lung disease in preterm infants. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD001146. DOI: 10.1002/14651858.CD001146.pub4.

Doyle LW, Cheong JL, Ehrenkranz RA, Halliday HL. Late (> 7 days) systemic postnatal corticosteroids for prevention of bronchopulmonary dysplasia in preterm infants. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD001145. DOI: 10.1002/14651858.CD001145.pub4

EARLY (≤ 7 DAYS) POSTNATAL STEROID THERAPY

META-ANALYSIS OF 30 RANDOMIZED CONTROLLED TRAILS

Outcome (N Studies)	Typical Risk Difference (95% CI)
CLD @ 28 DAYS (17)	-0.07 (-0.10,-0.03)
CLD @ 36 WEEKS (24)	-0.07 (-0.09, -0.04)
DEATH/CLD @ 36 WKS (25)	-0.06 (-0.09, -0.03)
MORTALITY (28)	-0.01 (-0.03, 0.01)

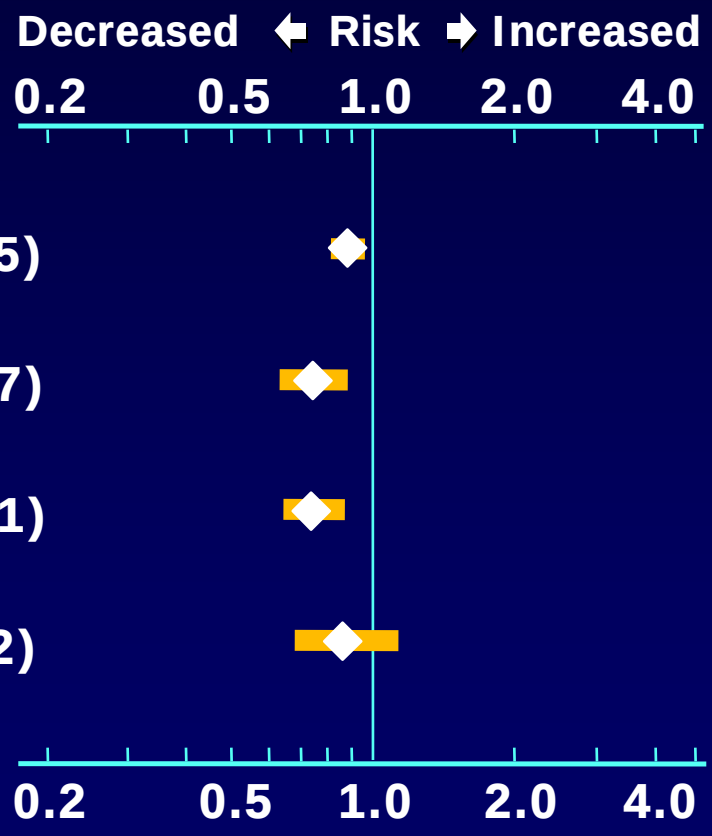


Doyle 2017

LATE (> 7 DAYS) POSTNATAL STEROID THERAPY

META-ANALYSIS OF 21 RANDOMIZED CONTROLLED TRAILS

Outcome (N Studies)	Typical Risk Difference (95% CI)
CLD @ 28 DAYS (6)	-0.11 (-0.17, -0.05)
CLD @ 36 WEEKS (11)	-0.15 (-0.22, -0.07)
DEATH/CLD @ 36 WKS (11)	-0.18 (-0.25, -0.11)
MORTALITY (19)	-0.03 (-0.07, 0.02)

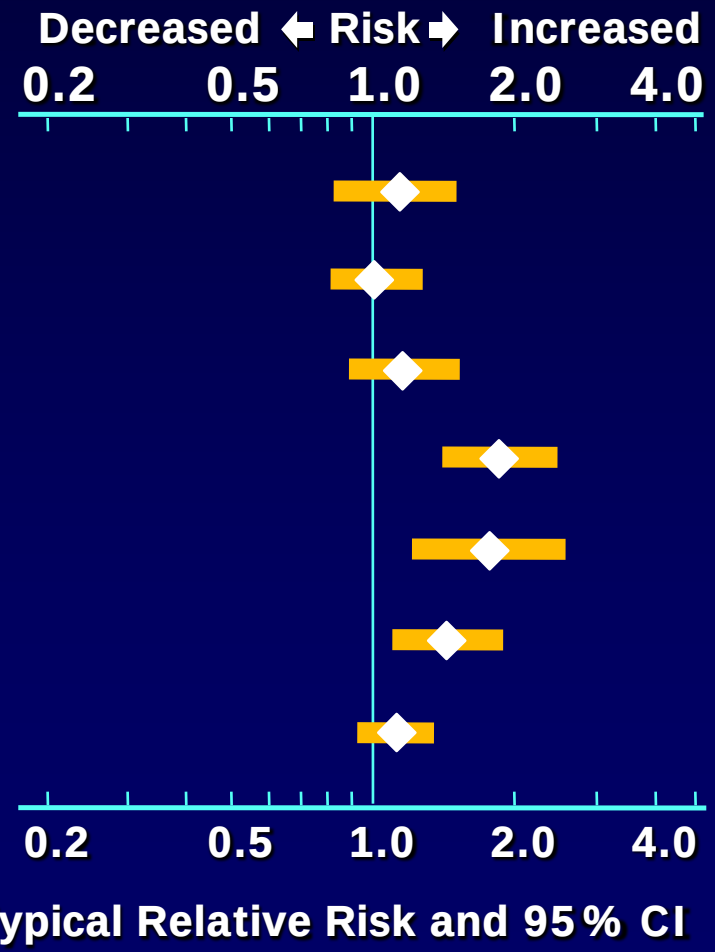


Doyle 2017

EARLY (≤ 7 DAYS) POSTNATAL STEROID THERAPY

NEURODEVELOPMENTAL OUTCOME IN SURVIVORS

OUTCOME (N Studies)	Typical Risk Difference (95% CI)
PVL (15)	0.00 (-0.01, 0.02)
BAYLEY MDI < 2SD (3)	0.01 (-0.06, 0.06)
BAYLEY PDI < 2SD (3)	0.02 (-0.02, 0.07)
ABNORMAL NEURO EXAM (5)	0.10 (0.05, 0.15)
DEVELOPMENTAL DELAY (1)	0.14 (0.03, 0.24)
CEREBRAL PALSY (13)	0.02 (-0.00, 0.05)
MOD/SEVERE IMPAIRMENT (7)	0.01 (-0.02, 0.05)

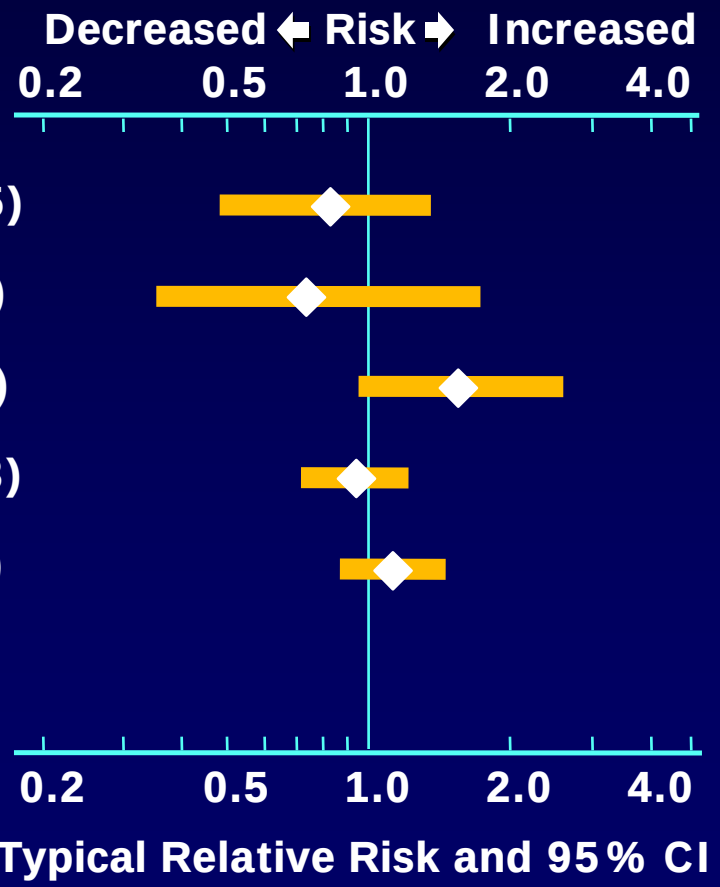


Doyle 2017

LATE (> 7 DAYS) POSTNATAL STEROID THERAPY

NEURODEVELOPMENTAL OUTCOME IN SURVIVORS

Outcome (N)	Typical Risk Difference (95% CI)
BAYLEY MDI < 2SD (7)	-0.03 (-0.10, 0.05)
BAYLEY PDI < 2SD (1)	-0.04 (-0.17, 0.09)
ABNORMAL NEURO EXAM (4)	0.15 (-0.00, 0.30)
CEREBRAL PALSY (15)	-0.02 (-0.08, 0.03)
MOD/SEVERE IMPAIRMENT (9)	0.03 (-0.03, 0.08)



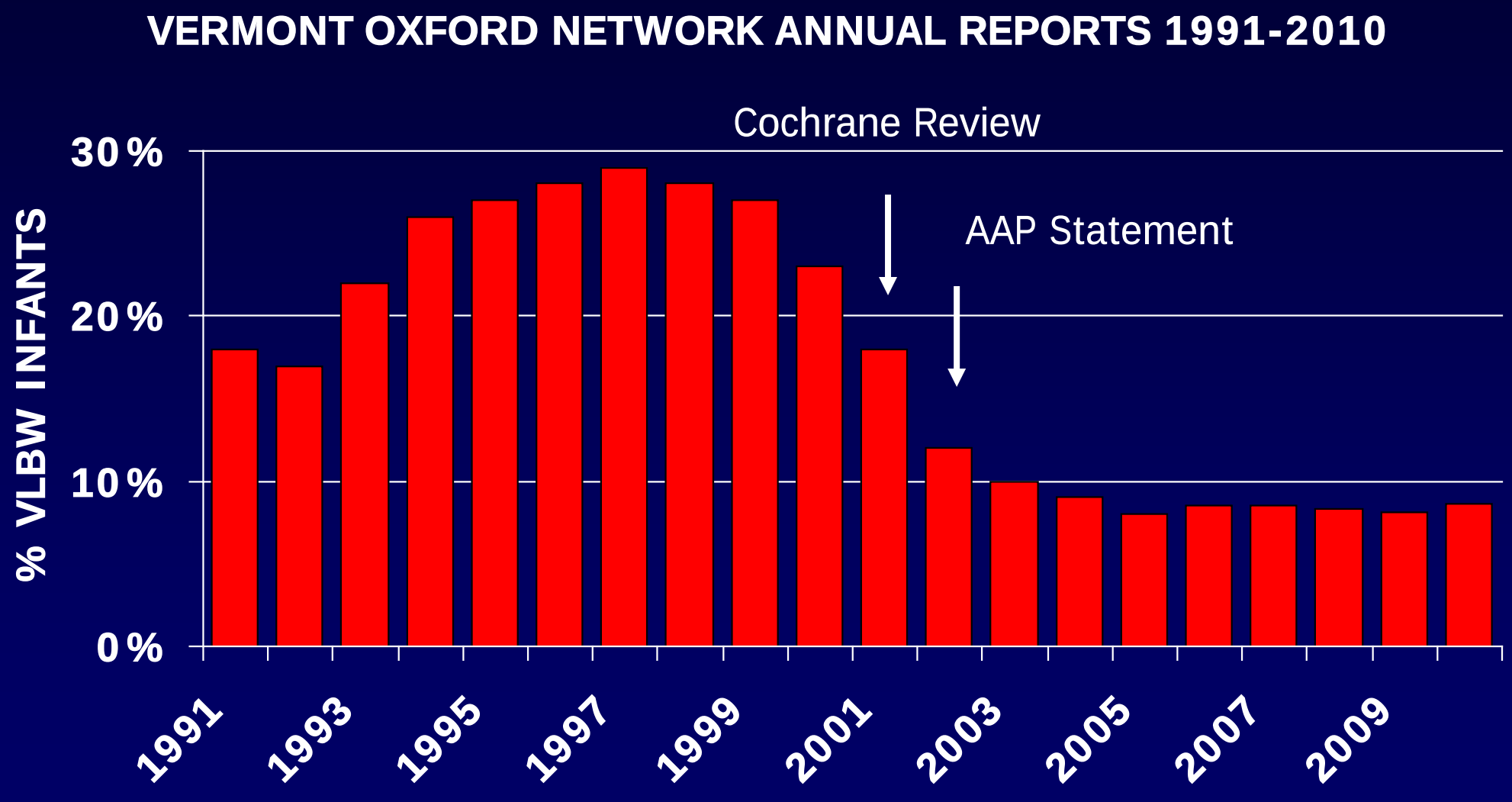
Doyle 2017

POSTNATAL CORTICOSTEROIDS TO TREAT OR PREVENT CHRONIC LUNG DISEASE IN PRETERM INFANTS

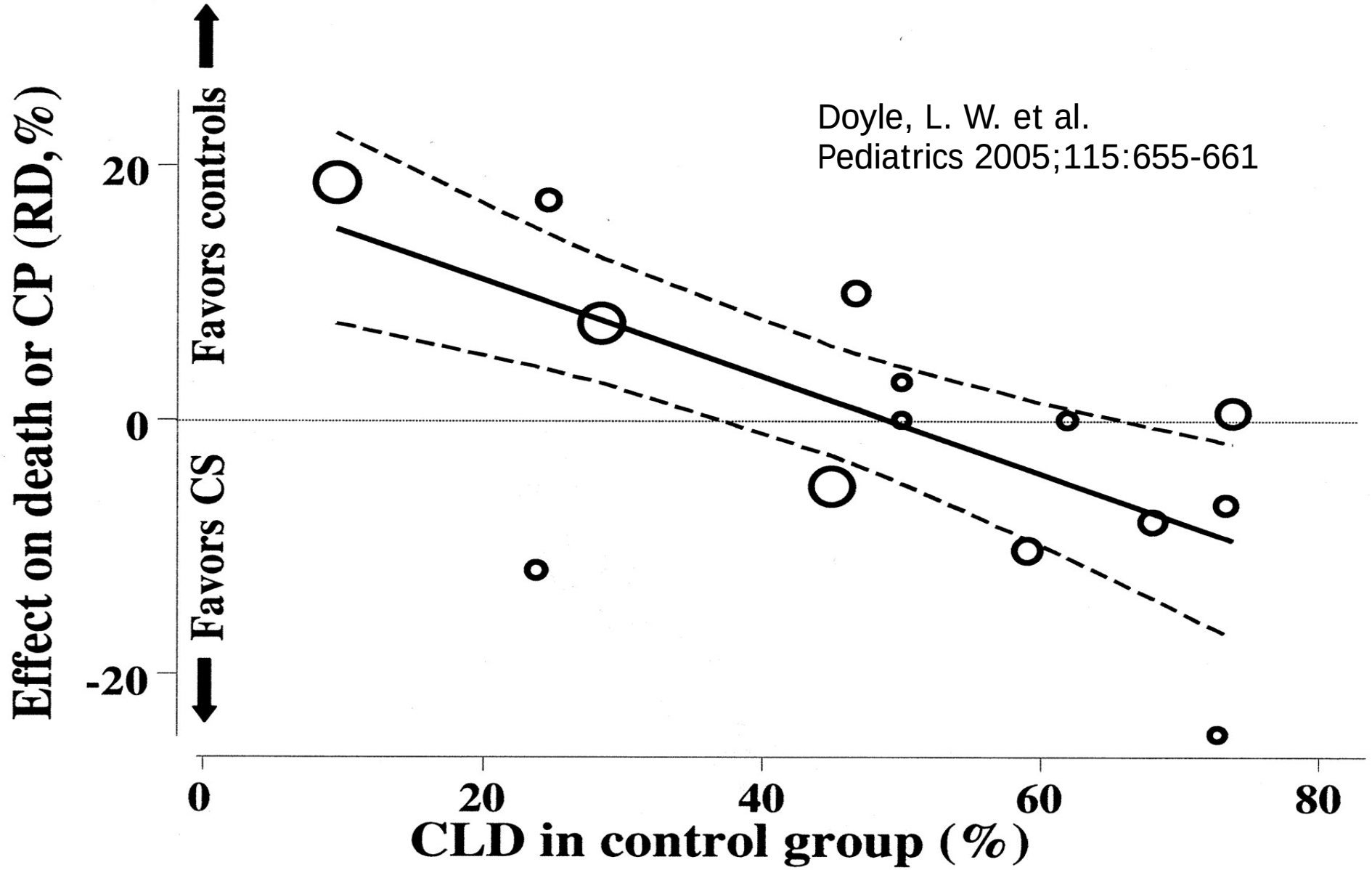
RECOMMENDATIONS FROM THE COMMITTEE ON THE FETUS AND NEWBORN 2002

On the basis of limited short-term benefits, the absence of long-term benefits, and the number of serious short-term and long-term complications, the routine use of systemic dexamethasone for the prevention or treatment of chronic lung disease in infants with very low birth weight is not recommended.

POSTNATAL CORTICOSTEROID USE IN VLBW INFANTS



Risk Difference (%) for Death or CP among all participants vs. rate of CLD (%) in the control group



Early Inhaled Corticosteroids For The Prevention Of Bronchopulmonary Dysplasia In Extremely Preterm Infants: The Neonatal European Study Of Inhaled Steroids (Neurosis)

Objective: To determine the effect of early use of inhaled budesonide in infants with gestational ages of 23 0/7 to 27 6/7 weeks requiring any form of positive pressure support on survival without BPD at 36 weeks' gestational age.

Methods: Randomized controlled trial. Budesonide or placebo were continued until infants were either off supplementary oxygen and positive pressure support or had reached a gestational age of 32 0/7 weeks regardless of their ventilator status. The primary outcome was death before 36 weeks of gestational age or survival with BPD, defined according to the physiological definition.

Bassler and colleagues. Arch Dis Child 2014;99:A1-A2

ADC

Early Inhaled Corticosteroids For The Prevention Of Bronchopulmonary Dysplasia In Extremely Preterm Infants: The Neonatal European Study Of Inhaled Steroids (Neurosis)

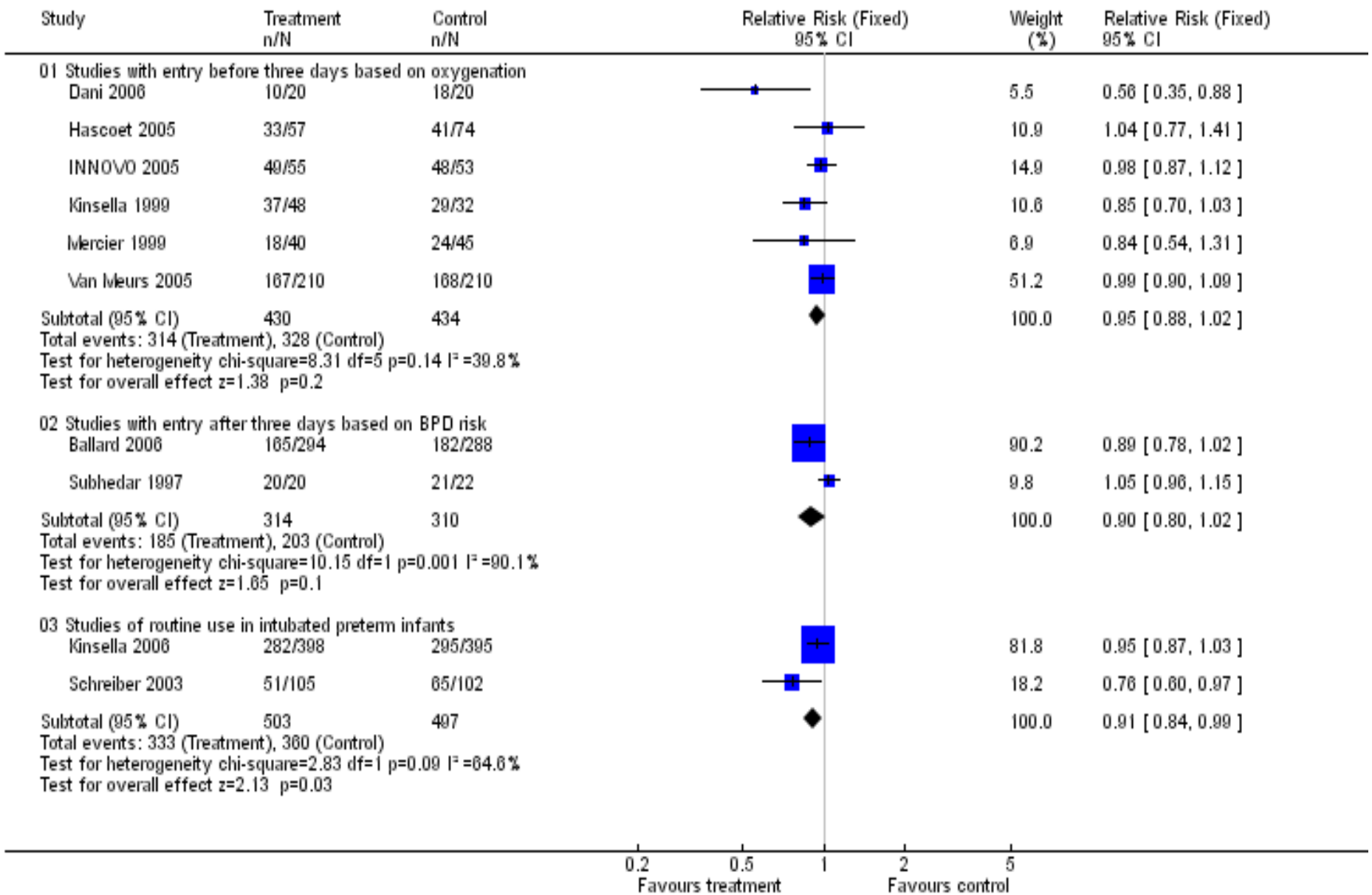
Primary Outcome	Placebo	Budesonide	Relative Risk (95% CI)	Relative Risk Adjusted for GA (95% CI)	P Value	Odds Ratio Adjusted for GA, birth weight, caffeine, mech. ventilation (95% CI)
Primary Outcome	194/419 (46.3)	175/437 (40.0)	0.86 (0.74-1.01)	0.86 (0.75-1.00)	0.053	0.71 (0.53-0.97)
Components of primary outcome						
Death at <36 wk of gestational age	57/419 (13.6)	74/437 (16.9)	1.24 (0.91-1.71)	1.24 (0.91-1.69)	0.165	
Survival with BPD	138/363 (38.0)	101/363 (27.8)	0.73 (0.59-0.90)	0.74 (0.60-0.91)	0.004	

D Bassler et al. Arch Dis Child 2014;99:A1-A2

ADC

NITRIC OXIDE FOR RESPIRATORY FAILURE IN PRETERM INFANTS

EFFECT ON DEATH OR BPD AT 36 WEEKS PMA



American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

CLINICAL REPORT

Use of Inhaled Nitric Oxide in Preterm Infants

The results of randomized controlled trials, traditional meta-analyses, and an individualized patient data meta-analysis study indicate that neither rescue nor routine use of iNO improves survival in preterm infants with respiratory failure (Evidence quality, A; Grade of recommendation, strong).

The preponderance of evidence does not support treating preterm infants who have respiratory failure with iNO for the purpose of preventing/ameliorating BPD, severe intraventricular hemorrhage, or other neonatal morbidities (Evidence quality, A; Grade of recommendation, strong).

Pediatrics 2014

Bronchopulmonary Dysplasia: Evidence for Best Practice

QUALITY IMPROVEMENT

VERMONT OXFORD NETWORK
NIC/Q PROJECT

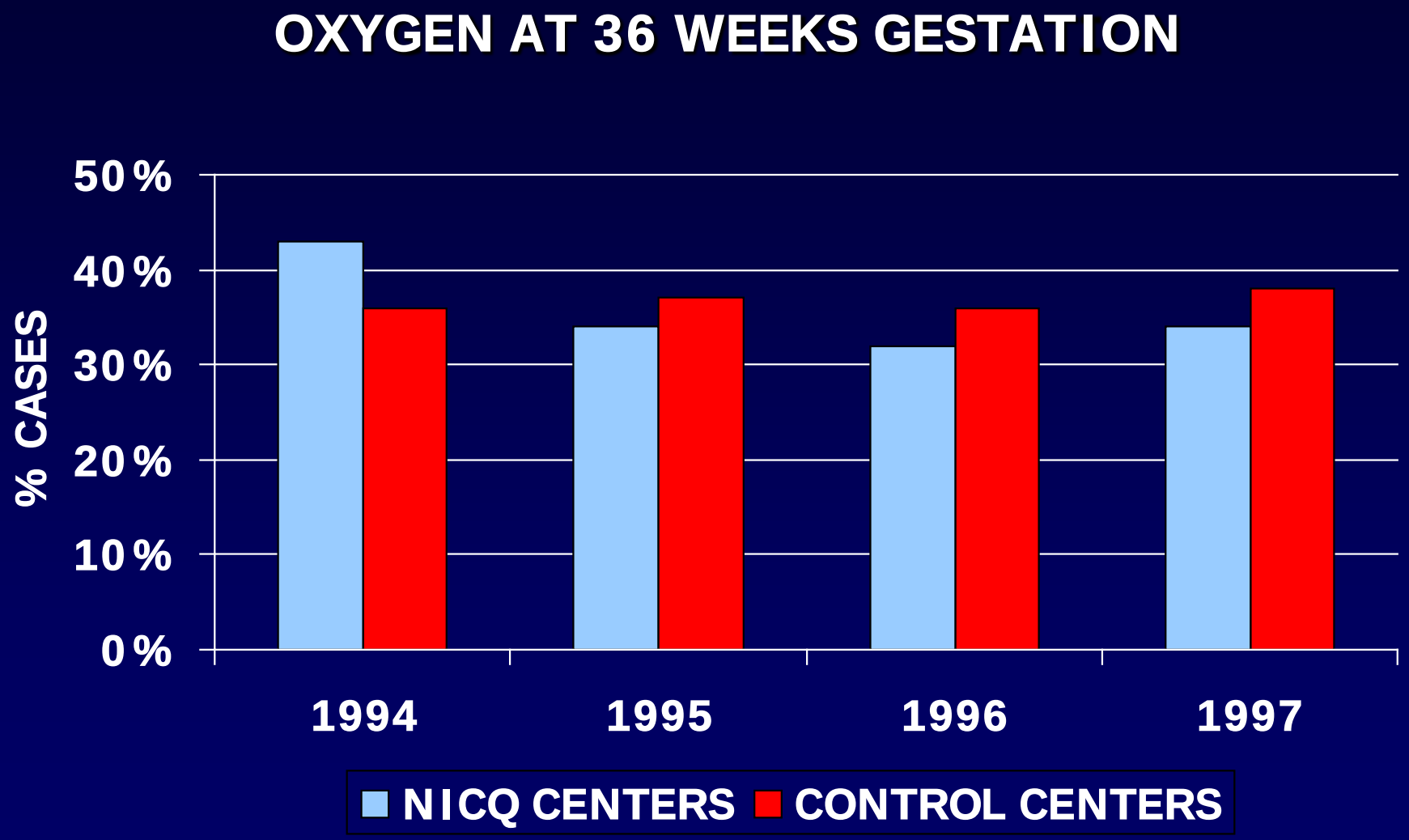
- Performance Feedback
- Quality Training
- Collaborative Learning
  - Site Visits and Benchmarking
  - Meetings, Listservs, Conference Calls

SUPPORTED BY A GRANT FROM THE DAVID AND LUCILE PACKARD FOUNDATION

CLD: Potentially Better Practices

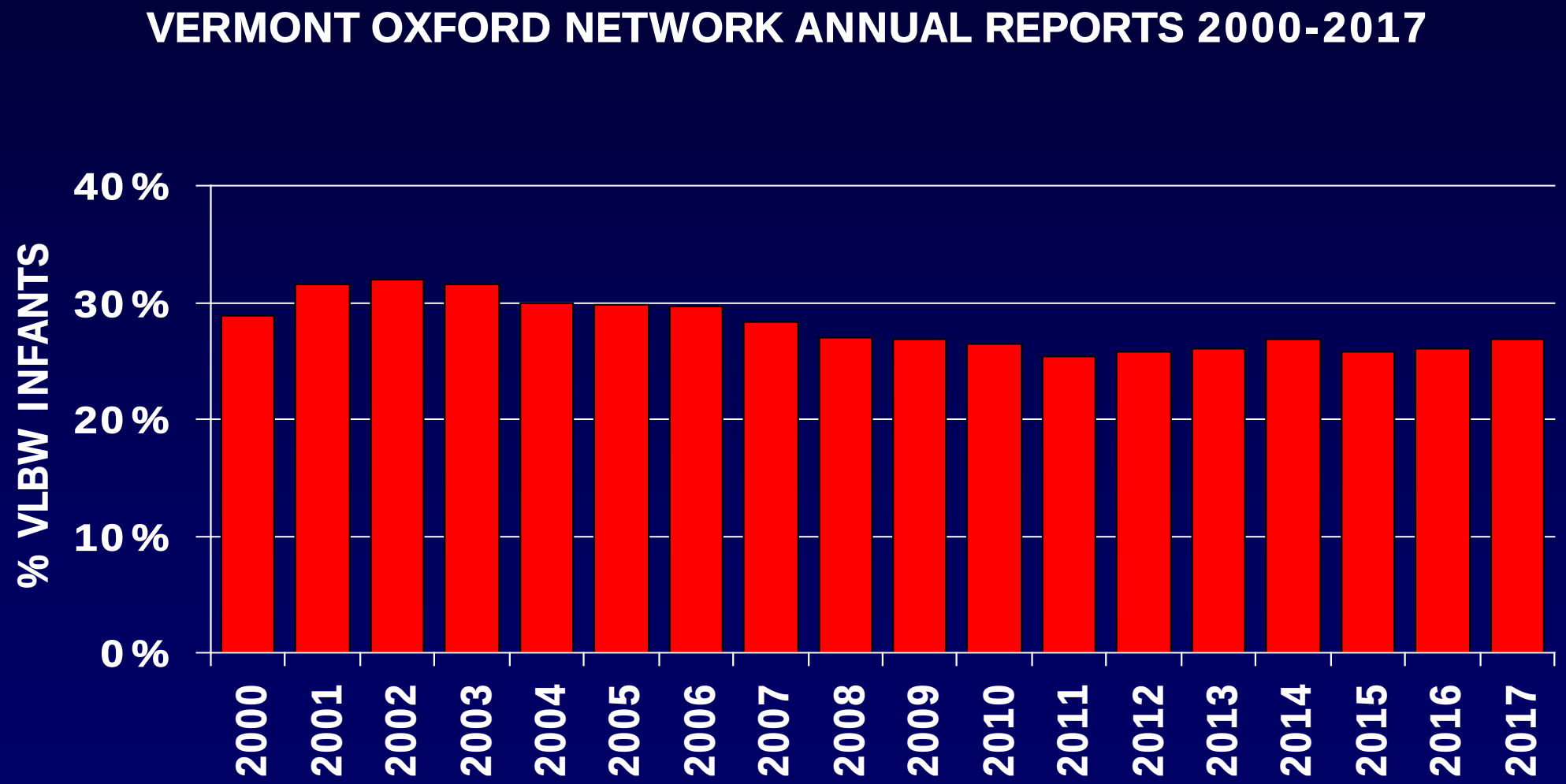
- Promote the use of antenatal steroids
- Prophylactic surfactant administration for infants with birth weight < 1000 grams
- Prophylactic indomethacin for infants < 1000 grams
- Stabilization on SIMV or HOFV
- Participate in RCT to assess effect of early steroids
- Restrict fluid intake
- Permissive hypercarbia
- Post-extubation NCPAP
- Developmentally supportive care

NICQ PROJECT: CHRONIC LUNG DISEASE



HORBAR J. PEDIATRICS 2001

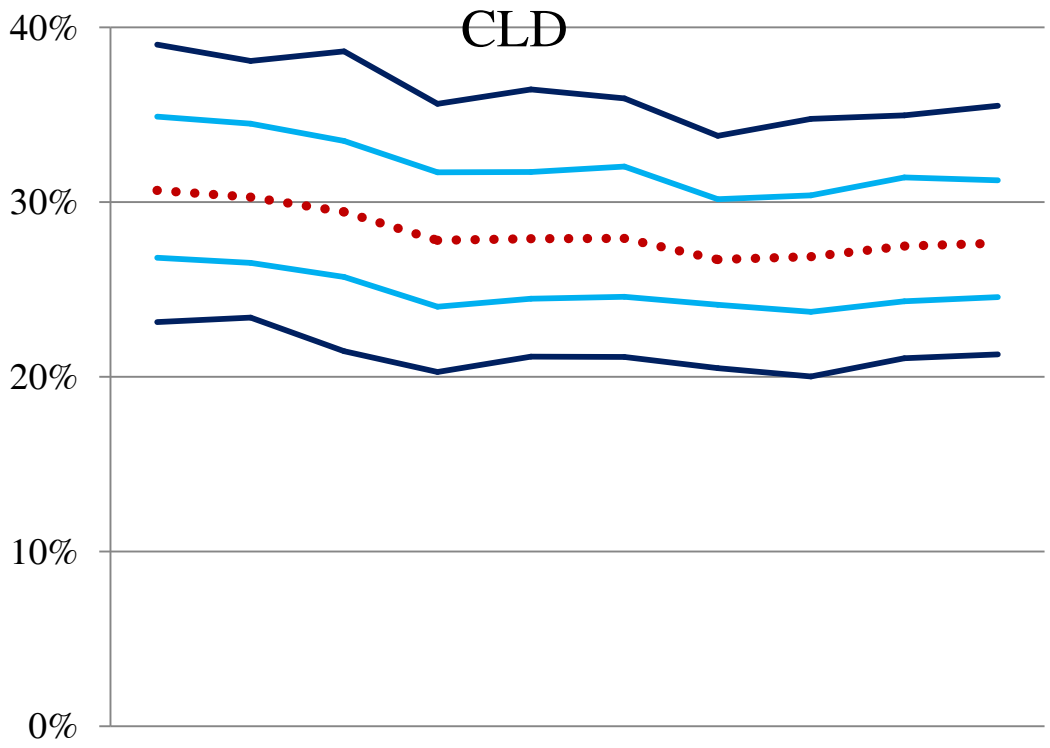
Chronic Lung Disease in VLBW Infants



JAMA Pediatrics

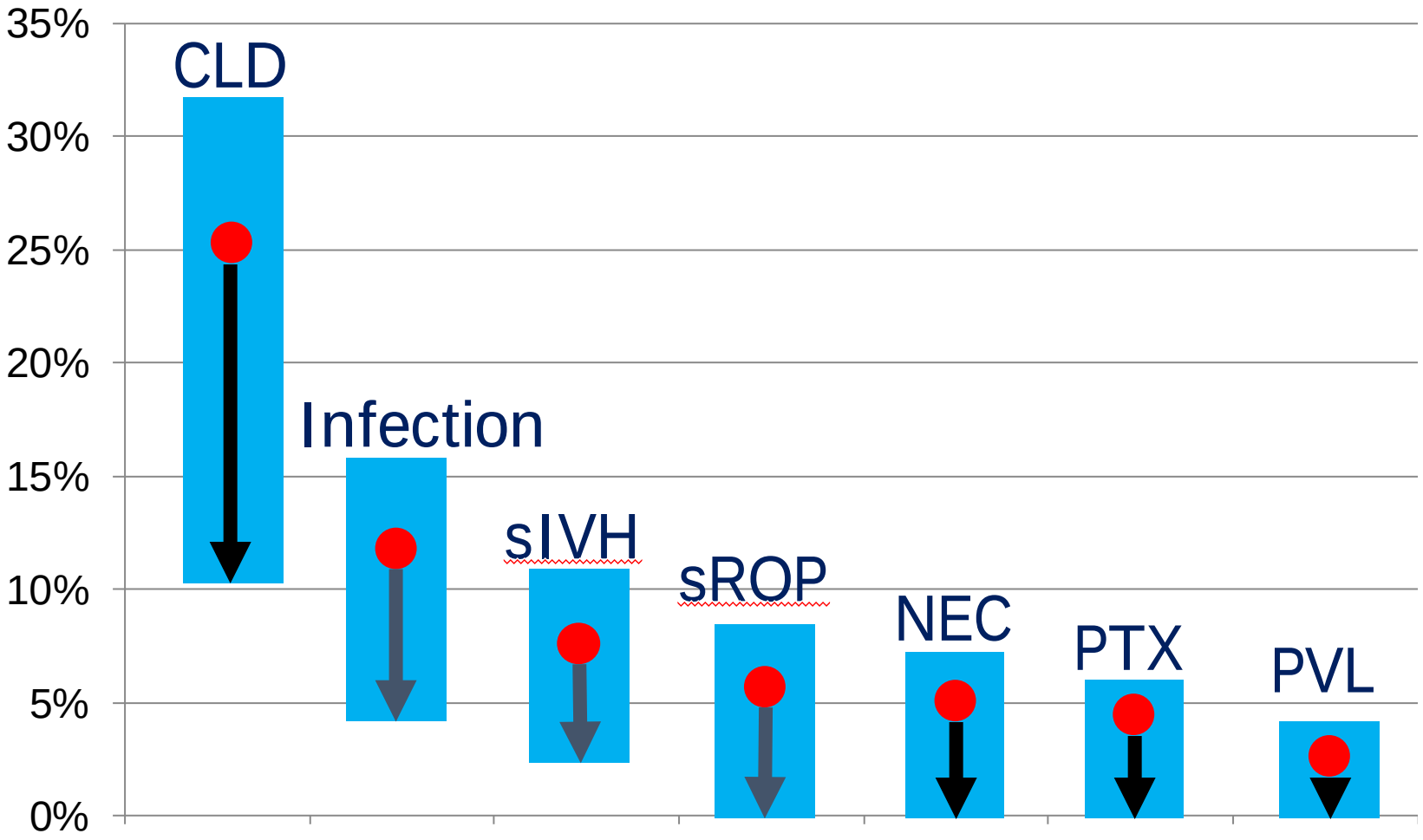
Chronic Lung Disease 2005 to 2014

Risk-Adjusted Rates of Outcomes in the NICU at the 10th, 25th, 50th, 75th, and 90th Percentiles, 2005-2014, With the Dark Blue, Light Blue, and Dotted Red Curves Indicating 10th/90th, 25th/75th, and 50th Percentiles, Respectively



Horbar JD, Edwards EM, Greenberg LT, et al. Variation in performance of neonatal intensive care units in the United States. JAMA Pediatr. Published online January 9, 2017. doi:10.1001/ jamapediatrics.2016.4396

Morbidities



60,000 VLBW Infants at 917 NICUs

Avoidable Morbidity for Infants and Families

CLD	2800
Infection	2300
Severe ROP	650
NEC	650
PVL	500
Severe IVH	400
PTX	350

Risk adjusted estimates based on 917 NICUs in 2013