Title of Program: Preventing and Treating Retinopathy of Prematurity: Evidence from Cochrane Systematic Reviews

Speakers/Moderators: Roger F. Soll, MD, James Hagadorn, MD

Planning Committee: Jeffery D. Horbar, MD, Madge E. Buus-Frank, RN, MS, APRN-BC, FAAN, Roger F. Soll, MD

Date: December 18, 2017

Learning Objectives:

Participants will be presented with evidence from clinical trials and systematic reviews and will be able to evaluate and translate the evidence in the field of neonatology to better serve their practices. Specifically, evidence for strategies regarding the prevention and treatment of retinopathy of prematurity will be presented and critiqued.

DISCLOSURE:

Is there anything to disclose? ***No financial interests to disclose***

COMMERCIAL SUPPORT ORGANIZATIONS ***(if applicable):*** ***No Commercial Support***

This activity has been planned and implemented by The Robert Larner College of Medicine at The University of Vermont and Cochrane Neonatal is accredited by the American Nurses Credentialing Center (ANCC), the Accreditation Council for Pharmacy Education (ACPE), and the Accreditation Council for Continuing Medical Education (ACCME), to provide continuing education for the healthcare team.

The University of Vermont designates this web seminar for a maximum of 1 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Cochrane Neonatal

Preventing and Treating Retinopathy of Prematurity: Evidence from Cochrane Systematic Reviews

Conference begins at 12 Noon EST
December 18, 2017

Supported by: Vermont Oxford Network

Trusted evidence. Informed decisions. Better health.

The Basics

· Follow the slides on your screen.

· Listen to the Audio Broadcast via your computer speakers.

· If the computer audio is not working well, click  at the bottom of the Participants panel and follow the prompts to call in on the telephone.

· Send questions and comments via Chat to "All Panelists".

Cochrane Neonatal

Cochrane

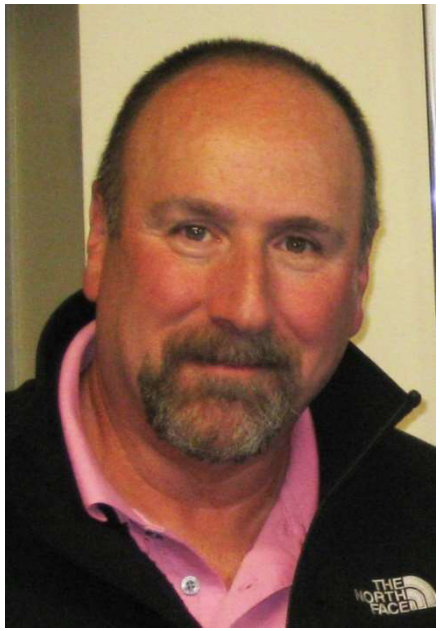
Preparing, maintaining and promoting the accessibility of systematic reviews of the effects of health care interventions

Cochrane Neonatal

Prepares and disseminates evidence-based reviews of the effects of therapies in the field of neonatal medicine

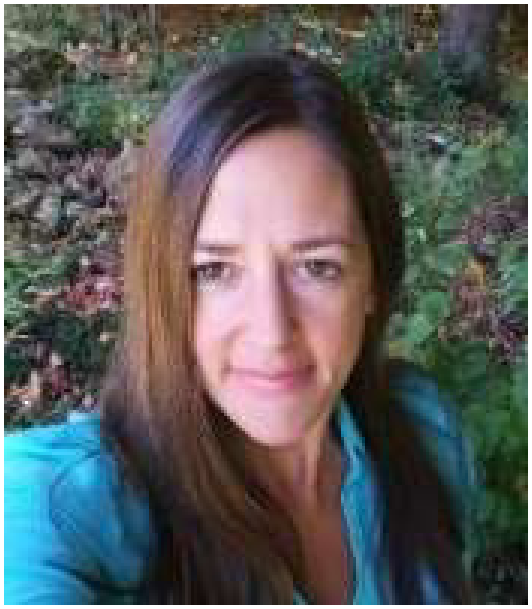
Cochrane Neonatal

Editorial Team



Roger F. Soll
Coordinating Editor

Colleen Ovelman
Managing Editor

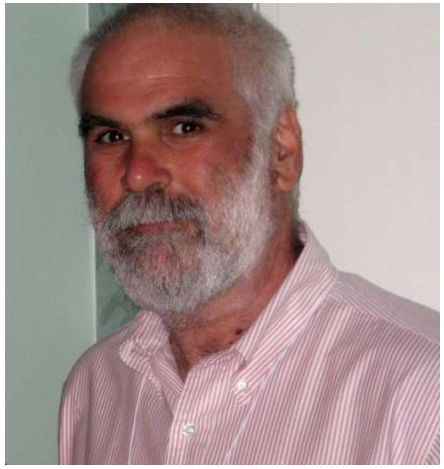


Jennifer Spano
Trial Search Coordinator

Cochrane Neonatal

Editorial Team

Michael Bracken
Yale University



Jeffrey Horbar
University of Vermont

Bill McGuire
Hull York Medical School

Gautham Suresh
Baylor University

Cochrane Neonatal

Guest Discussant

James Hagadorn, MD
Associate Professor of Pediatrics
University of Connecticut School of Medicine

Cochrane Neonatal

In Memory

Jerold F. Lucey, MD
Professor Emeritus
University of Vermont College of Medicine

Remembering Dr. Jerry Lucey, teacher, mentor, colleague, and friend.

Support

Cochrane Neonatal acknowledges the generous support from Vermont Oxford Network in producing these seminars

Disclosure

Roger F. Soll is the
Coordinating Editor of Cochrane Neonatal
and
President of Vermont Oxford Network

Cochrane Neonatal

Why These Webinars?

To develop an understanding of
the evidence supplied by systematic reviews in neonatal perinatal medicine
(as well as other large well conducted trials)
and discuss how this evidence might influence your practice.

Cochrane Neonatal

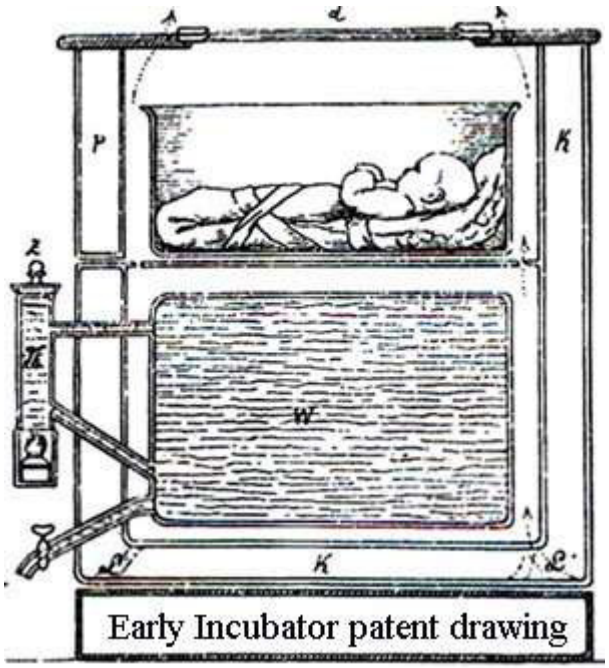
Retinopathy of Prematurity

We will review the evidence from randomized trials and meta-analyses and discuss the different approaches that teams around the world are using regarding the prevention and treatment of retinopathy of prematurity.

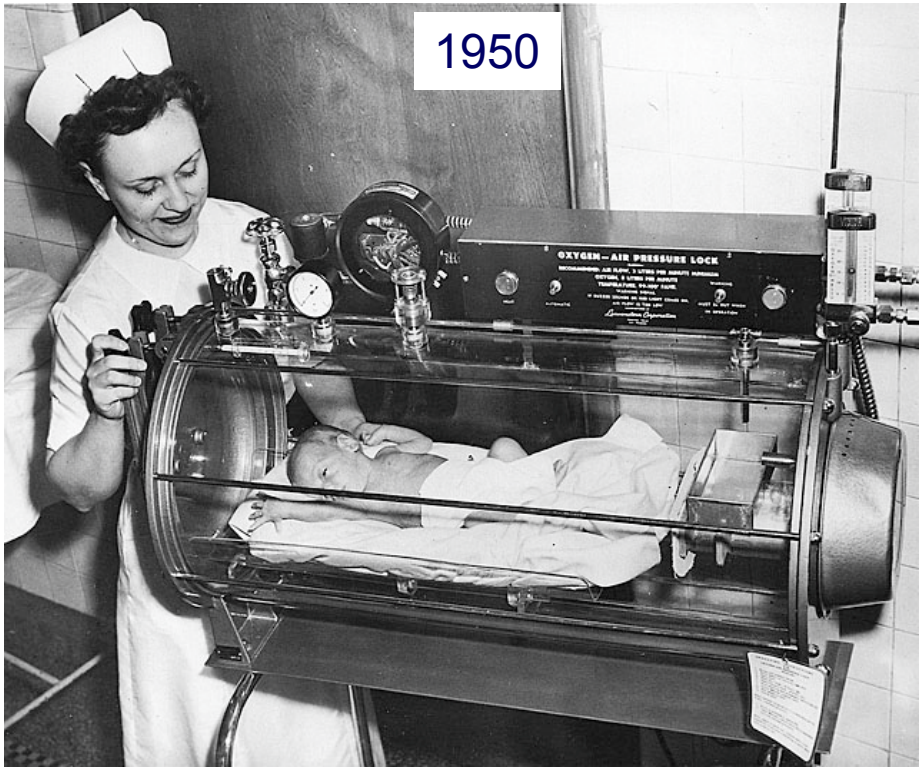
Cochrane Neonatal

Retinopathy of Prematurity is in many ways the story of oxygen use in the preterm newborn….

1887



1950



Cochrane Neonatal

Oxygen in the Preterm Infant

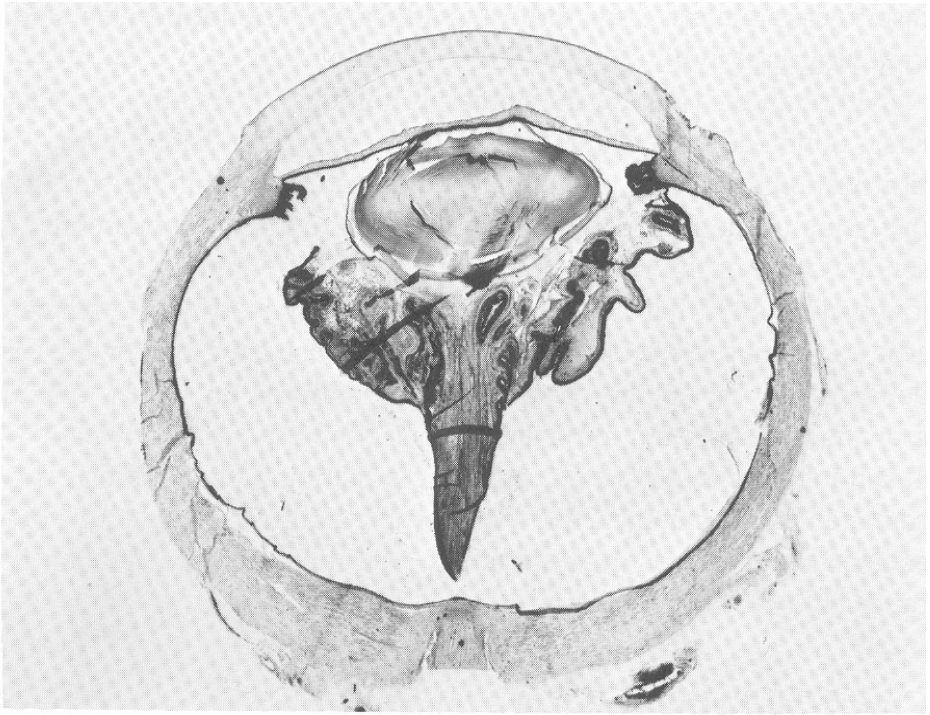
"In the 1940s, Wilson and colleagues observed that periodic breathing in premature infants was nearly eliminated with the use of 70% oxygen.

Although Wilson cautioned against unrestricted use of oxygen, other investigators and the American Academy of Pediatrics advocated its liberal use…."

Polin NEJM 2013

Cochrane Neonatal

Retinopathy of Prematurity (Retrolental Fibroplasia)



First described in 1942:

"Grayish white opaque membrane behind each crystalline lens"

Terry 1942

Cochrane Neonatal

Retinopathy of Prematurity Pathogenesis

Phase 1: Relative retinal hyperoxia and interruption of normal vascularization

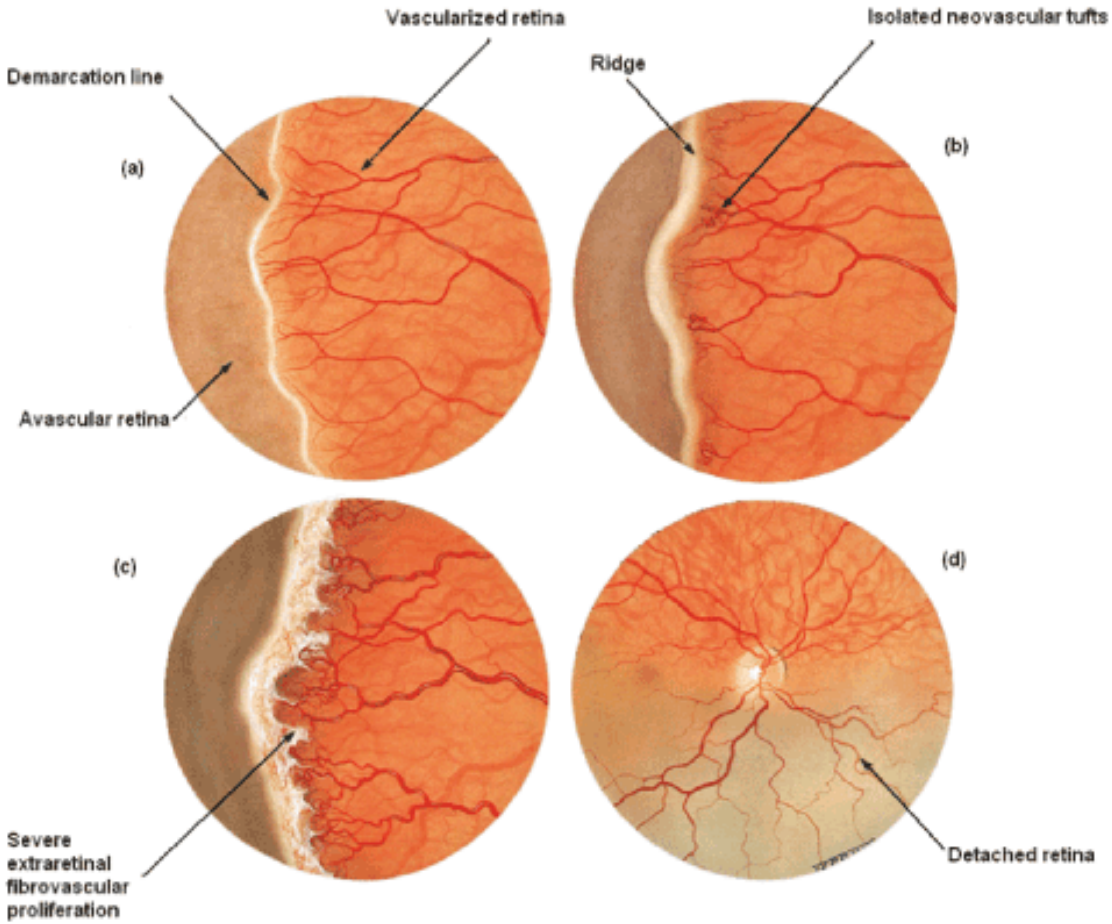
- retinal response to hyperoxia is vasoconstriction
- reduced vascular endothelial growth factor (VEGF)

Phase 2: Hypoxia-revascularization

- VEGF is upregulated in response to hypoxia
- Abnormal neovascularization can occur

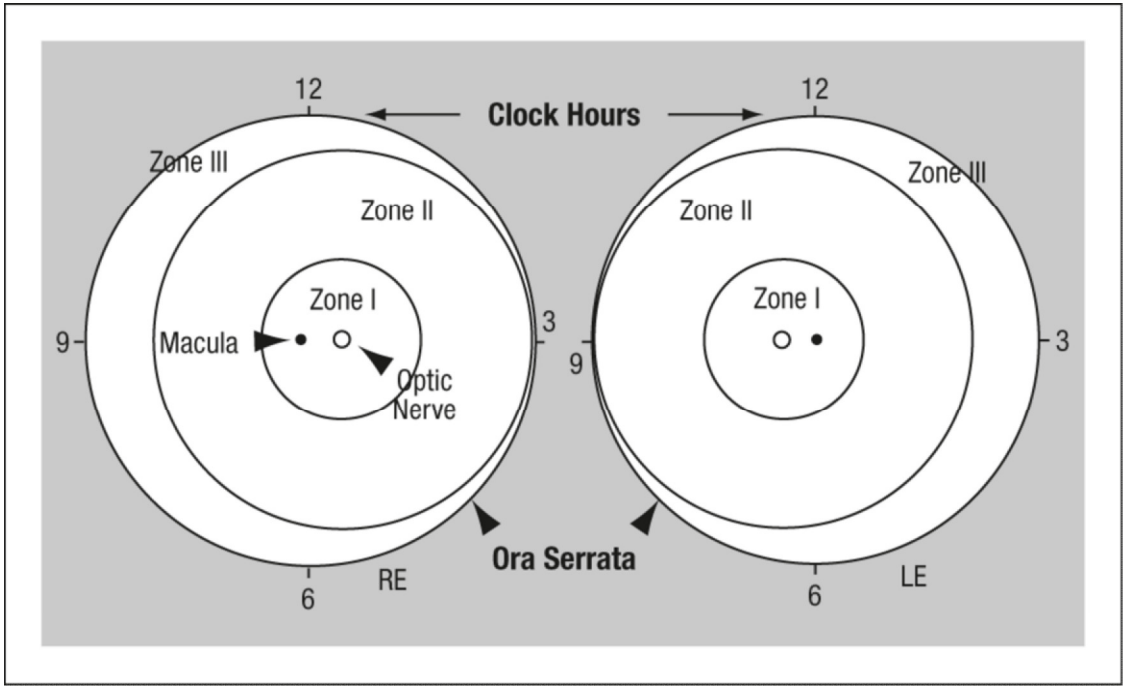
Cochrane Neonatal

Stages of Retinopathy of Prematurity



Retinopathy of Prematurity

From: **The International Classification of Retinopathy of Prematurity Revisited**
Arch Ophthalmol. 2005;123(7):991-999. doi:10.1001/archopht.123.7.991

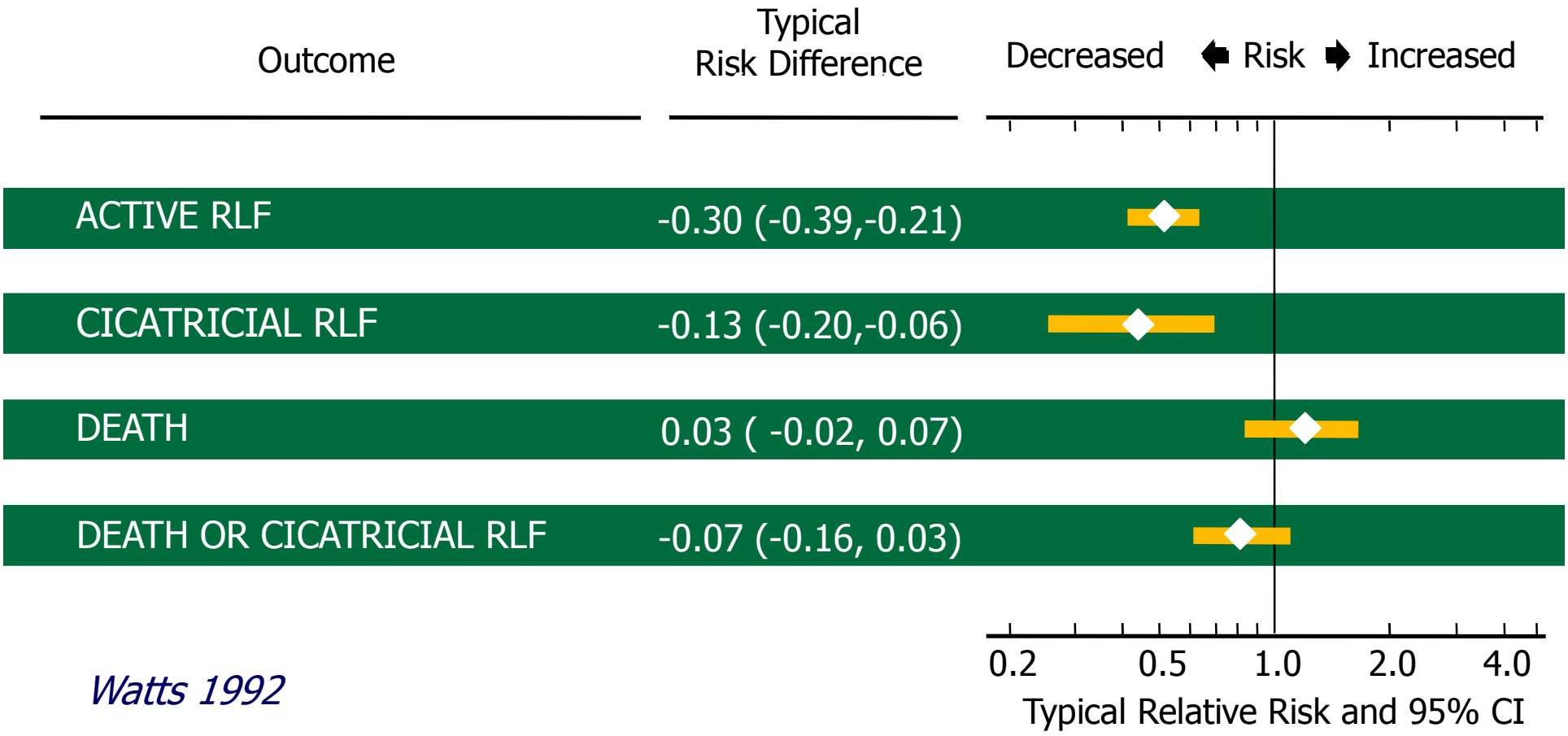


Scheme of retina of right eye (RE) and left eye (LE) showing zone borders and clock hours used to describe the location and extent of retinopathy of prematurity (adapted the Committee for the Classification of Retinopathy of Prematurity).

Cochrane Neonatal

Effect of Restricted Oxygen on Retrolental Fibroplasia

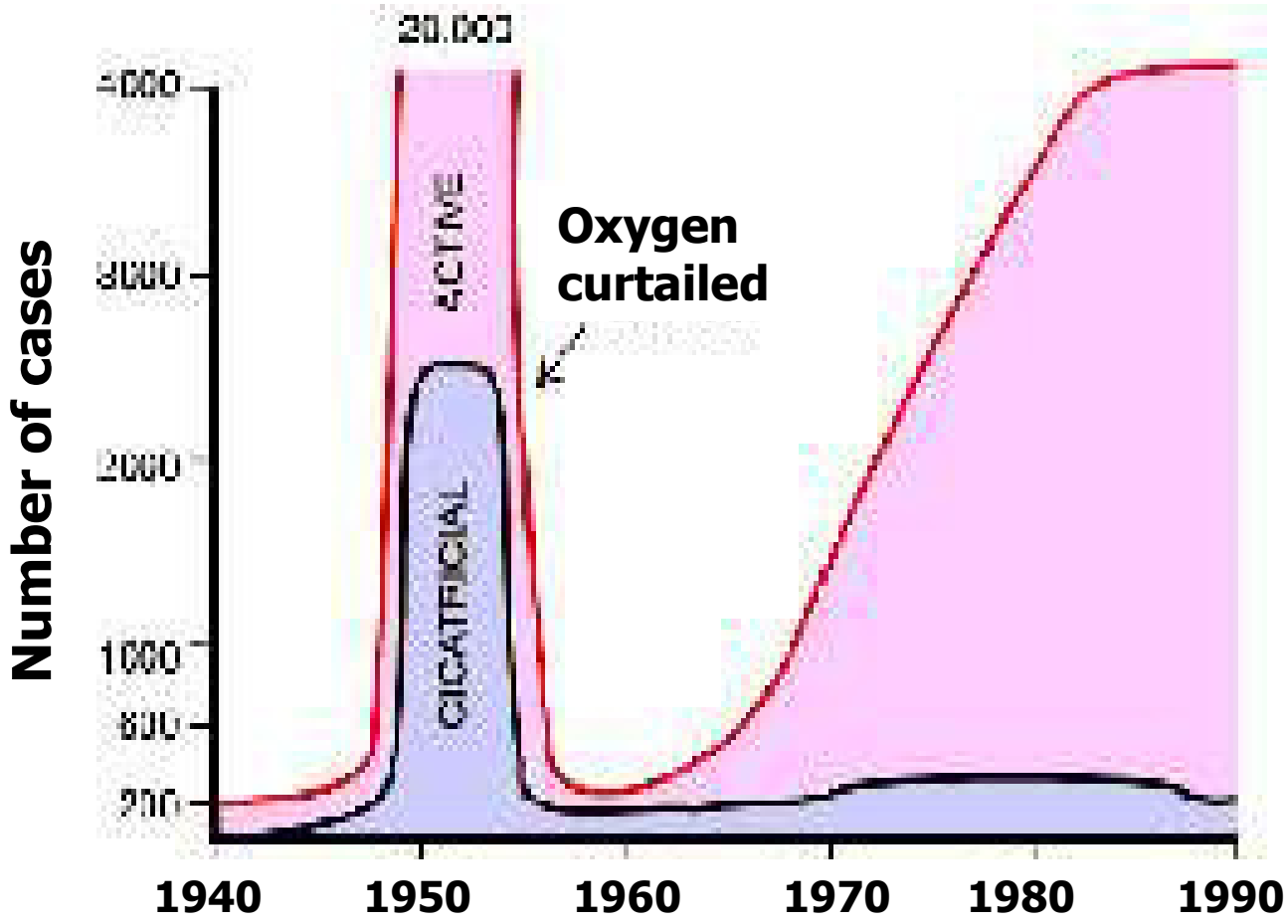
Overview of 3 Randomized Controlled Trials



Watts 1992

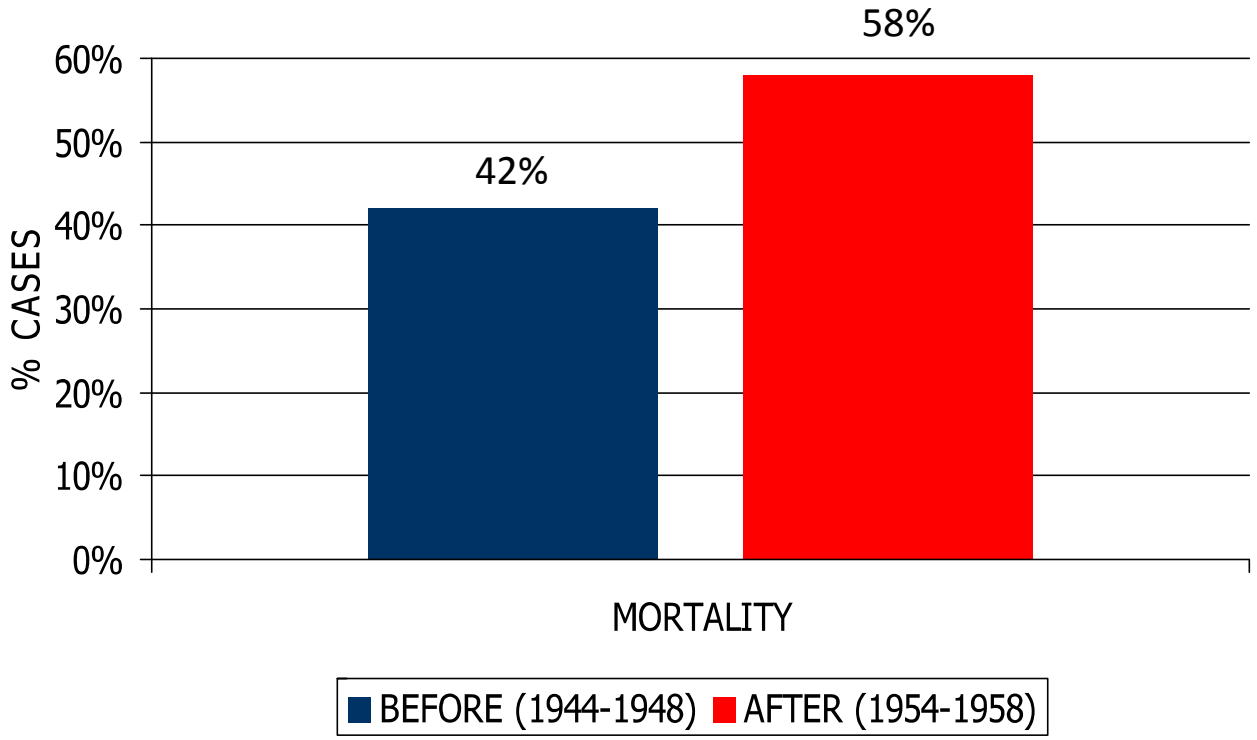
Cochrane Neonatal

Epidemic of ROP



Effect of Restricted Oxygen on Mortality

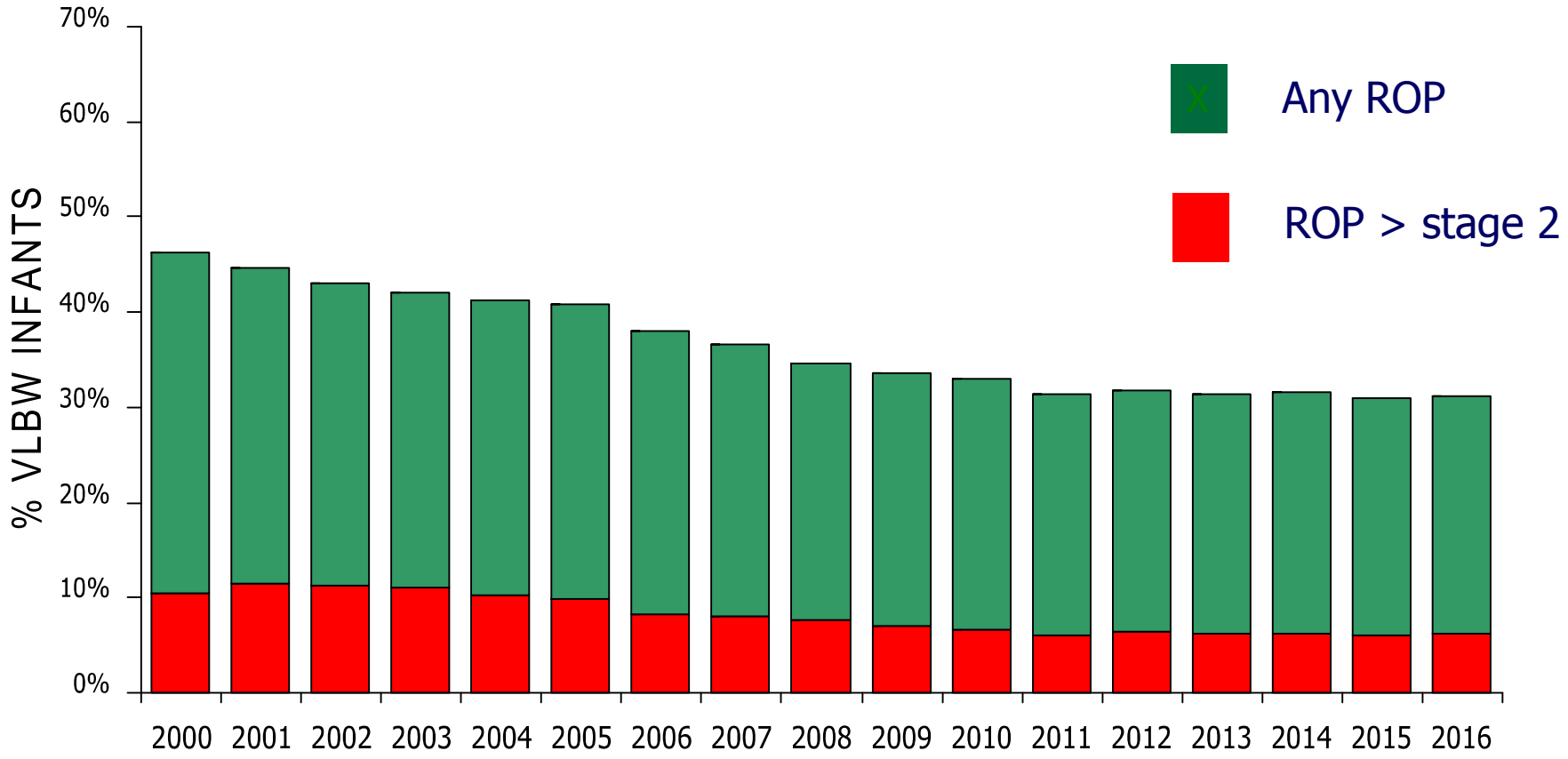
MORTALITY BEFORE (1944-1948) AND AFTER (1954-1958) INTRODUCTION OF A POLICY OF OXYGEN RESTRICTION IN INFANTS BIRTH WEIGHT 1000-1499 GRAMS



AVERY et al. Recent increase in mortality from hyaline membrane disease. J Pediatrics 1960

Retinopathy of Prematurity

VERMONT OXFORD NETWORK ANNUAL REPORTS 2000-2016



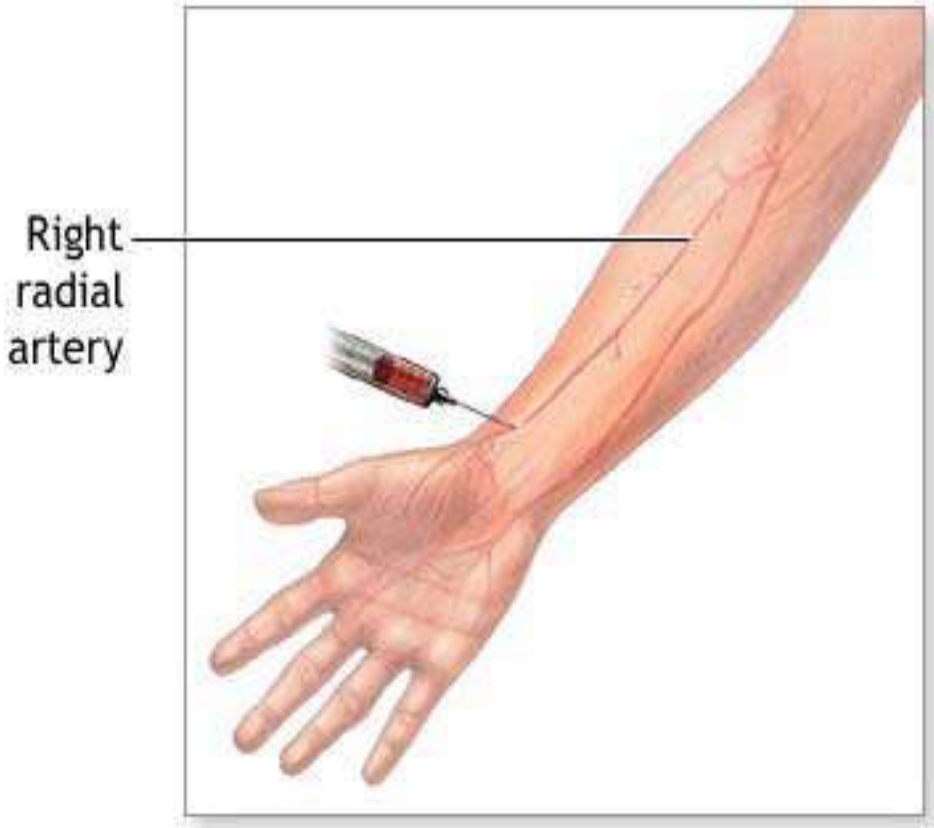
Oxygen Monitoring and Retinopathy of Prematurity

Use of Oxygen and Retinopathy of Prematurity

- Blood gases
- Transcutaneous Monitoring
- Policies/guidelines to decrease oxygen exposure
- Recent multicenter trials (NeoProM)

Oxygen Monitoring and Retinopathy of Prematurity

BLOOD GASES



Oxygen Monitoring and Retinopathy of Prematurity

Blood gases

Like watching a football game and checking in on the score every quarter…

First Quarter	Giants 12	Patriots 9
Second Quarter	Giants 18	Patriots 12
Third Quarter	Giants 25	Patriots 15
Fourth Quarter	Giants 31	Patriots 18

Oxygen Monitoring and Retinopathy of Prematurity

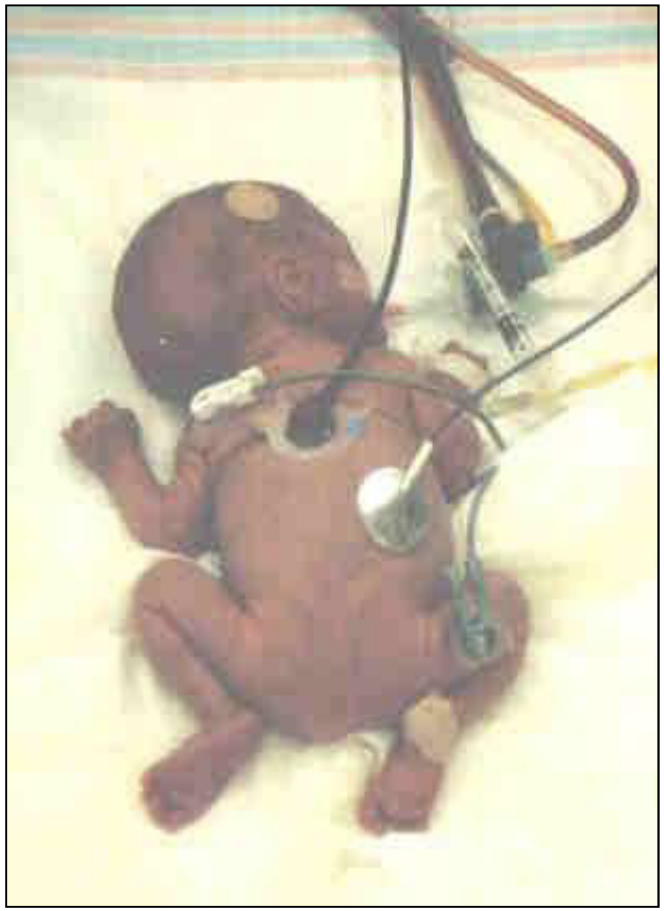
Blood gases

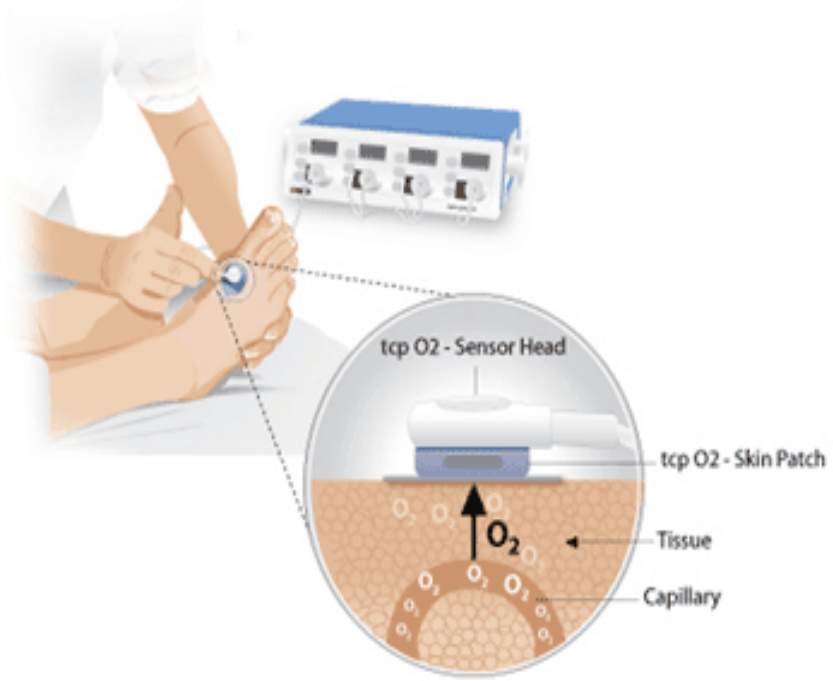
So what happened in the First Quarter?

Did the Giants score 4 field goals, or a touchdown, a missed extra point and 2 field goals, or a touchdown and a field goal and a safety?

Have to watch the game more closely to know!

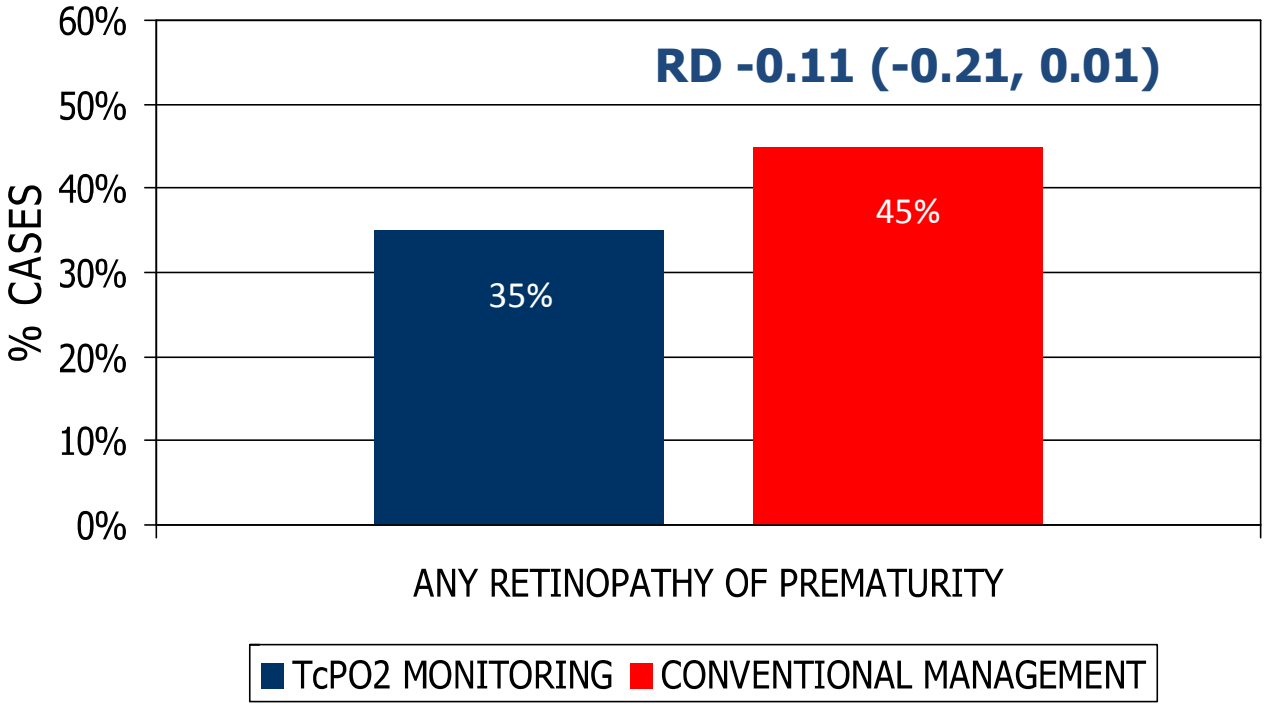
Transcutaneous oxygen monitoring





Continuous TcPO2 Monitoring Compared to Intermittent PaO2 Monitoring

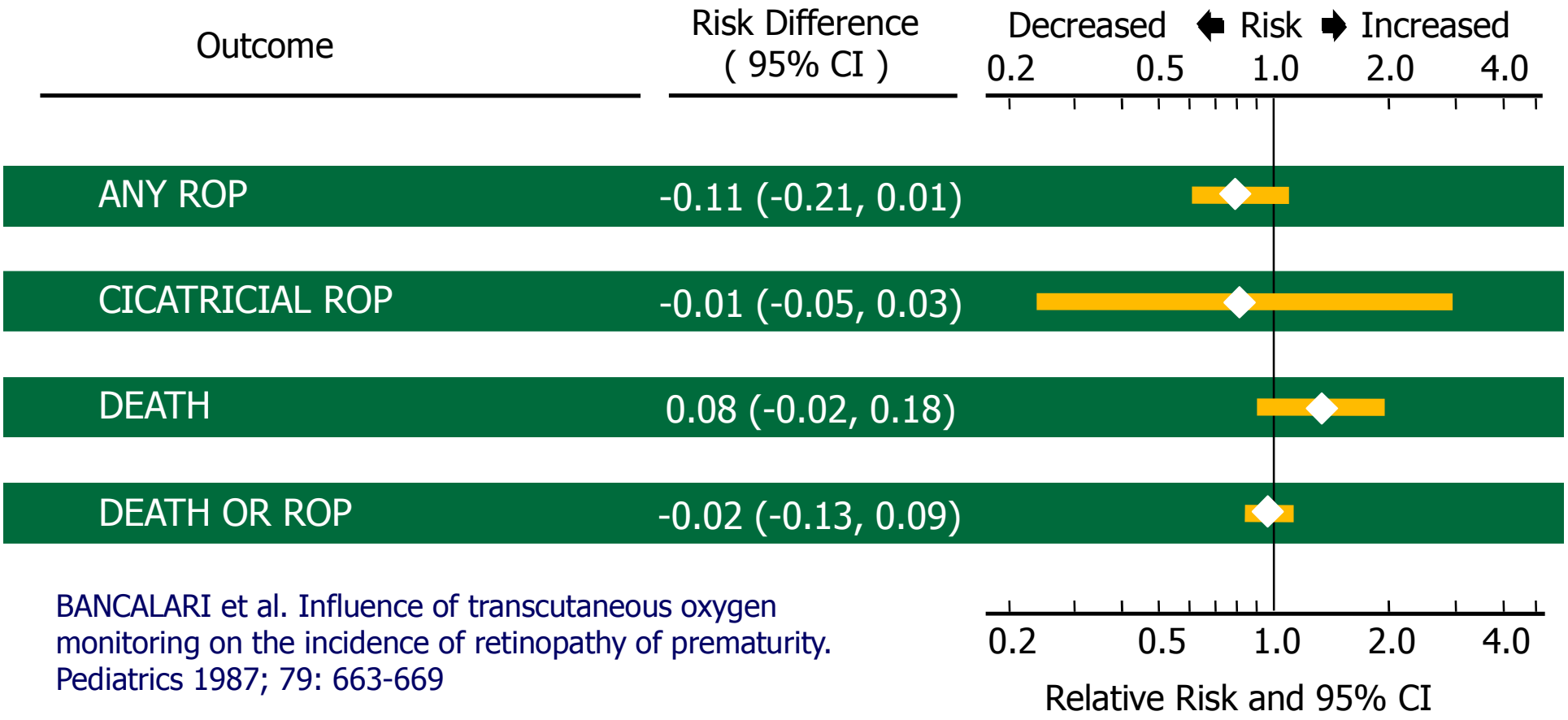
Retinopathy of prematurity
All Study Infants BW 500-1300 grams



BANCALARI et al. Influence of transcutaneous oxygen monitoring on the incidence of retinopathy of prematurity. Pediatrics 1987; 79: 663-669

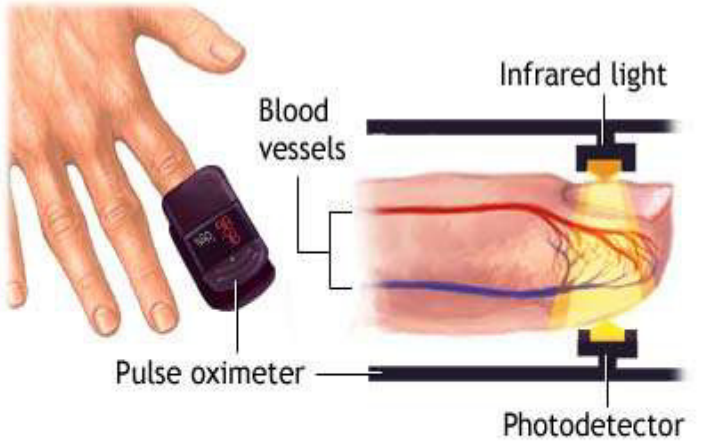
Continuous TcPO2 Monitoring Compared to Intermittent PaO2 Monitoring

BANCALARI AND COWORKERS 1987



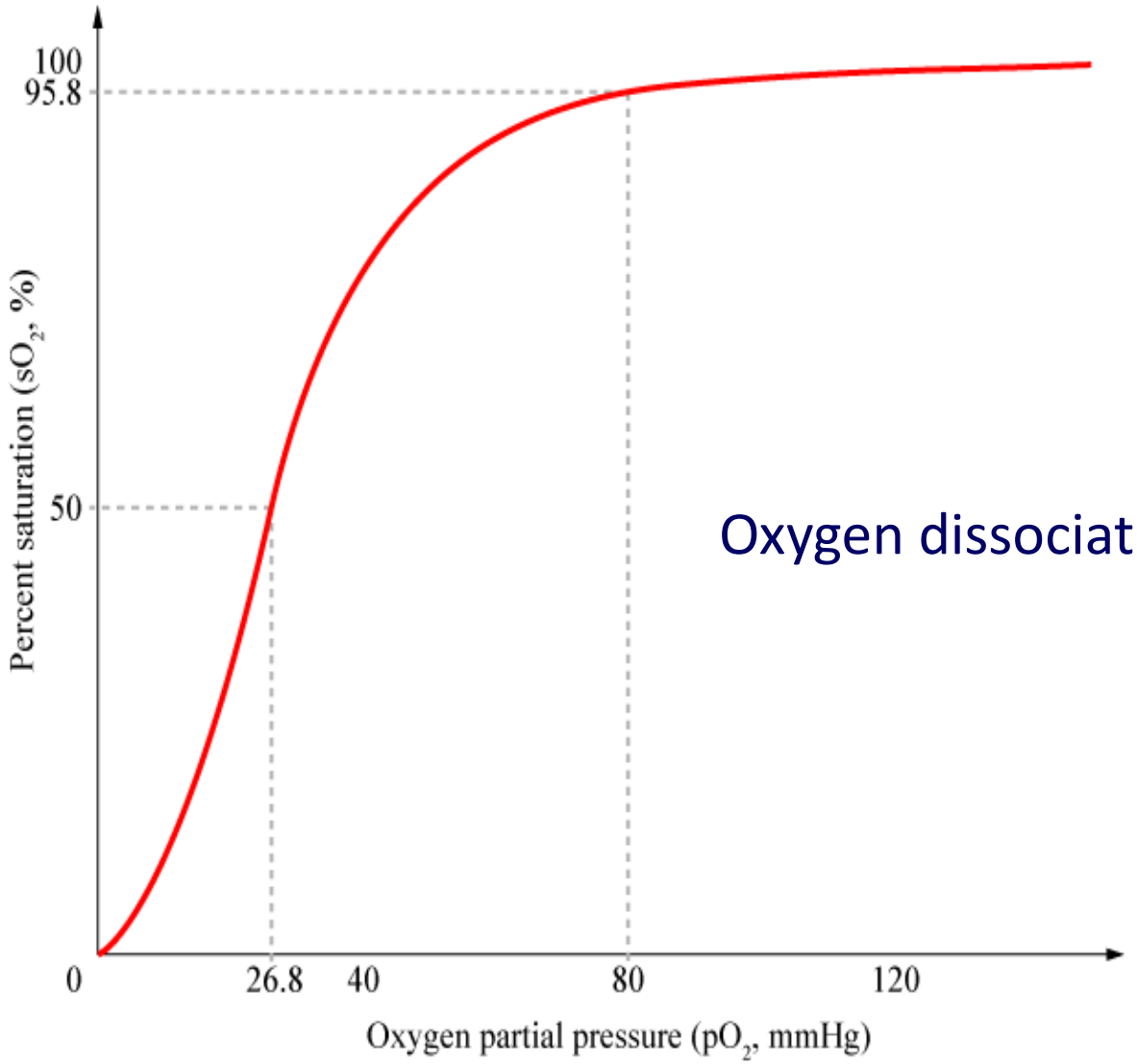
BANCALARI et al. Influence of transcutaneous oxygen monitoring on the incidence of retinopathy of prematurity. Pediatrics 1987; 79: 663-669

Oxygen saturation monitoring



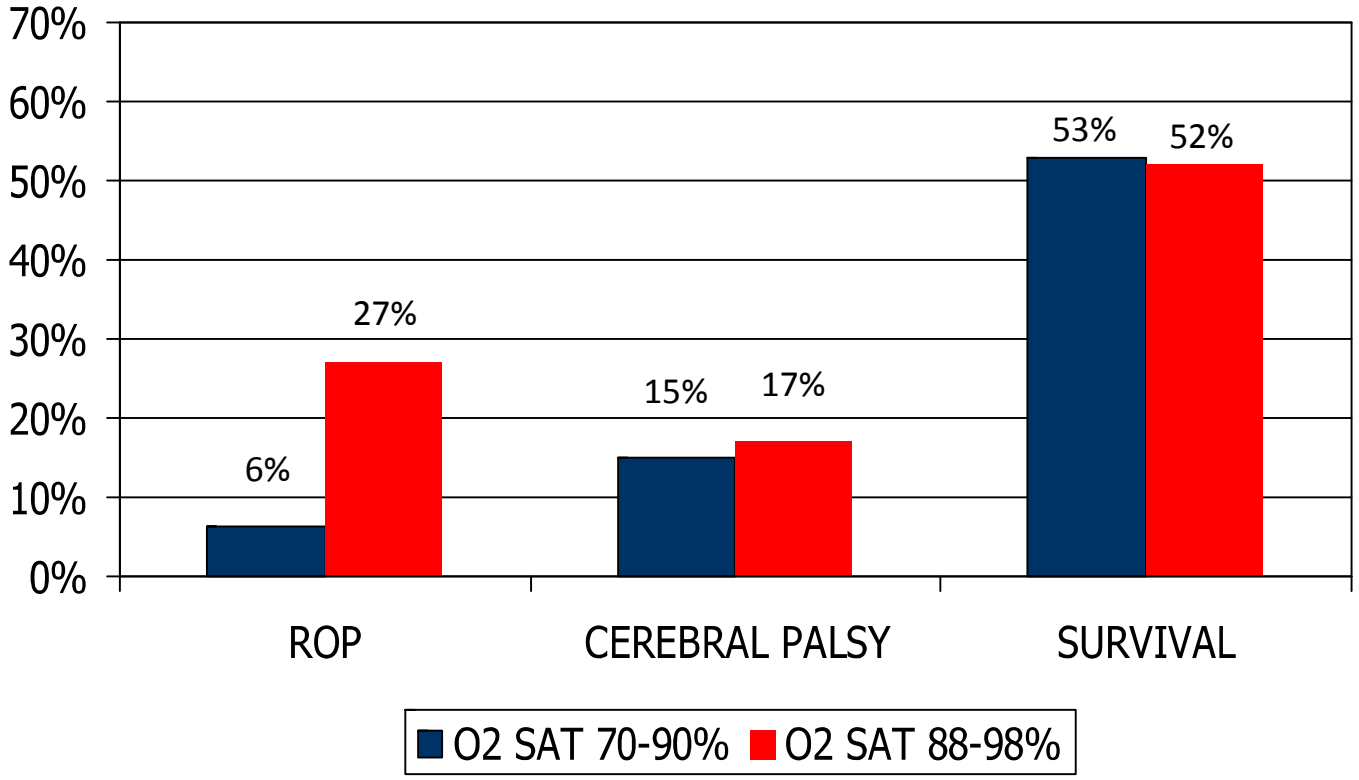
A pulse oximeter estimates the amount of oxygen carried in the bloodstream using infrared technology across the skin

A.D.A.M.



Oxygen dissociation curve

Lower Oxygen Saturation and the Impact on Retinopathy of Prematurity



Tin W et al. Pulse oximetry, severe retinopathy, and outcome at one year in babies of less than 28 weeks gestation. Arch Dis Child Fetal Neonatal Ed 2001;84:F106-110

Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Askie LM, Darlow BA, Davis PG, Finer N, Stenson B, Vento M, Whyte R.

Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD011190. DOI: 10.1002/14651858.CD011190.pub2.

Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Objectives:

1. What are the effects of targeting lower versus higher oxygen saturation ranges on death or major neonatal and infant morbidities, or both, in extremely preterm infants?

2. Do these effects differ in different types of infants, including those born at a very early gestational age, or in those who are outborn, without antenatal corticosteroid coverage, of male sex, small for gestational age or of multiple birth, or by mode of delivery?

NeOProM

Askie et al. BMC Pediatrics 2011, 11:6
http://www.biomedcentral.com/1471-2431/11/6

BMC Pediatrics

STUDY PROTOCOL Open Access

NeOProM: Neonatal Oxygenation Prospective Meta-analysis Collaboration study protocol

Lisa M Askie[1*], Peter Brocklehurst[2], Brian A Darlow[3], Neil Finer[4], Barbara Schmidt[5,6], William Tarnow-Mordi[7,8], for the NeOProM Collaborative Group[1]

Characteristics of randomized trials included in the NeoProM Collaboration

Trial acronym	BOOST II-Australia	BOOST II-UK	BOOST-NZ	SUPPORT	COT
Registration number	ACTRN12605000055606	ISRCTN00842661	ACTRN12605000253606	NCT00233324	ISRCTN62491227
Planned sample size	1200	1200	320	1310	1200
Countries of recruitment	Australia	United Kingdom	New Zealand	United States	Canada, USA, Argentina, Germany, Israel, Finland
Participants	Infants < 28 wks gestation inborn or outborn < 24 hrs old	Infants < 28 wks gestation < 12 hrs old (24 hrs if outborn)	Infants < 28 wks gestation inborn or outborn < 24 hrs old	Infants 24-27 wks gestation < 2 hrs old	Infants 23 0/7-27 6/7 wks gestation < 24 hrs old
Masked?	Yes	Yes	Yes	Yes	Yes
Intervention	Lower oxygen saturation (85%-89%)	Lower oxygen saturation (85%-89%)	Lower oxygen saturation (85%-89%)	Lower oxygen saturation (85%-89%)	Lower oxygen saturation (85%-89%)
Comparator	Higher oxygen saturation (91%-95%)	Higher oxygen saturation (91%-95%)	Higher oxygen saturation (91%-95%)	Higher oxygen saturation (91%-95%)	Higher oxygen saturation (91%-95%)
Intervention & comparator duration	Oximeter applied asap after admission to NICU, continued for minimum 2 wks. Thereafter continued until 36 wks corrected age or SpO_2 > 96% in room air for 95% of time over 3 days.	Oximeter applied from randomisation until postmenstrual age (PMA) of 36 wks or until baby is breathing air. All monitoring at any time prior to 36 wks to be done using study oximeter. BPD defined at 36 wks using a physiological test.	Oximeter applied asap after admission to NICU, continued for minimum 2 wks. Thereafter continued until 36 wks corrected age or SpO_2 > 96% in room air for 95% of time over 3 days.	Oximeter applied within 2 hrs following admission to NICU until infant has been in room air for 72 hrs or until 36 wks corrected age, assessed by physiologic oxygen test.	Oximeter applied from day of birth until a minimum 36 wks PMA. If breathing room air without any form of respiratory assistance from 35 wks PMA onward, study oximetry discontinued at a 36 wks PMA. If receiving any form of respiratory assistance and/or oxygen therapy from 35 wks PMA onward study oximetry continues until 40 wks PMA. Study oximetry stopped at any time before 40 wks PMA if baby discharged home (with or without respiratory assistance and/or oxygen).

Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Results:

- Five trials, which together enrolled 4965 infants, were eligible for inclusion.

- The investigators of these five trials had prospectively planned to combine their data as part of the NeOProM (Neonatal Oxygen Prospective Meta-analysis) Collaboration.

SUPPORT TRIAL

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 27, 2010 VOL. 362 NO. 21

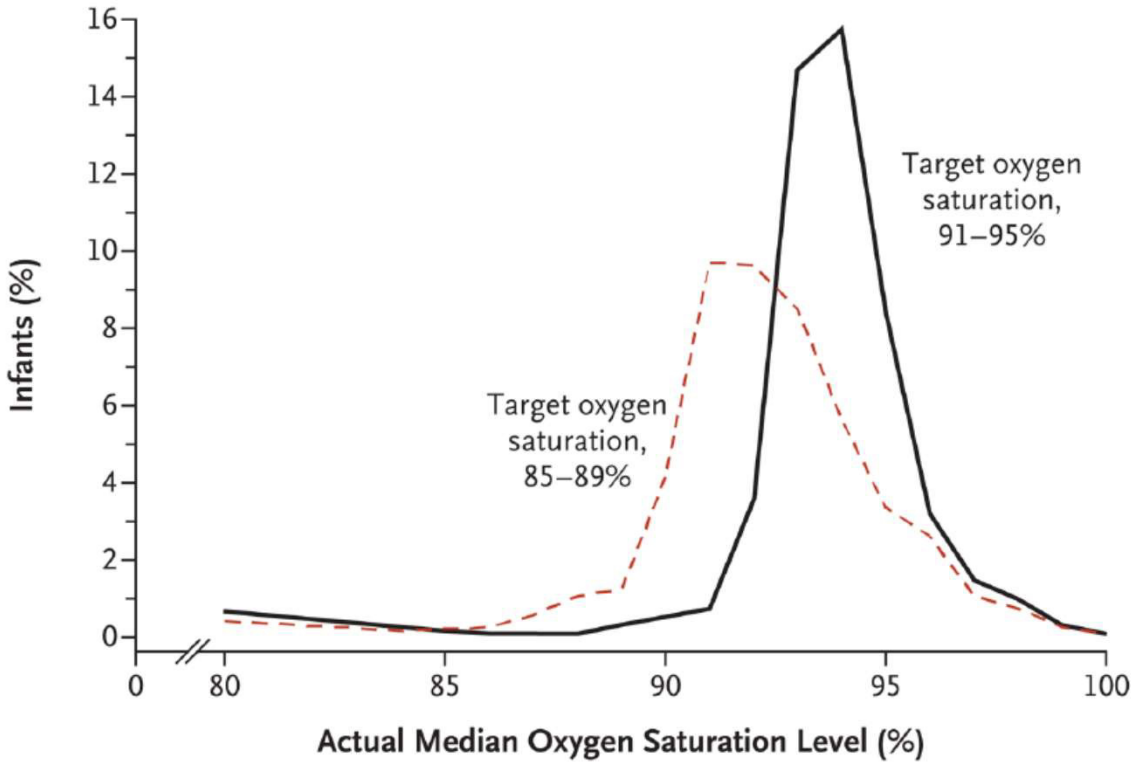
Target Ranges of Oxygen Saturation in Extremely Preterm Infants

SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network*

N Engl J Med. 2010 May 27;362(21):1959-69. Epub 2010 May 16.

SUPPORT TRIAL

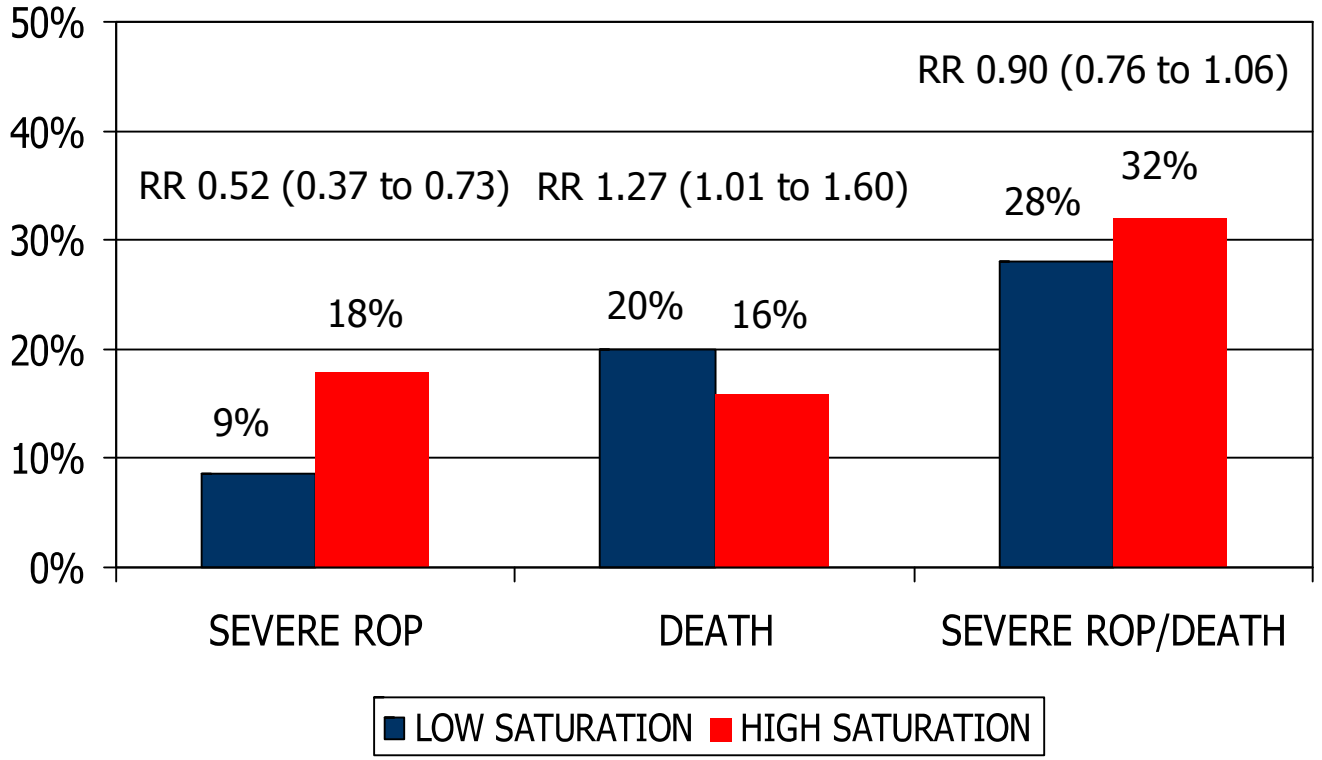
Median Oxygen Saturation with Oxygen Supplementation in the Low Target and High Target Groups



N Engl J Med. 2010 May 27;362(21):1959-69. Epub 2010 May 16.

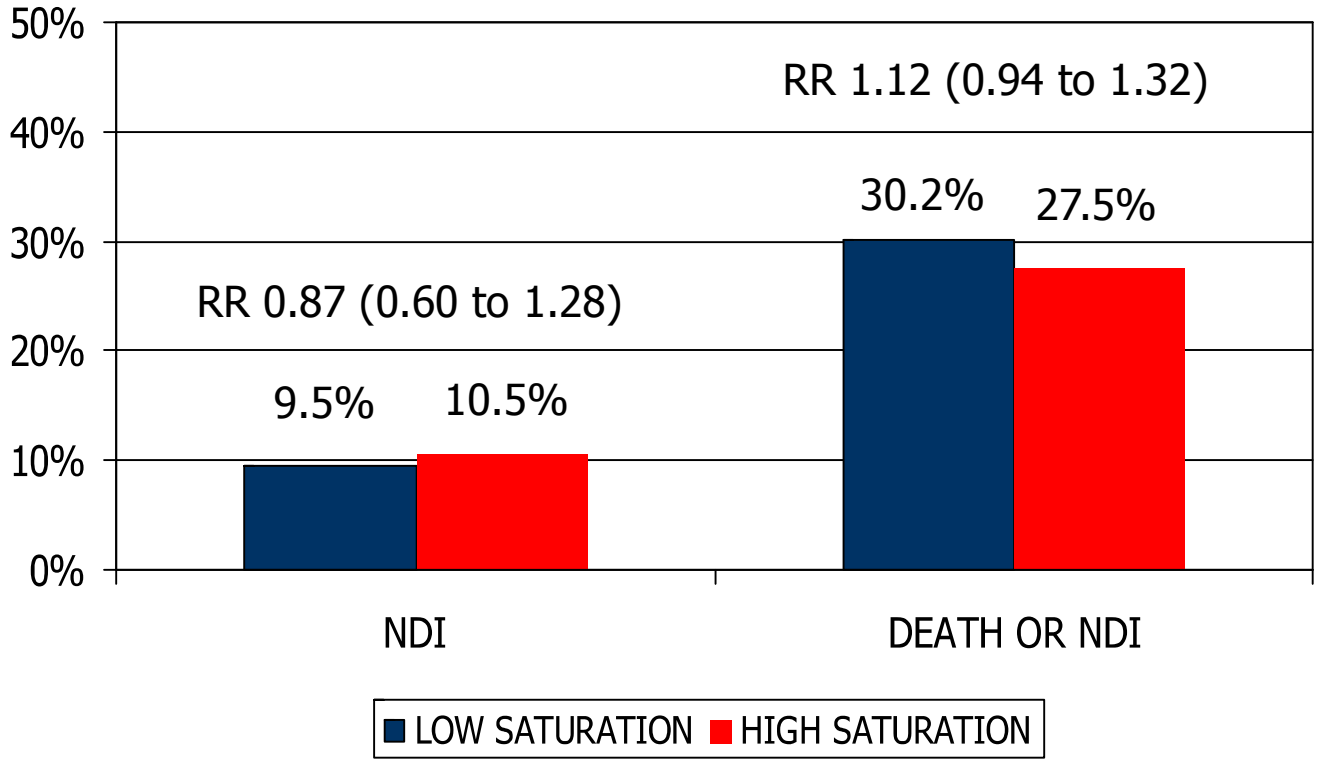
OXYGEN SATURATION TARGETS AND OUTCOMES IN EXTREMELY PREMATURE INFANTS

OUTCOME OF INFANTS IN THE SUPPORT TRIAL



SUPPORT NEJM 2010

OUTCOME OF INFANTS IN THE SUPPORT TRIAL: DEVELOPMENTAL FOLLOW UP



SUPPORT TRIAL PAS 2012

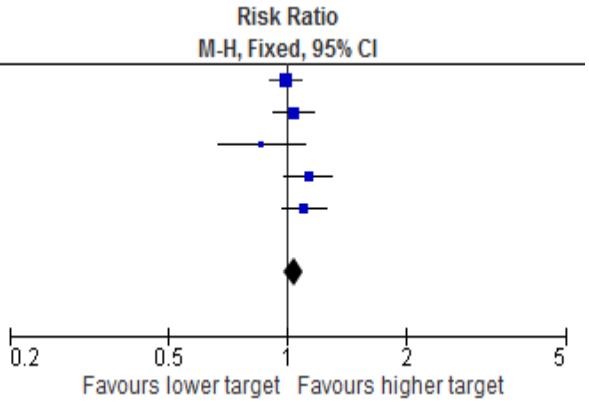
Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Effect on Death or Major Disability to 18 to 24 months

	Lower oxygen saturation		Higher oxygen saturation			Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year
Vaucher 2012	363	613	374	624	31.7%	0.99 [0.90, 1.08]	2012
Schmidt 2013	298	578	283	569	24.4%	1.04 [0.92, 1.16]	2013
BOOST NZ 2014	65	167	76	168	6.5%	0.86 [0.67, 1.11]	2014
BOOST-II Australia 2016	247	549	217	545	18.6%	1.13 [0.98, 1.30]	2016
BOOST-II UK 2016	245	473	220	468	18.9%	1.10 [0.97, 1.25]	2016
Total (95% CI)		**2380**		**2374**	**100.0%**	**1.04 [0.98, 1.10]**	
Total events	1218		1170				

Heterogeneity: Chi² = 5.50, df = 4 (P = 0.24); I² = 27%

Test for overall effect: Z = 1.35 (P = 0.18)



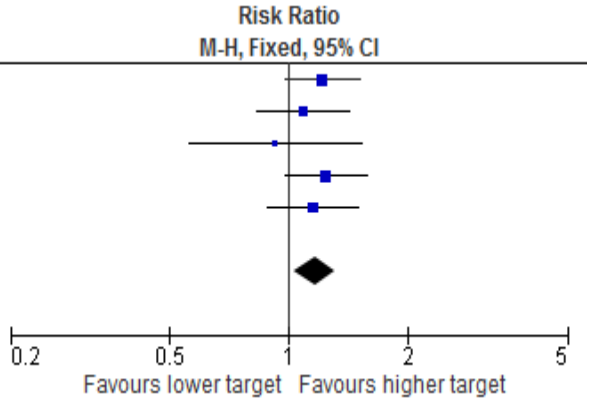
Typical RR 1.04 (95% CI 0.98 to 1.10)

Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Effect on Death to 18 to 24 months

Study or Subgroup	Lower oxygen saturation Events	Total	Higher oxygen saturation Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Vaucher 2012	140	633	118	648	27.9%	1.21 [0.98, 1.51]
Schmidt 2013	97	585	88	577	21.2%	1.09 [0.83, 1.42]
BOOST NZ 2014	25	170	27	170	6.5%	0.93 [0.56, 1.53]
BOOST-II UK 2016	122	484	98	483	23.5%	1.24 [0.98, 1.57]
BOOST-II Australia 2016	100	561	87	562	20.8%	1.15 [0.89, 1.50]
Total (95% CI)		**2433**		**2440**	**100.0%**	**1.16 [1.03, 1.31]**
Total events	484		418			

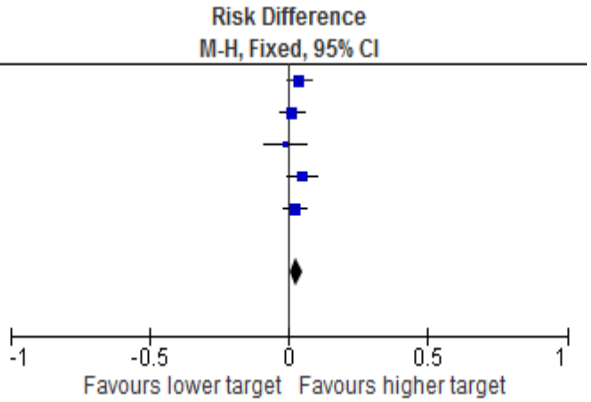
Heterogeneity: Chi² = 1.51, df = 4 (P = 0.83); I² = 0%
Test for overall effect: Z = 2.50 (P = 0.01)



Typical RR 1.16 (95% CI 1.03 to 1.31)

Study or Subgroup	Lower oxygen saturation Events	Total	Higher oxygen saturation Events	Total	Weight	Risk Difference M-H, Fixed, 95% CI
Vaucher 2012	140	633	118	648	26.3%	0.04 [-0.00, 0.08]
Schmidt 2013	97	585	88	577	23.8%	0.01 [-0.03, 0.06]
BOOST NZ 2014	25	170	27	170	7.0%	-0.01 [-0.09, 0.06]
BOOST-II UK 2016	122	484	98	483	19.8%	0.05 [-0.00, 0.10]
BOOST-II Australia 2016	100	561	87	562	23.0%	0.02 [-0.02, 0.07]
Total (95% CI)		**2433**		**2440**	**100.0%**	**0.03 [0.01, 0.05]**
Total events	484		418			

Heterogeneity: Chi² = 2.41, df = 4 (P = 0.66); I² = 0%
Test for overall effect: Z = 2.50 (P = 0.01)



Typical RD 0.03 (95% CI 0.01 to 0.05)

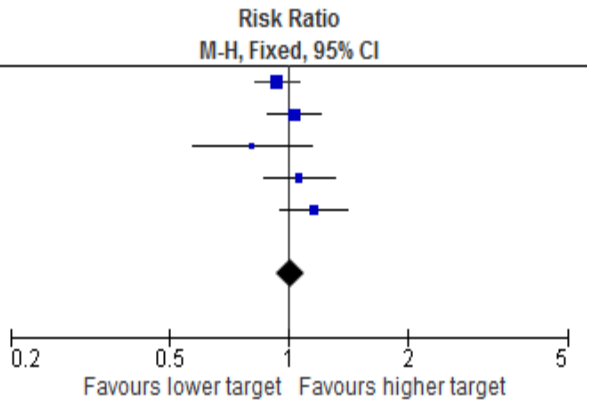
Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Effect on Major Disability to 18 to 24 months

Study or Subgroup	Lower oxygen saturation Events	Total	Higher oxygen saturation Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Vaucher 2012	223	473	256	506	33.5%	0.93 [0.82, 1.06]
Schmidt 2013	201	488	195	489	26.4%	1.03 [0.89, 1.20]
BOOST NZ 2014	40	142	49	141	6.7%	0.81 [0.57, 1.15]
BOOST-II UK 2016	123	351	122	370	16.1%	1.06 [0.87, 1.30]
BOOST-II Australia 2016	147	449	130	458	17.4%	1.15 [0.95, 1.40]
Total (95% CI)		**1903**		**1964**	**100.0%**	**1.01 [0.93, 1.09]**
Total events	734		752			

Heterogeneity: $Chi^2 = 5.13$, $df = 4$ ($P = 0.27$); $I^2 = 22\%$

Test for overall effect: $Z = 0.25$ ($P = 0.80$)



Typical RR 1.01 (95% CI 0.93 to 1.09)

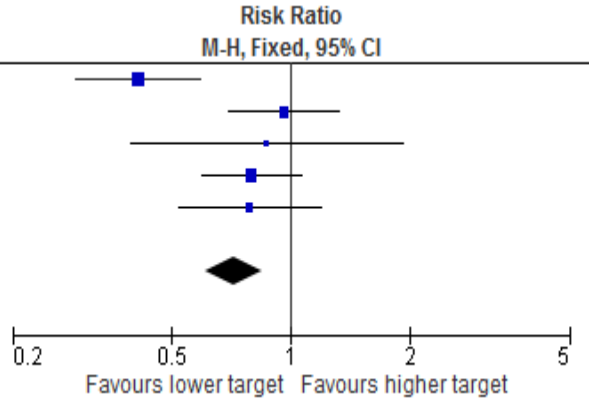
Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Effect on Severe Retinopathy of Prematurity

Study or Subgroup	Lower targeting Events	Total	Higher targeting Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Vaucher 2012	36	482	93	514	29.9%	0.41 [0.29, 0.59]
Schmidt 2013	63	500	66	503	21.9%	0.96 [0.70, 1.33]
BOOST NZ 2014	11	158	12	150	4.1%	0.87 [0.40, 1.91]
BOOST-II UK 2016	67	395	86	403	28.3%	0.79 [0.60, 1.06]
BOOST-II Australia 2016	37	487	48	497	15.8%	0.79 [0.52, 1.19]
Total (95% CI)		**2022**		**2067**	**100.0%**	**0.72 [0.61, 0.85]**
Total events	214		305			

Heterogeneity: Chi² = 12.90, df = 4 (P = 0.01); I² = 69%

Test for overall effect: Z = 3.97 (P < 0.0001)

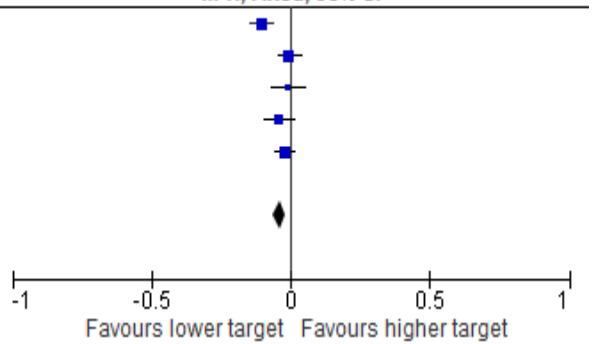


Typical RR 0.72 (95% CI 0.61 to 0.85)

Study or Subgroup	Lower targeting Events	Total	Higher targeting Events	Total	Weight	Risk Difference M-H, Fixed, 95% CI
Vaucher 2012	36	482	93	514	24.3%	-0.11 [-0.15, -0.07]
Schmidt 2013	63	500	66	503	24.5%	-0.01 [-0.05, 0.04]
BOOST NZ 2014	11	158	12	150	7.5%	-0.01 [-0.07, 0.05]
BOOST-II UK 2016	67	395	86	403	19.5%	-0.04 [-0.10, 0.01]
BOOST-II Australia 2016	37	487	48	497	24.1%	-0.02 [-0.06, 0.01]
Total (95% CI)		**2022**		**2067**	**100.0%**	**-0.04 [-0.06, -0.02]**
Total events	214		305			

Heterogeneity: Chi² = 15.10, df = 4 (P = 0.004); I² = 74%

Test for overall effect: Z = 4.03 (P < 0.0001)



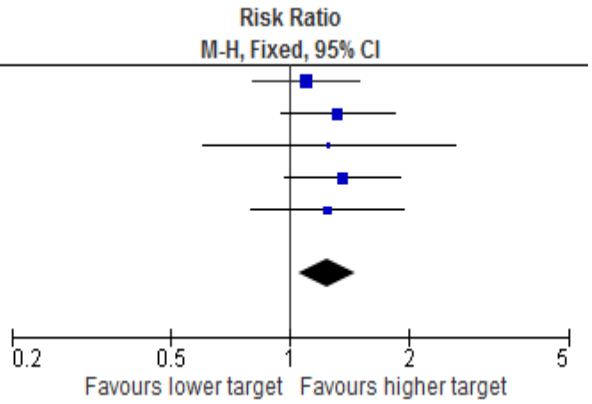
Typical RD -0.04 (95% CI -0.06 to -0.02)

Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Effect on Necrotizing Enterocolitis

Study or Subgroup	Lower oxygen saturation Events	Total	Higher oxygen saturation Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Vaucher 2012	76	641	70	649	31.2%	1.10 [0.81, 1.49]
Schmidt 2013	74	602	56	599	25.2%	1.31 [0.95, 1.83]
BOOST NZ 2014	15	170	12	170	5.4%	1.25 [0.60, 2.59]
BOOST-II UK 2016	71	484	52	480	23.4%	1.35 [0.97, 1.89]
BOOST-II Australia 2016	41	567	33	567	14.8%	1.24 [0.80, 1.94]
Total (95% CI)		**2464**		**2465**	**100.0%**	**1.24 [1.05, 1.47]**
Total events	277		223			

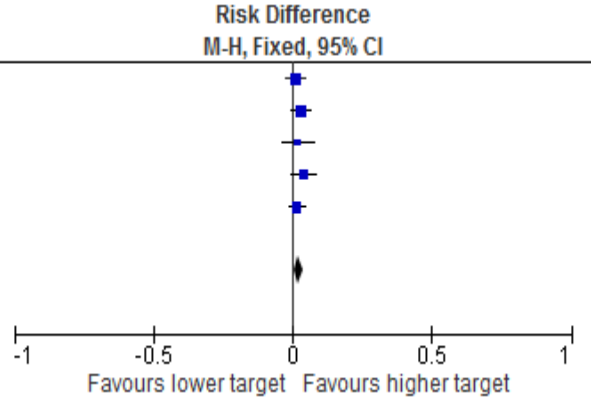
Heterogeneity: Chi² = 0.98, df = 4 (P = 0.91); I² = 0%
Test for overall effect: Z = 2.55 (P = 0.01)



Typical RR 1.24 (95% CI 1.05 to 1.47)

Study or Subgroup	Lower oxygen saturation Events	Total	Higher oxygen saturation Events	Total	Weight	Risk Difference M-H, Fixed, 95% CI
Vaucher 2012	76	641	70	649	26.2%	0.01 [-0.02, 0.05]
Schmidt 2013	74	602	56	599	24.4%	0.03 [-0.01, 0.06]
BOOST NZ 2014	15	170	12	170	6.9%	0.02 [-0.04, 0.08]
BOOST-II UK 2016	71	484	52	480	19.6%	0.04 [-0.00, 0.08]
BOOST-II Australia 2016	41	567	33	567	23.0%	0.01 [-0.01, 0.04]
Total (95% CI)		**2464**		**2465**	**100.0%**	**0.02 [0.01, 0.04]**
Total events	277		223			

Heterogeneity: Chi² = 1.47, df = 4 (P = 0.83); I² = 0%
Test for overall effect: Z = 2.56 (P = 0.01)



Typical RD 0.02 (95% CI 0.01 to 0.04)

Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Author's Conclusions:

In extremely preterm infants, targeting lower (85% to 89%) SpO_2 compared to higher (91% to 95%) SpO_2 had no significant effect on the composite outcome of death or major disability or on major disability alone, including blindness, but increased the average risk of mortality by 28 per 1000 infants treated.

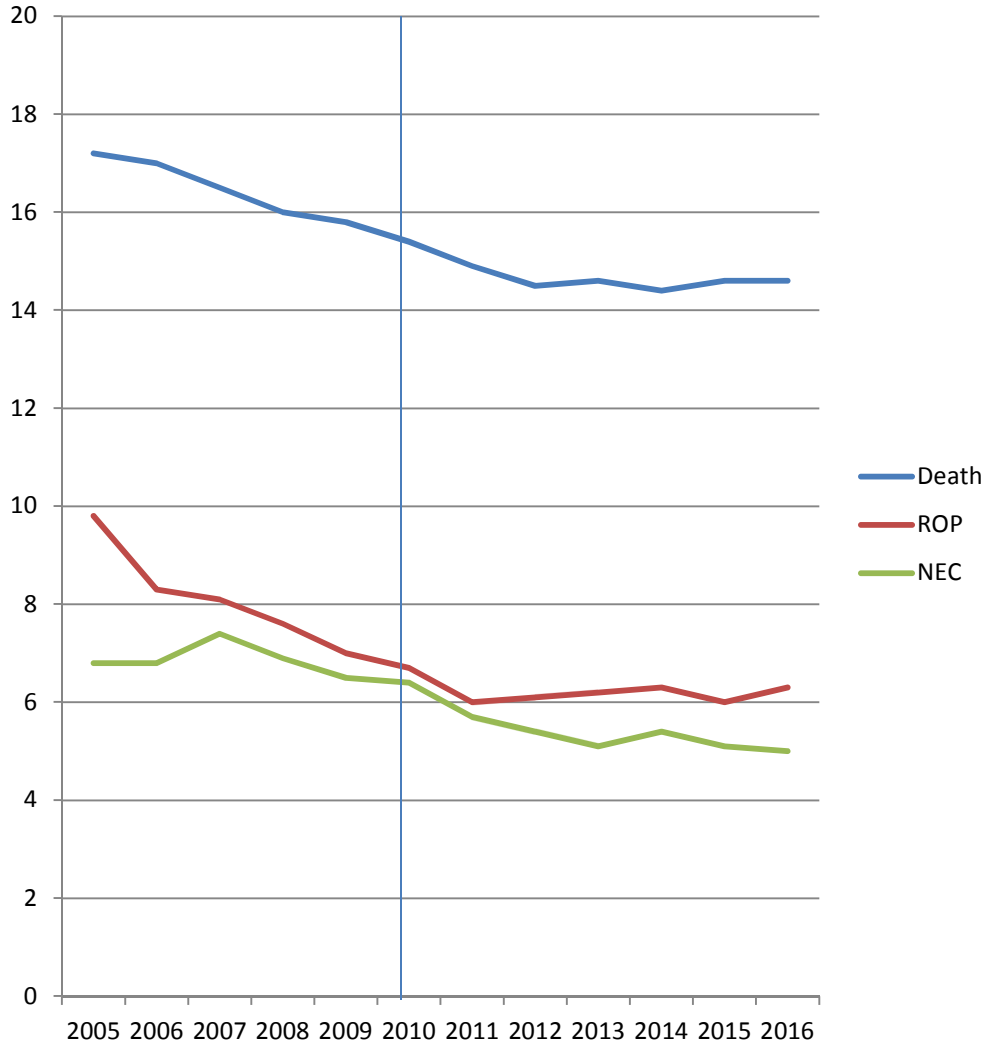
The trade-offs between the benefits and harms of the different oxygen saturation target ranges may need to be assessed within local settings (e.g. alarm limit settings, staffing, baseline outcome risks) when deciding on oxygen saturation targeting policies.

Effects of targeting lower versus higher arterial oxygen saturations on death or disability in preterm infants

Outcome of concern	Appropriate choice of saturation range (SpO_2)
Composite outcome of death or major disability	lower (85% to 89%) *or* higher (91% to 95%)
Death	higher (91% to 95%)
Retinopathy of Prematurity	lower (85% to 89%)
Necrotizing Enterocolitis	higher (91% to 95%)

Death, Severe ROP and NEC in the Vermont Oxford Network 2005-16

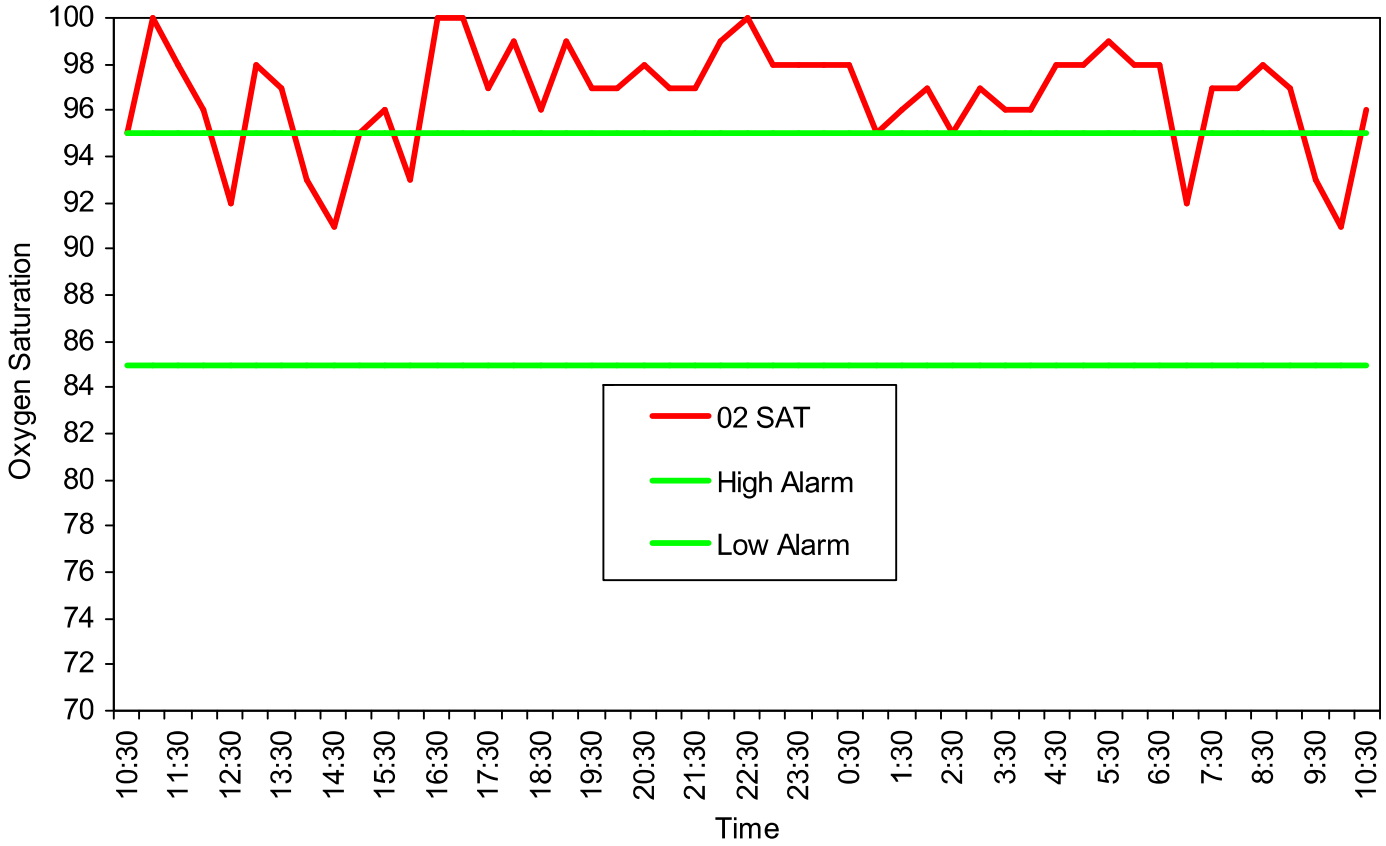
% of VLBW
(All centres)



Courtesy of Ben Stenson, MD
Vermont Oxford Network, unpublished data used by permission

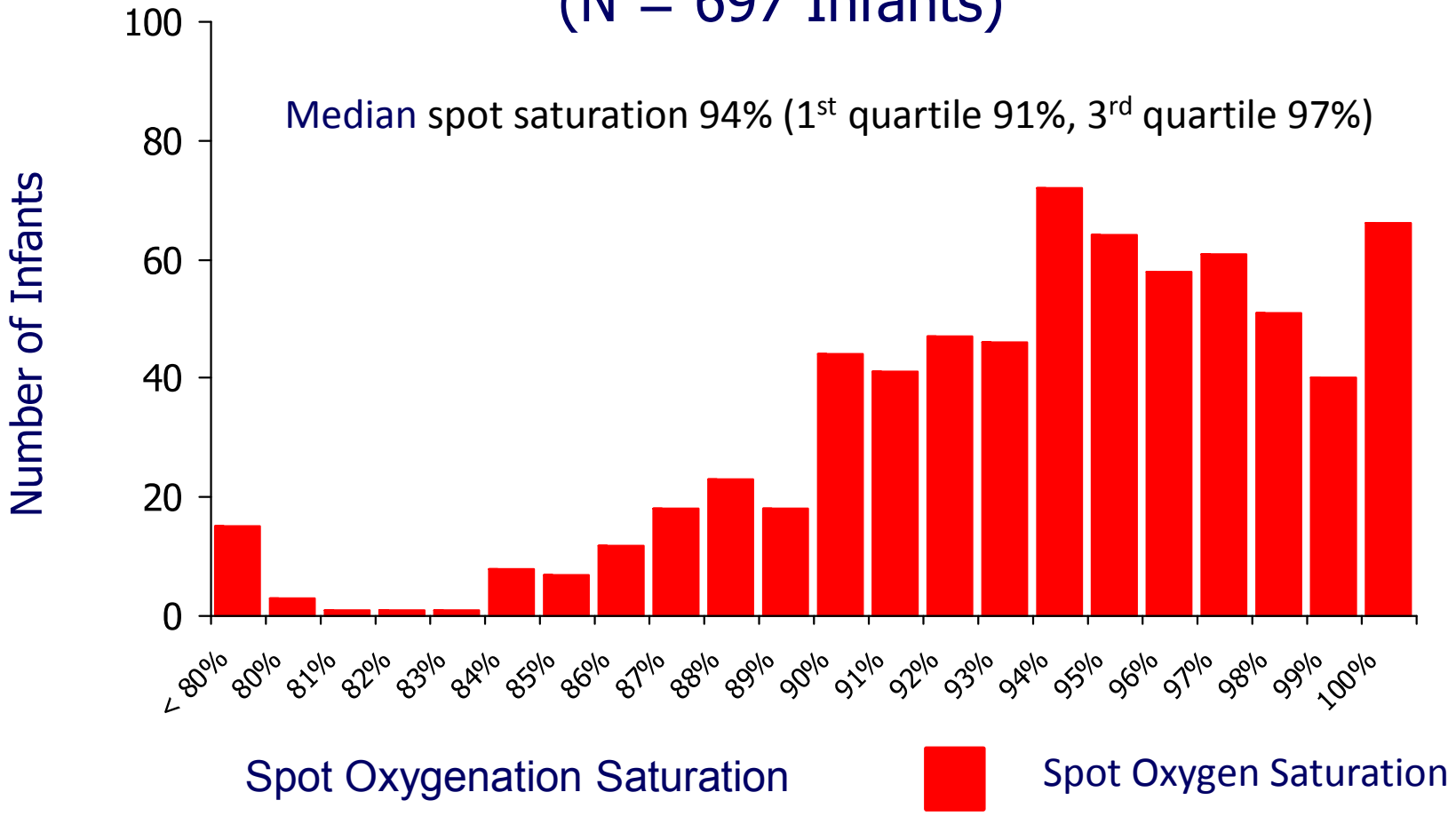
VON Vermont Oxford NETWORK

Hitting our targets is easier said than done!



VON Day Oxygen Monitoring Audit
Spot Oxygen Saturation

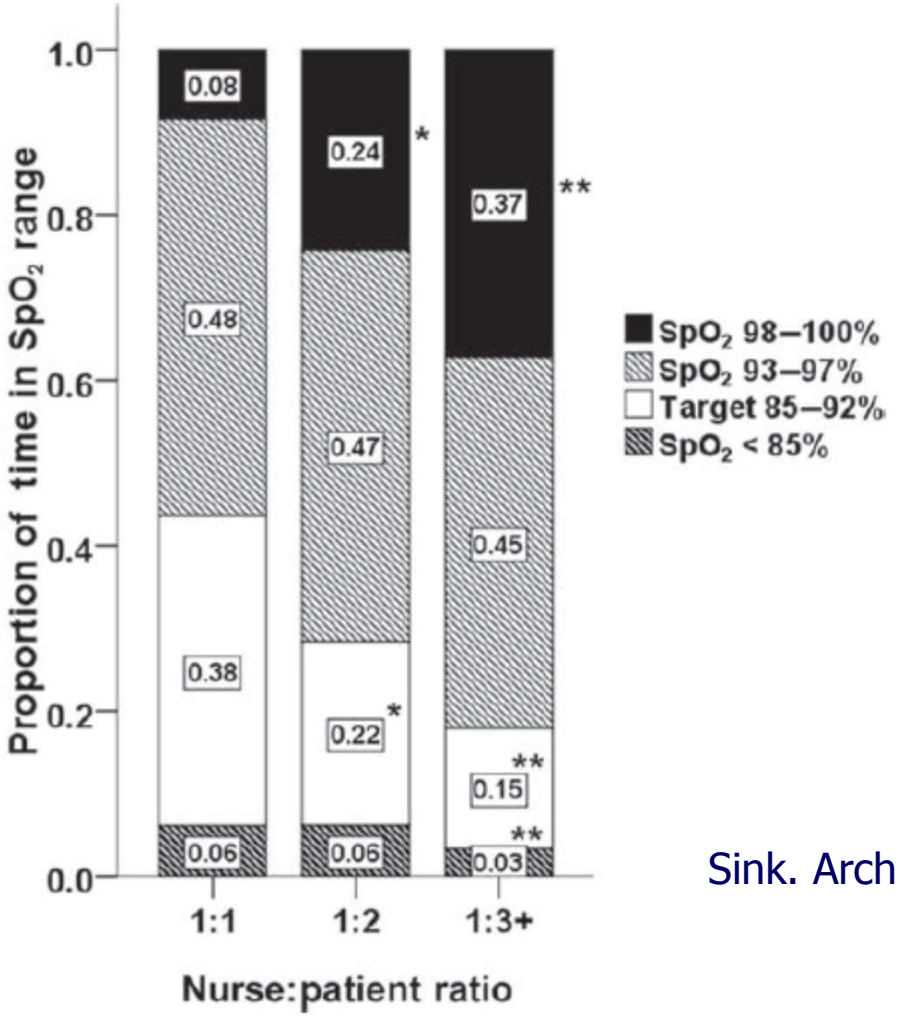
Infants on Oxygen and Respiratory Support (N = 697 Infants)



Vermont Oxford NETWORK

What's missing from this discussion?

Nurse:patient ratio and achievement of oxygen saturation goals in premature infants



Sink. Arch Dis Child Fetal Neonatal Ed. 2011

Mean proportion of time in specified oxygen saturation range

Compliance with alarm limits for pulse oximetry in very preterm infants

Dependent on:

Staff knowledge of unit policies and guidelines
Nurse / patient ratio
Patient acuity
Patient age

Trials have now shown us the appropriate range to maintain oxygen saturation.

Maintaining appropriate oxygen saturation is a complex task that includes oxygen targets, alarm settings and staff response and unit culture.

MORE ON OXYGEN!

SUPPLEMENTAL THERAPEUTIC OXYGEN FOR PRETHRESHOLD ROP

Eligibility Criteria

- Preterm infants screened for ROP
- Prethreshold ROP in at least one eye
- Median pulse oximetry saturation < 94%

The STOP-ROP Multicenter Study Group 2000

SUPPLEMENTAL THERAPEUTIC OXYGEN FOR PRETHRESHOLD ROP

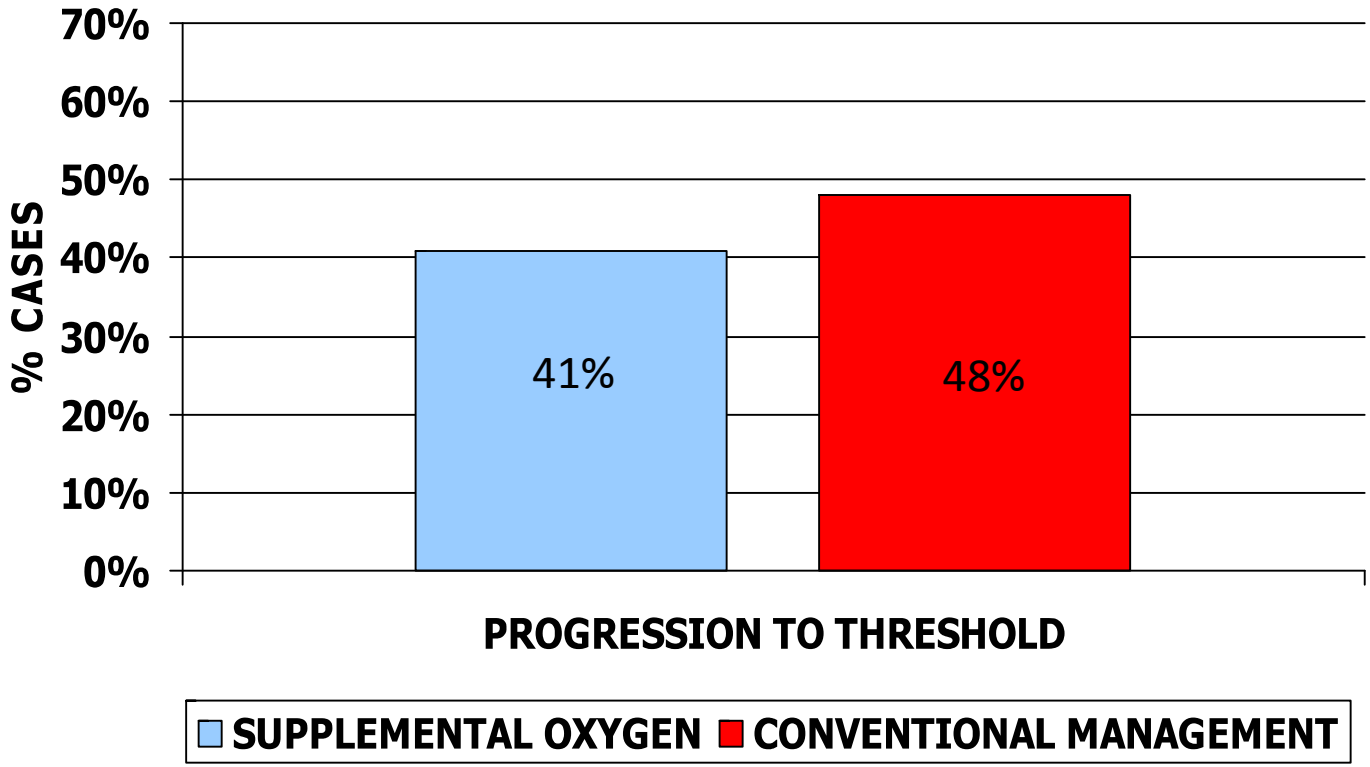
Intervention

- Continuous pulse oximetry monitoring
- Conventional arm: maintain oxygen saturation 89-94%
- Supplemental arm: maintain oxygen saturation 96-99%

The STOP-ROP Multicenter Study Group 2000

SUPPLEMENTAL THERAPEUTIC OXYGEN FOR PRETHRESHOLD ROP

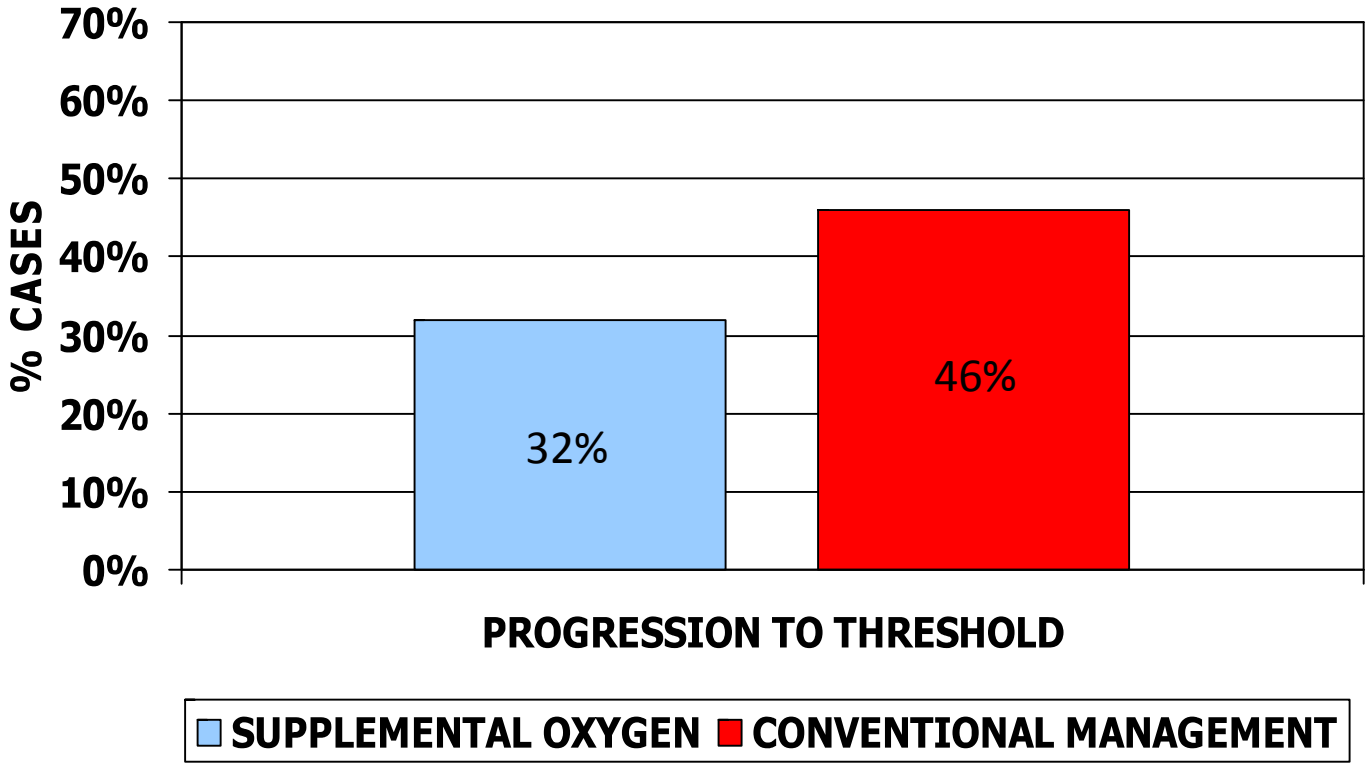
PROGRESSION TO THRESHOLD



The STOP-ROP Multicenter Study Group 2000

SUPPLEMENTAL THERAPEUTIC OXYGEN FOR PRETHRESHOLD ROP

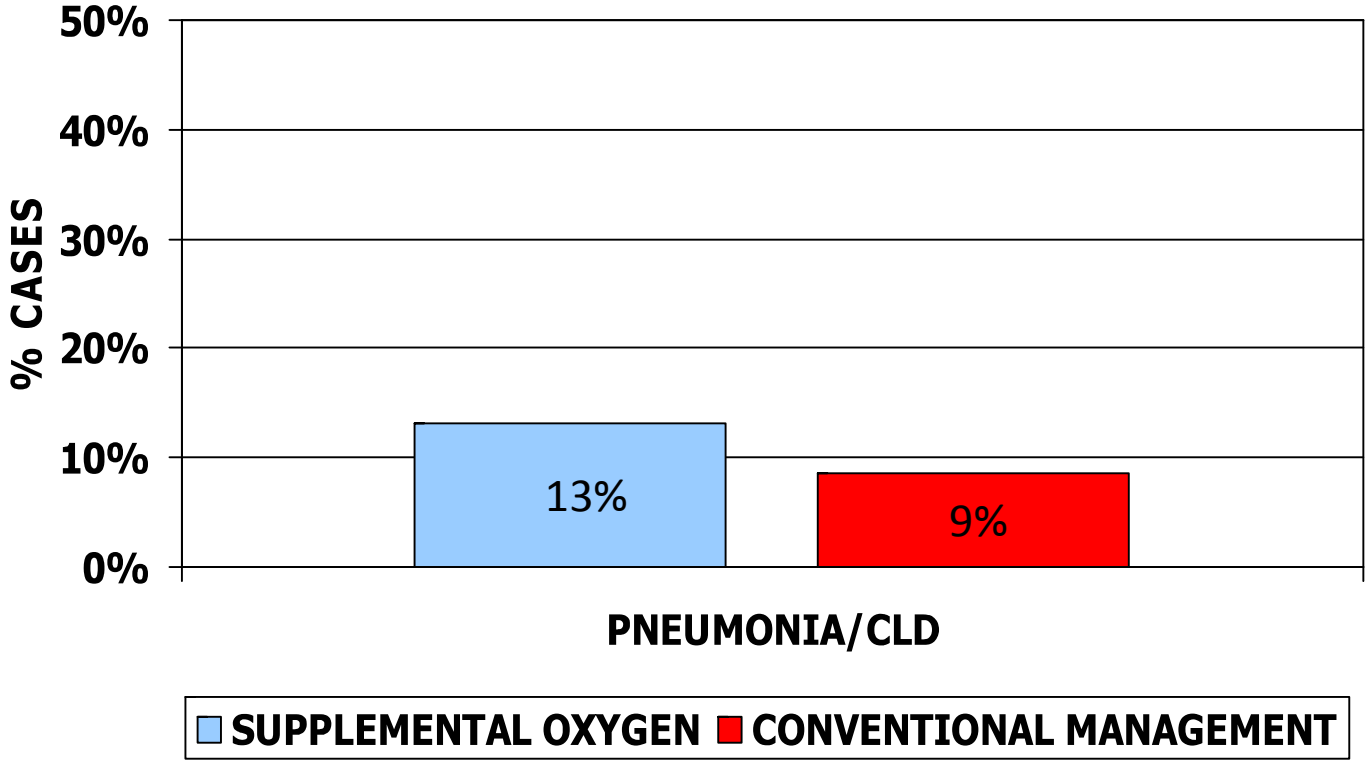
SUBGROUP ANALYSIS: INFANTS WITH PLUS DISEASE PROGRESSION TO THRESHOLD



The STOP-ROP Multicenter Study Group 2000

SUPPLEMENTAL THERAPEUTIC OXYGEN FOR PRETHRESHOLD ROP

PNEUMONIA/EXACERBATION OF CHRONIC LUNG DISEASE



The STOP-ROP Multicenter Study Group 2000

Moving on from oxygen, How else can we prevent or treat ROP?

LIGHT REDUCTION IN PREVENTING RETINOPATHY OF PREMATURITY

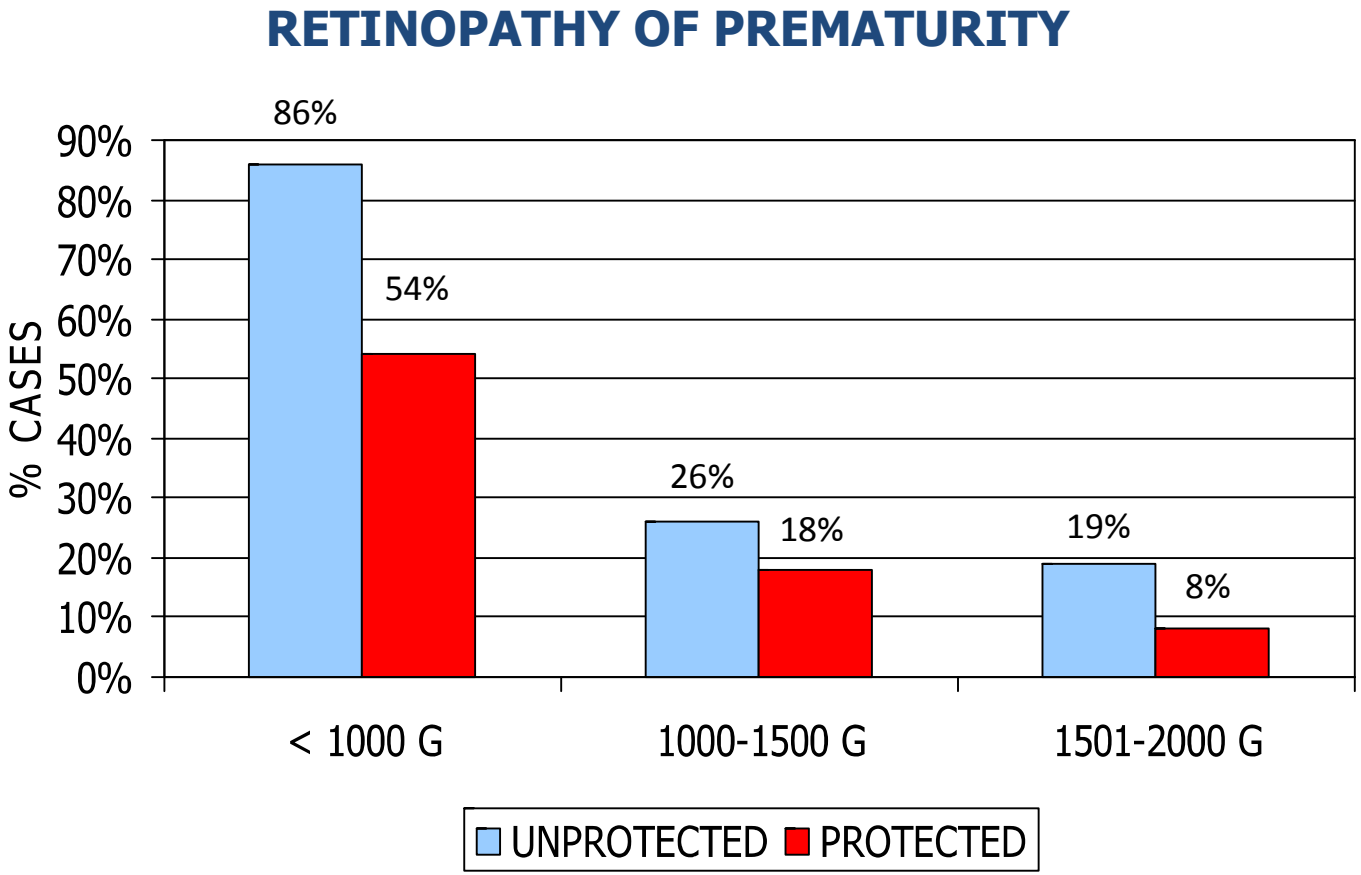
Glass and coworkers 1985

investigated effect of exposure to light in two intensive care nurseries

- standard bright nursery environment
- reduced light level environment

Effect of bright light in the Hospital Nursery on Retinopathy of Prematurity 1985

LIGHT REDUCTION IN PREVENTING RETINOPATHY OF PREMATURITY



Effect of bright light in the Hospital Nursery on Retinopathy of Prematurity 1985

Early light reduction for preventing retinopathy of prematurity in very low birth weight infants

Jorge EC, Jorge EN, El Dib RP. Early light reduction for preventing retinopathy of prematurity in very low birth weight infants. Cochrane Database of Systematic Reviews 2001, Issue 1. Art. No.: CD000122. DOI: 10.1002/14651858.CD000122.

Early light reduction for preventing retinopathy of prematurity in very low birth weight infants

Seiberth 1994: 169 infants of less than 1501 grams birth weight from one nursery were enrolled and then randomized to no patching or patching of both eyes from the day of birth until 35 weeks' postmenstrual age.

Braz 2006: 226 infants of less than 1600 grams birth weight or < 32 weeks' gestation were enrolled and randomized. In the experimental group, patching of both eyes began on the day of birth and continued until 35 weeks' postmenstrual age.

Kennedy 1997: 71 infants weighing 1250 grams or less, or of gestational age 32 weeks or less, were enrolled and randomized at 0 to 6 hours after birth to wearing goggles until 31 weeks' postmenstrual age.

Reynolds 1998: 409 infants of less than 31 weeks' gestation and less than 1251 grams birth weight were randomized to wearing goggles or control. The goggles were placed on the infant within 24 hours of birth, reducing light by 97% (100% of ultraviolet) and were continued until the infant was 31 weeks' postmenstrual age or four weeks chronological age, whichever occurred later.

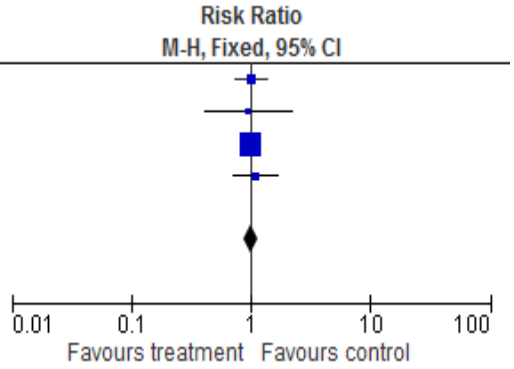
Jorge EC, Jorge EN, El Dib RP. Early light reduction for preventing retinopathy of prematurity in very low birth weight infants. Cochrane Database of Systematic Reviews 2001, Issue 1. Art. No.: CD000122. DOI: 10.1002/14651858.CD000122.

Early light reduction for preventing retinopathy of prematurity in very low birth weight infants

Effect on Any Retinopathy of Prematurity in infants < 2001 grams

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Braz 2006	44	95	43	93	21.6%	1.00 [0.74, 1.36]
Kennedy 1997	7	24	8	26	3.8%	0.95 [0.41, 2.22]
Reynolds 1998	130	188	121	173	62.5%	0.99 [0.86, 1.13]
Seiberth 1994	26	62	25	65	12.1%	1.09 [0.71, 1.67]
Total (95% CI)		**369**		**357**	**100.0%**	**1.00 [0.89, 1.13]**
Total events	207		197			

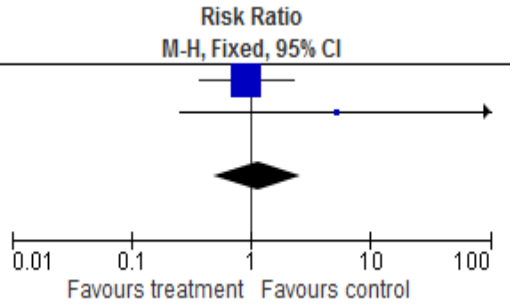
Heterogeneity: Chi² = 0.21, df = 3 (P = 0.98); I² = 0%
Test for overall effect: Z = 0.04 (P = 0.97)



Effect on "poor" Retinopathy of Prematurity outcomes in infants < 2001 grams

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Reynolds 1998	9	188	9	173	95.0%	0.92 [0.37, 2.26]
Seiberth 1994	2	62	0	65	5.0%	5.24 [0.26, 106.98]
Total (95% CI)		**250**		**238**	**100.0%**	**1.13 [0.49, 2.61]**
Total events	11		9			

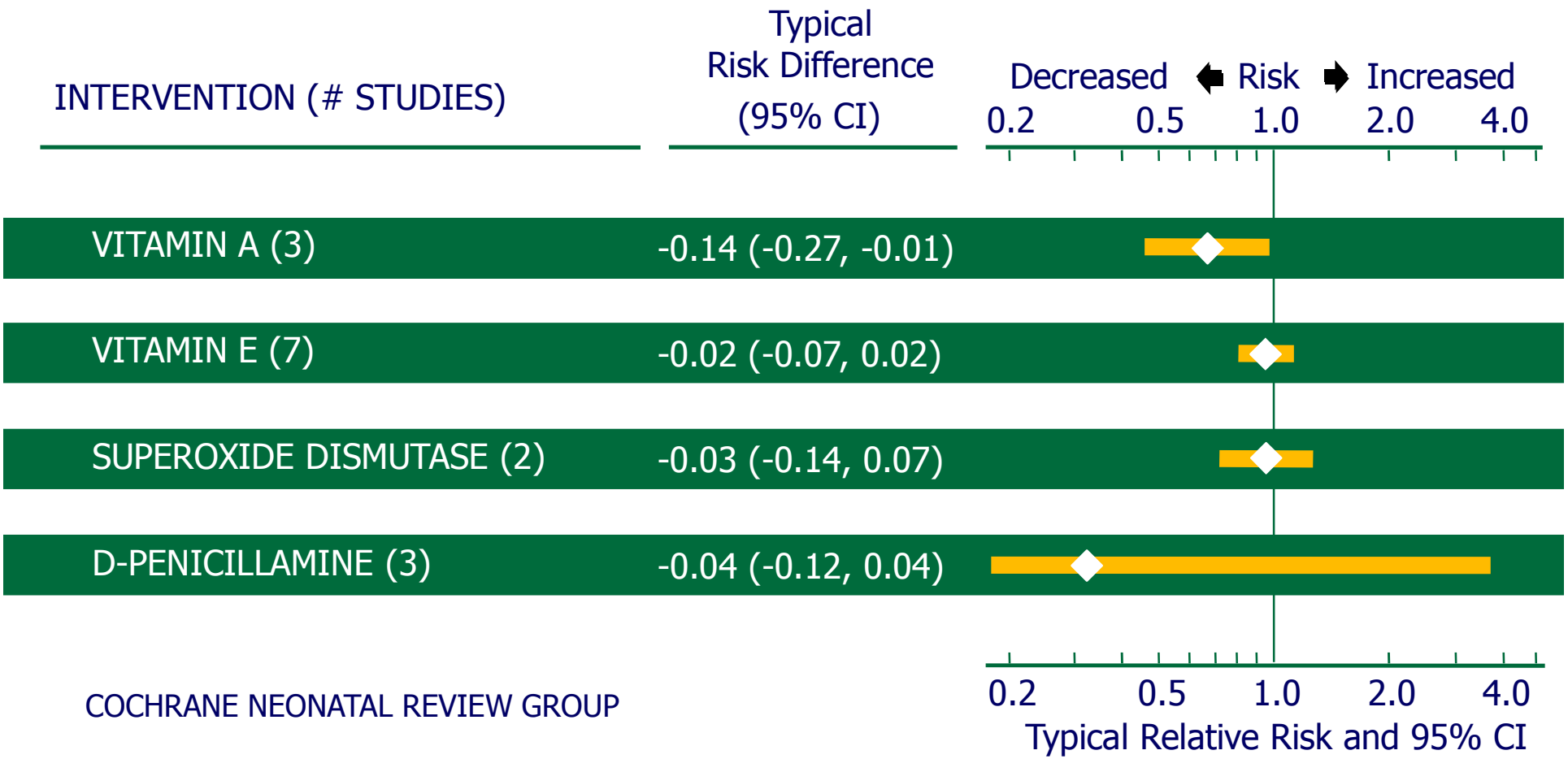
Heterogeneity: Chi² = 1.20, df = 1 (P = 0.27); I² = 16%
Test for overall effect: Z = 0.30 (P = 0.77)



Jorge EC, Jorge EN, El Dib RP. Early light reduction for preventing retinopathy of prematurity in very low birth weight infants. Cochrane Database of Systematic Reviews 2001, Issue 1. Art. No.: CD000122. DOI: 10.1002/14651858.CD000122.

EFECT OF ANTI OXIDANT THERAPY ON RETINOPATHY OF PREMATURITY

OVERVIEW OF RANDOMIZED CONTROLLED TRIALS



COCHRANE NEONATAL REVIEW GROUP

Beta-blockers for prevention and treatment of retinopathy of prematurity in preterm infants

Kaempfen S, Neumann RP, Jost K, Schulzke SM. Beta-blockers for prevention and treatment of retinopathy of prematurity in preterm infants. Cochrane Database of Systematic Reviews 2015, Issue 9. Art. No.: CD011893. DOI: 10.1002/14651858.CD011893. (full review pending publication January 2018)

Beta-blockers for prevention and treatment of retinopathy of prematurity in preterm infants

Background: The use of beta-adrenergic blocking agents (beta-blockers), which modulate the vasoproliferative retinal process, may reduce the progression of ROP or even restore established ROP.

Objectives: To determine the effect of beta-blockers on short-term structural outcomes, long-term functional outcomes, and the need for additional treatment, when used either as prophylaxis in preterm infants without ROP, stage 1 ROP (zone I), or stage 2 ROP (zone II) without plus disease or as treatment in preterm infants with at least prethreshold ROP.

Beta-blockers for prevention and treatment of retinopathy of prematurity in preterm infants

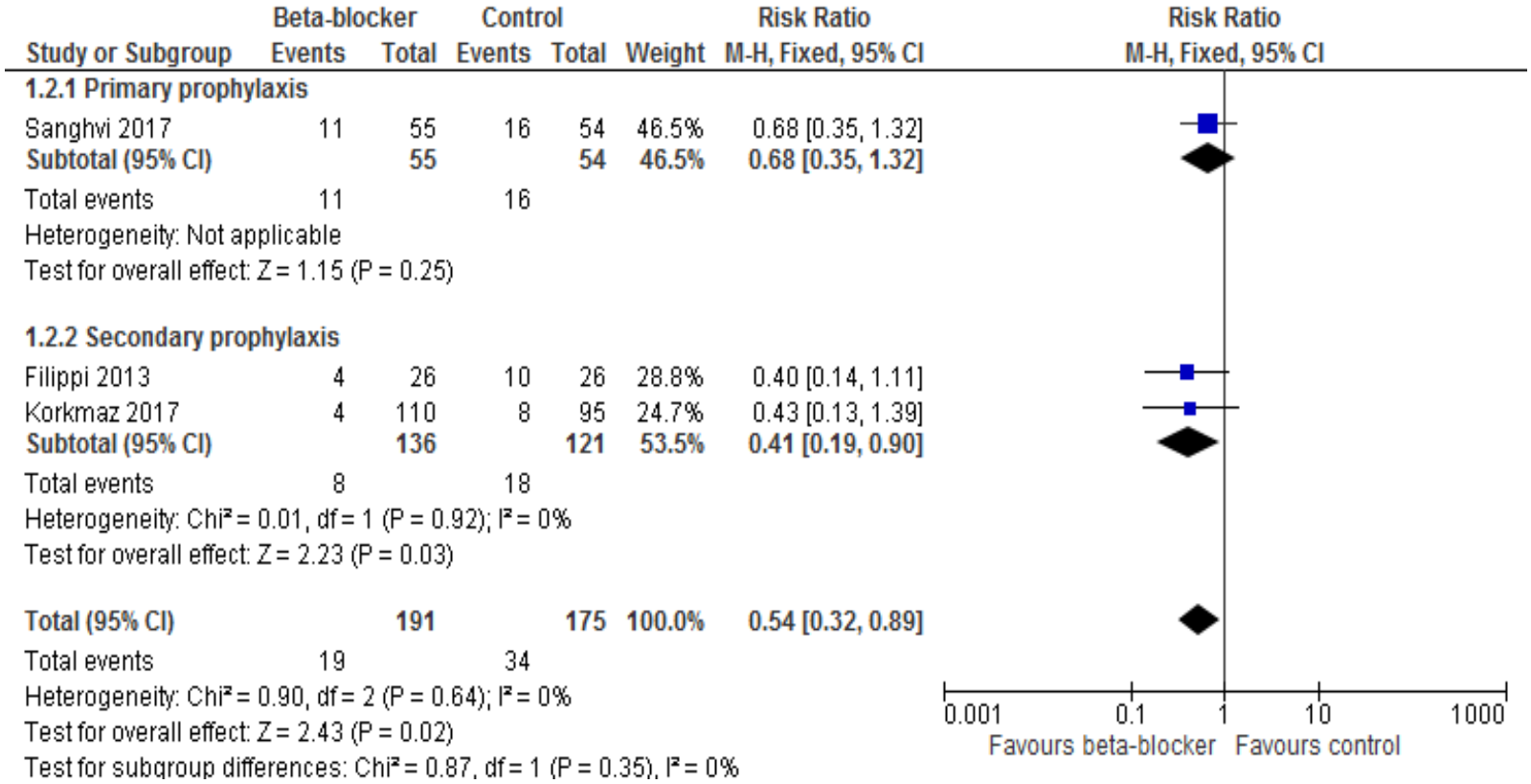
Three studies incorporating a total of 366 preterm infants met inclusion criteria of this review (Filippi 2013; Korkmaz 2017; Sanghvi 2017).

These trials were conducted as ROP prevention trials and included preterm infants diagnosed with ≤ stage 2 ROP without plus disease (Filippi 2013; Korkmaz 2017) or preterm neonates in whom ROP was not assessed at enrolment but very unlikely to be present as they were < 8 days old (Sanghvi 2017).

Of the three included trials, two trials were placebo-controlled (Korkmaz 2017; Sanghvi 2017), while the third trial compared beta-blocker administration to no treatment (Filippi 2013).

Beta-blockers for prevention and treatment of retinopathy of prematurity in preterm infants

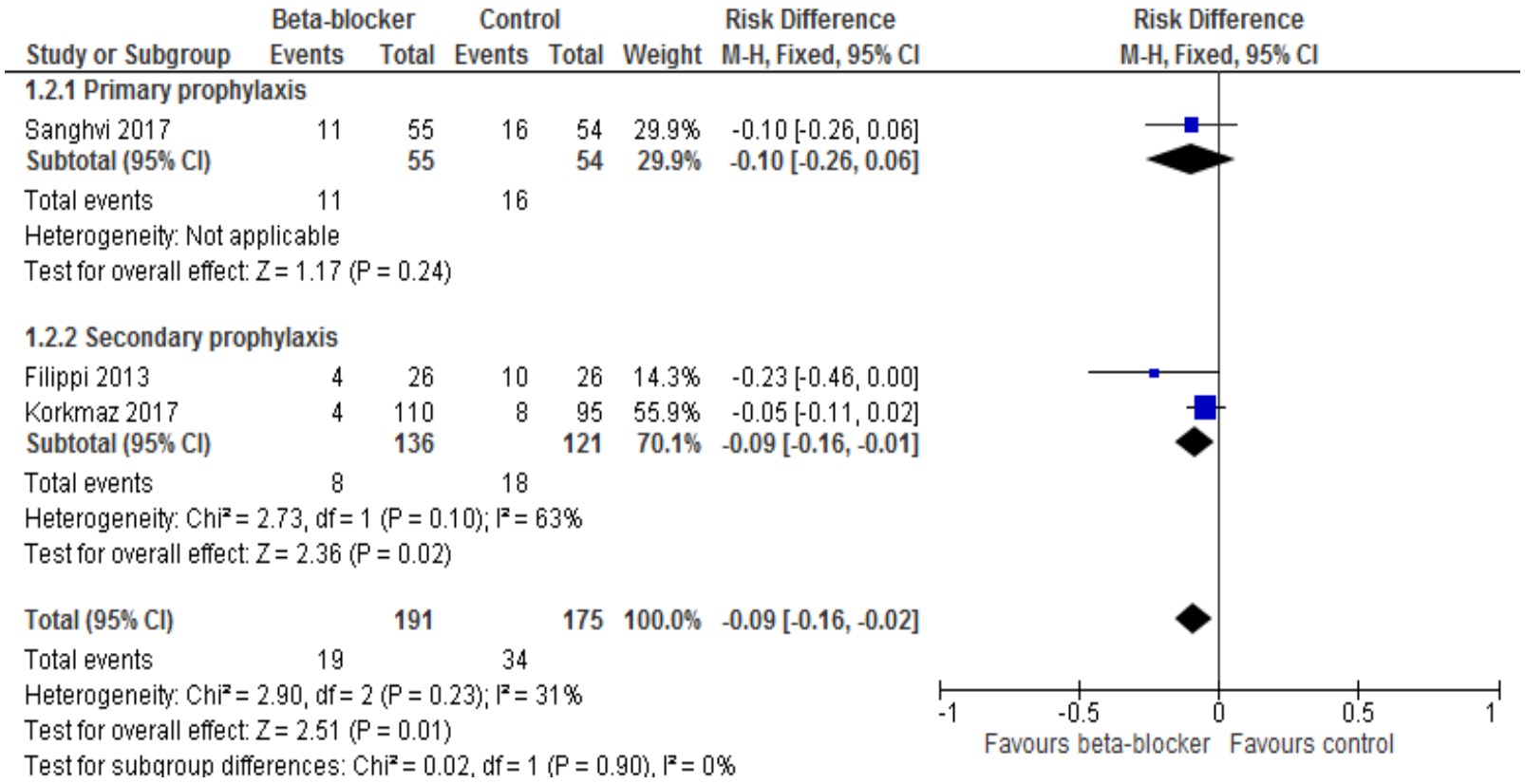
Effect on use or retinal ablation surgery



Typical RR 0.54 (95% CI 0.32 to 0.89)

Beta-blockers for prevention and treatment of retinopathy of prematurity in preterm infants

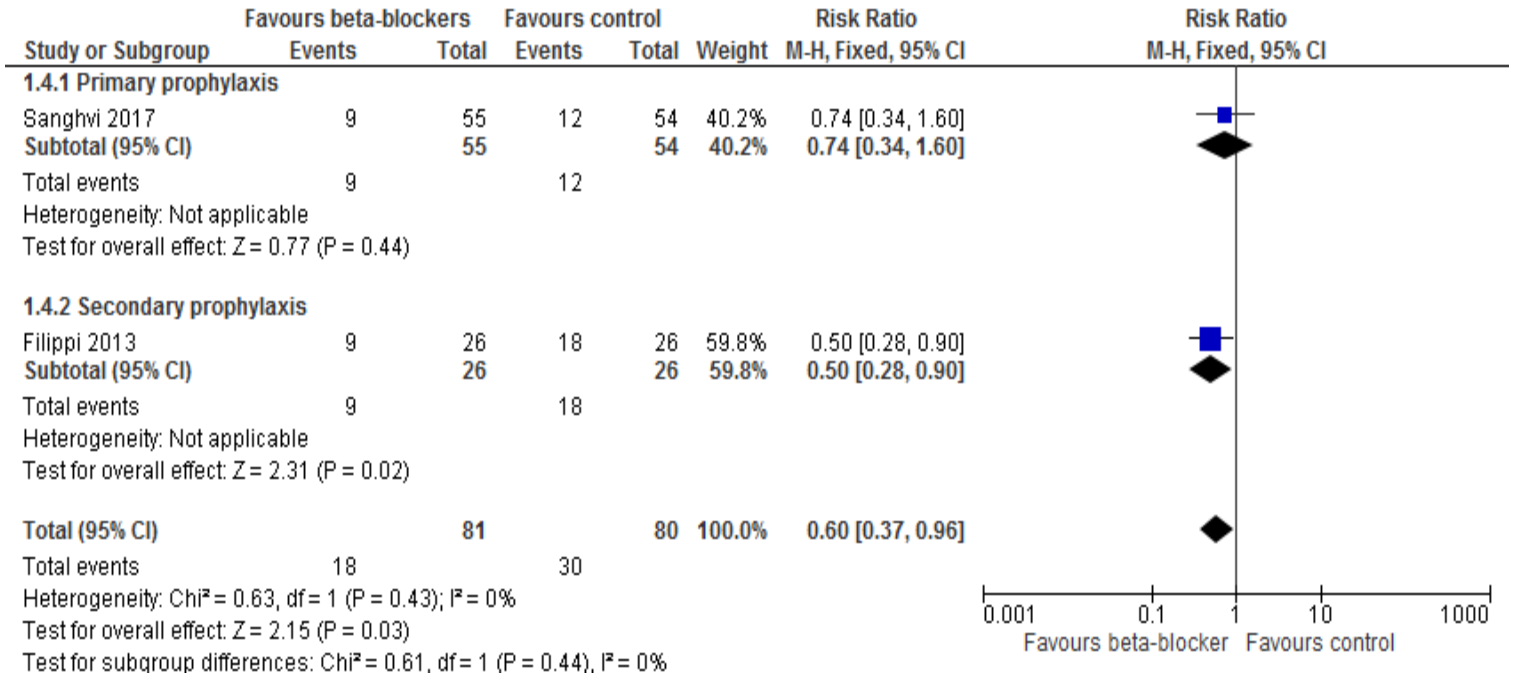
Effect on use or retinal ablation surgery



Typical RD -0.09 (95% CI -0.16 to -0.02)

Beta-blockers for prevention and treatment of retinopathy of prematurity in preterm infants

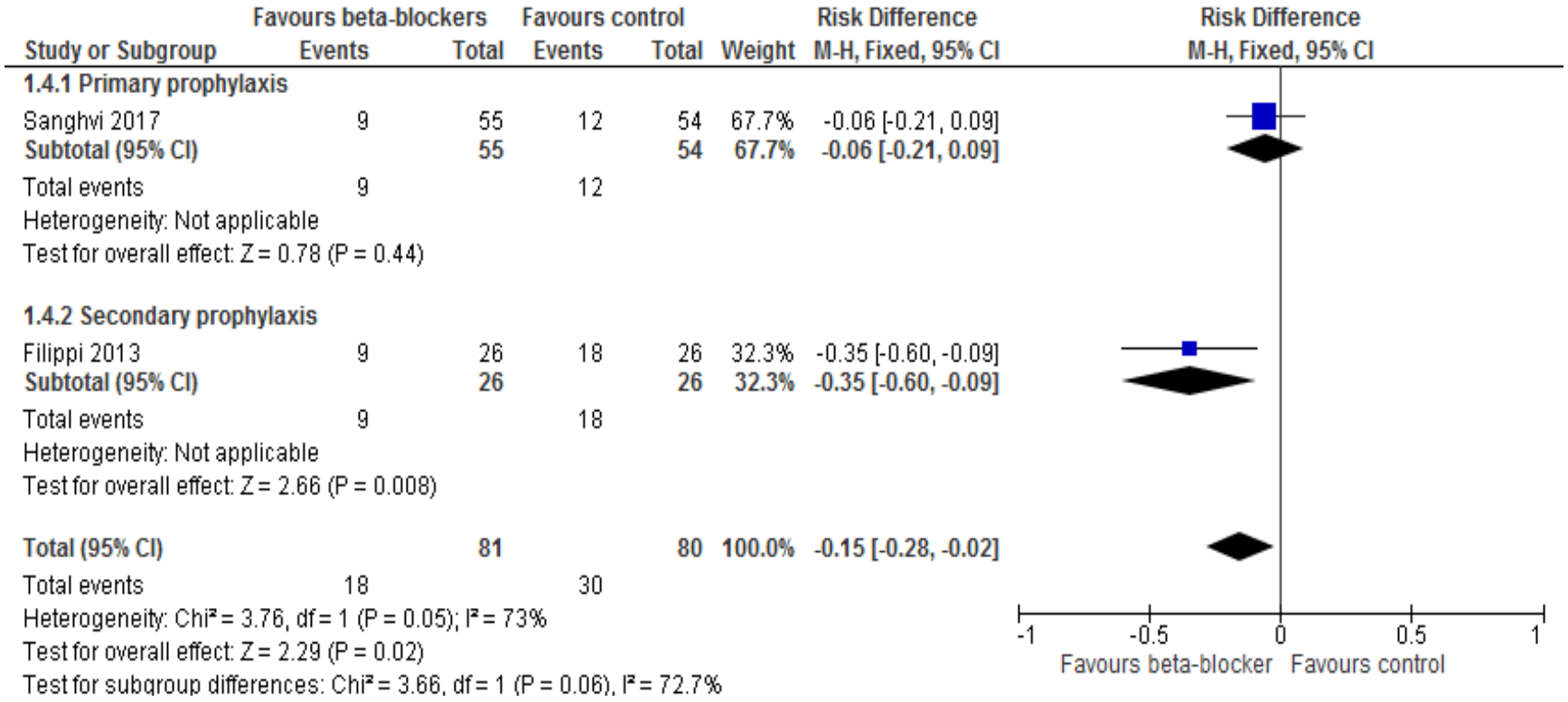
Effect on progression to stage 3 ROP



Typical RR 0.60 (95% CI 0.37 to 0.96)

Beta-blockers for prevention and treatment of retinopathy of prematurity in preterm infants

Effect on progression to stage 3 ROP



Typical RD -0.15 (95% CI -0.28 to -0.02)

Beta-blockers for prevention and treatment of retinopathy of prematurity in preterm infants

Concern and impression regarding other important clinical outcomes

Outcome (# studies)	Typical RR (95% CI)
Hypotension (3)	7.00 (0.38 to 129.11)
Bronchopulmonary Dysplasia (2)	1.14 (0.75 to 1.73)
Necrotizing Enterocolitis (2)	2.45 (0.50 to 12.11)
Mortality (2)	0.99 (0.30 to 3.29)

Beta-blockers for prevention and treatment of retinopathy of prematurity in preterm infants

Authors' conclusions: Limited evidence of low to moderate quality suggests that prophylactic administration of oral beta-blockers might reduce progression towards stage 3 ROP and decrease the need of anti-VEGF agents or laser therapy.

The clinical relevance of those findings is unclear as no data on long-term visual impairment were reported.

Adverse events attributed to oral propranolol at a dose of 2 mg/kg/d raise concerns regarding systemic administration of this drug for prevention of ROP at the given dose.

Inositol in preterm infants at risk for or having respiratory distress syndrome

Howlett A, Ohlsson A, Plakkal N. Inositol in preterm infants at risk for or having respiratory distress syndrome. Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD000366. DOI: 10.1002/14651858.CD000366.pub3.

Inositol in preterm infants at risk for or having respiratory distress syndrome

Background: Inositol is an essential nutrient required by human cells in culture for growth and survival. Inositol promotes maturation of several components of surfactant and may play a critical role in fetal and early neonatal life.

Objectives: To assess the effectiveness and safety of supplementary inositol in preterm infants with or without respiratory distress syndrome (RDS) in reducing adverse neonatal outcomes.

Results: Four published RCTs and one ongoing RCT were identified

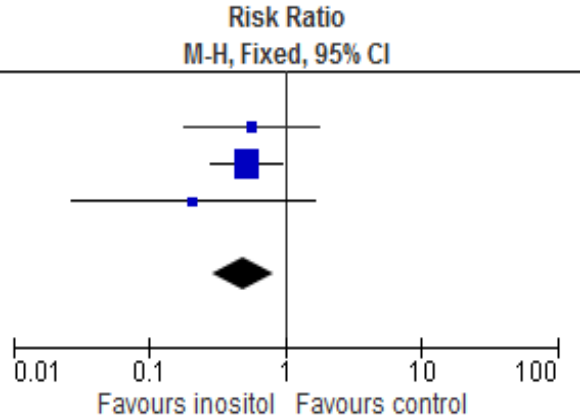
Inositol in preterm infants at risk for or having respiratory distress syndrome

Effect on Neonatal Mortality

Study or Subgroup	Inositol Events	Inositol Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Friedman 1995	0	24	0	24		Not estimable
Hallman 1986	4	37	7	37	18.5%	0.57 [0.18, 1.79]
Hallman 1992	13	114	26	119	67.4%	0.52 [0.28, 0.96]
Phelps 2016	1	28	6	35	14.1%	0.21 [0.03, 1.63]
Total (95% CI)		**203**		**215**	**100.0%**	**0.49 [0.29, 0.82]**
Total events	18		39			

Heterogeneity: Chi² = 0.78, df = 2 (P = 0.68); I² = 0%

Test for overall effect: Z = 2.70 (P = 0.007)

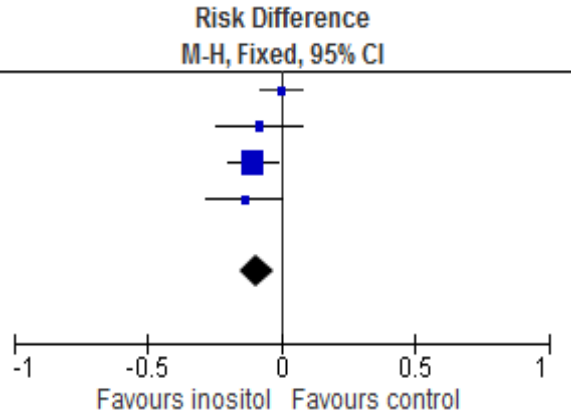


Typical RR 0.49 (95% CI 0.29 to 0.82)

Study or Subgroup	Inositol Events	Inositol Total	Control Events	Control Total	Weight	Risk Difference M-H, Fixed, 95% CI
Friedman 1995	0	24	0	24	11.5%	0.00 [-0.08, 0.08]
Hallman 1986	4	37	7	37	17.7%	-0.08 [-0.24, 0.08]
Hallman 1992	13	114	26	119	55.8%	-0.10 [-0.20, -0.01]
Phelps 2016	1	28	6	35	14.9%	-0.14 [-0.28, 0.01]
Total (95% CI)		**203**		**215**	**100.0%**	**-0.09 [-0.16, -0.03]**
Total events	18		39			

Heterogeneity: Chi² = 5.93, df = 3 (P = 0.11); I² = 49%

Test for overall effect: Z = 2.83 (P = 0.005)

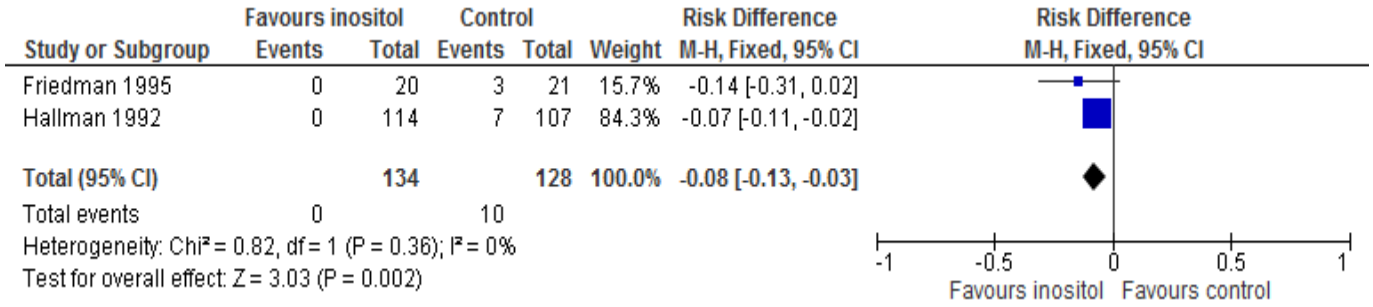


Typical RD -0.09 (95% CI -0.16 to -0.03)

Inositol in preterm infants at risk for or having respiratory distress syndrome

Effect on Retinopathy of Prematurity Stage ≥ 3

Typical RR 0.09 (95% CI 0.01 to 0.67)



Typical RD -0.08 (95% CI -0.13 to -0.03)

NICHD Neonatal Research Network Inositol Trial
Concerning preliminary reports

Objective: To test the safety and efficacy of inositol to improve survival without severe ROP, defined as Type 1 ROP, in very preterm infants.

Design/Methods: We conducted a randomized, placebo controlled trial of Inositol (INS) in preterm infants.

18 centers of the NICHD Neonatal Research Network conducted a randomized controlled trial of 5% inositol given daily to infants < 28 weeks' gestation until 10 weeks chronologic age, 34 weeks' postmenstrual age, or discharge.

Preliminary results: The Data Safety Monitoring Committee ultimately recommended cessation of the trial for a safety concern, unrelated to the manufacturing issue after enrollment of 638 infants.

The unfavorable outcome of Type 1 ROP or death prior to ROP determination was 21% in the placebo group, and 29% in the INS group, $p<0.01$.

Late onset sepsis was more common in the INS group (26%, vs 20% in placebo), although the difference was not statistically significant ($p=0.06$). Other diagnoses including BPD and severe IVH, adverse events, and serious adverse events occurred at similar rates in the two groups.

Conclusion(s): Daily inositol at 80mg/kg/day for up to10 weeks did not benefit infants < 28 weeks' gestation, and may be harmful for extremely preterm infants. The biologic mechanism for these findings is unknown.

Treatment of Retinopathy of Prematurity

Peripheral retinal ablation for threshold retinopathy of prematurity in preterm infants

Andersen C, Phelps D. Peripheral retinal ablation for threshold retinopathy of prematurity in preterm infants. Cochrane Database of Systematic Reviews 1999, Issue 3. Art. No.: CD001693. DOI: 10.1002/14651858.CD001693.

MULTICENTER TRIAL OF CRYOTHERAPY

- Infants weighing less than 1251 grams
- Ophthalmologic examinations to begin at 4-6 weeks of age
- Repeated every two weeks until “prethreshold”
- Repeated weekly until “threshold”

Cryotherapy for Retinopathy of Prematurity Cooperative Group 1988

MULTICENTER TRIAL OF CRYOTHERAPY

"threshold" disease

at least five contiguous or eight cumulative 30 degree sectors of stage 3 ROP in zone 1 or 2 in the presence of plus disease

Cryotherapy for Retinopathy of Prematurity Cooperative Group 1988

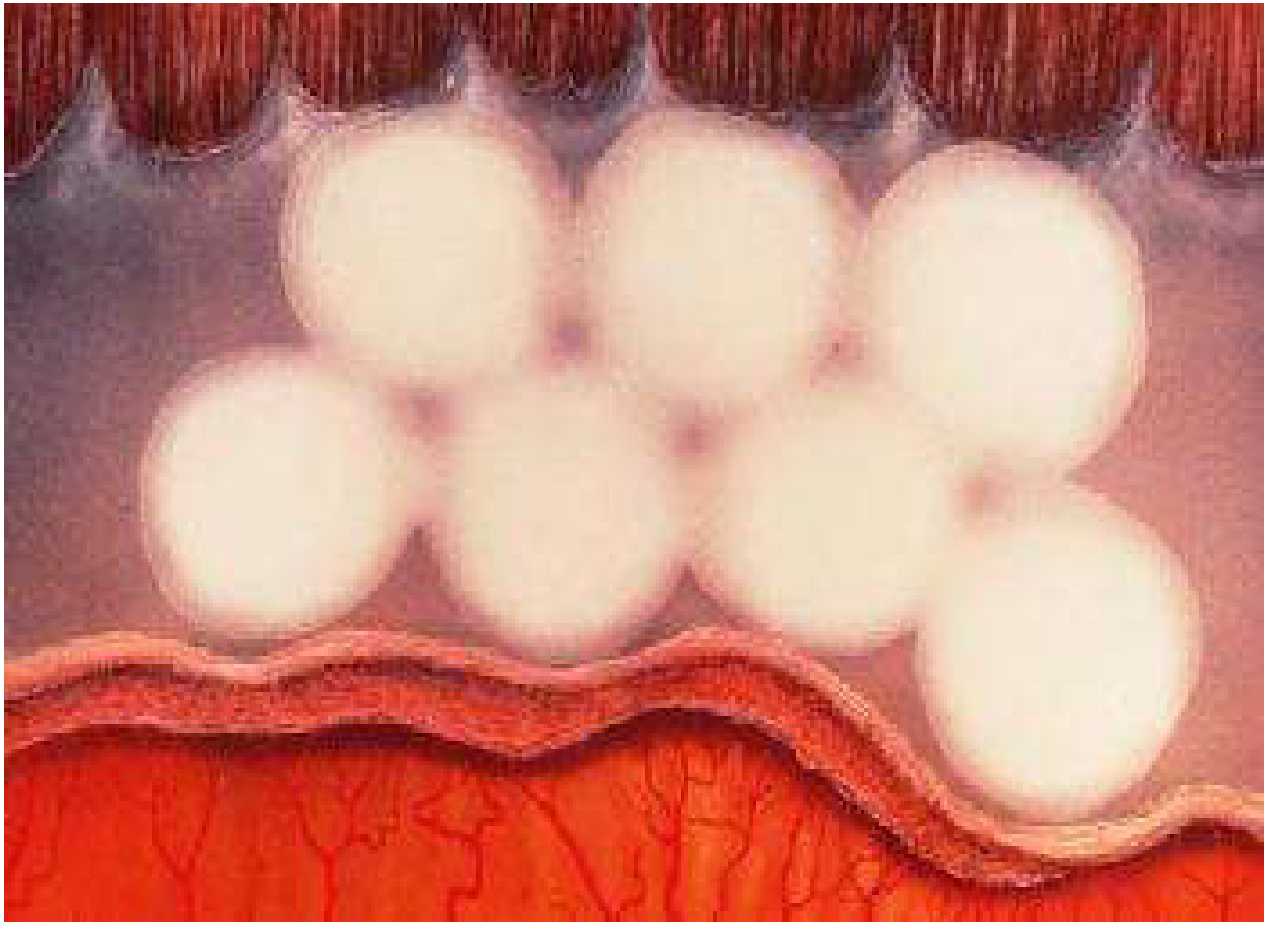
MULTICENTER TRIAL OF CRYOTHERAPY

Randomization

- "symmetric": both eyes meet threshold
  one eye randomly assigned to treatment
- "asymmetric": one eye met threshold
  randomize worst eye

Cryotherapy for Retinopathy of Prematurity Cooperative Group 1988

MULTICENTER TRIAL OF CRYOTHERAPY



Cryotherapy for Retinopathy of Prematurity Cooperative Group 1988

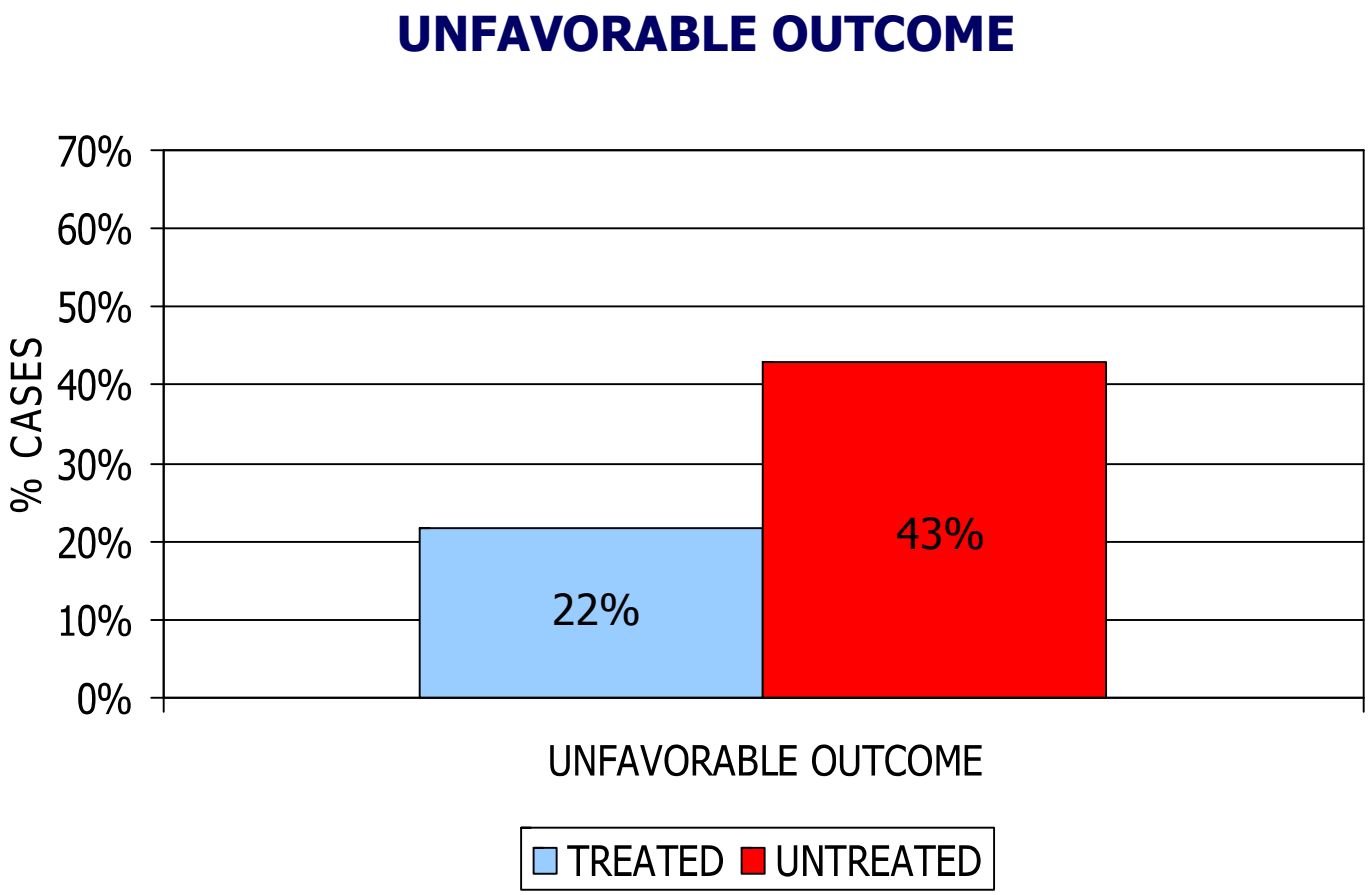
MULTICENTER TRIAL OF CRYOTHERAPY

Unfavorable outcome

- a retinal fold involving the macula
- retinal detachment involving zone 1
- retrolental tissue or "mass"

Cryotherapy for Retinopathy of Prematurity Cooperative Group 1988

MULTICENTER TRIAL OF CRYOTHERAPY



Cryotherapy for Retinopathy of Prematurity Cooperative Group 1988

COMPLICATIONS OF CRYOTHERAPY

Intraoperative ocular complications

- conjunctival hematoma 10%
- conjunctival hemorrhage 5%

Systemic complications

- bradycardia/arrhythmia 9%
- cyanosis 2%

Cryotherapy for Retinopathy of Prematurity Cooperative Group 1988

LASER PHOTOCOAGULATION VS. CRYOTHERAPY FOR THRESHOLD ROP

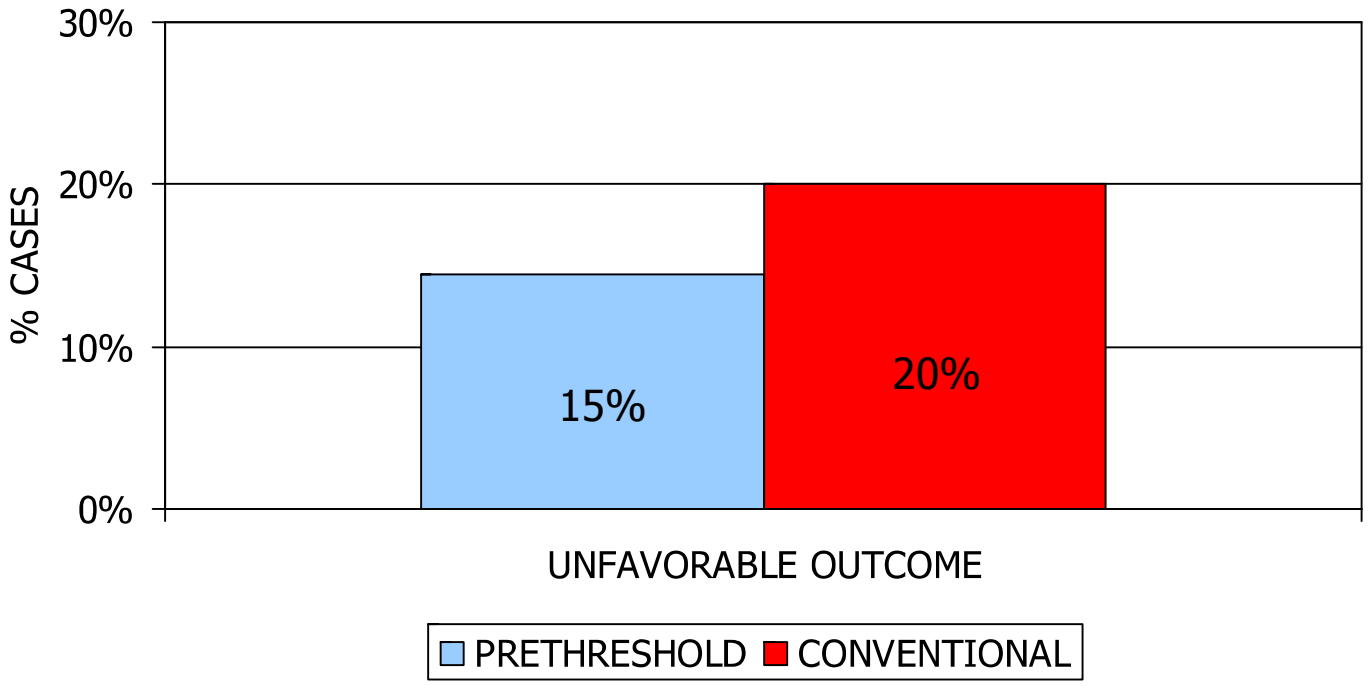
VISUAL ACUITY

- Follow up at ten years of age
- Good outcome defined as 20/50 or better
- Odds ratio for "good outcome":
  5.2 (95% CI 1.4, 19.8)

NG and coworkers Ophthalmology 2002: 928-934

EARLY TREATMENT FOR RETINOPATHY OF PREMATURITY TRIAL

UNFAVORABLE OUTCOME



Early Treatment for Retinopathy of Prematurity Cooperative Group. Arch Ophthalmol. 2003; 121: 1684-1696

Retinopathy of Prematurity

ROP Surgery

VERMONT OXFORD NETWORK ANNUAL REPORTS 2000-2016

ANTI VEGF
IN THE TREATMENT
OF RETINOPATHY
OF PREMATURITY

Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity

Sankar M Jeeva, Sankar J, Mehta M, Bhat V, Srinivasan R. Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity. Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD009734. DOI: 10.1002/14651858.CD009734.pub2. (update pending publication December 2017)

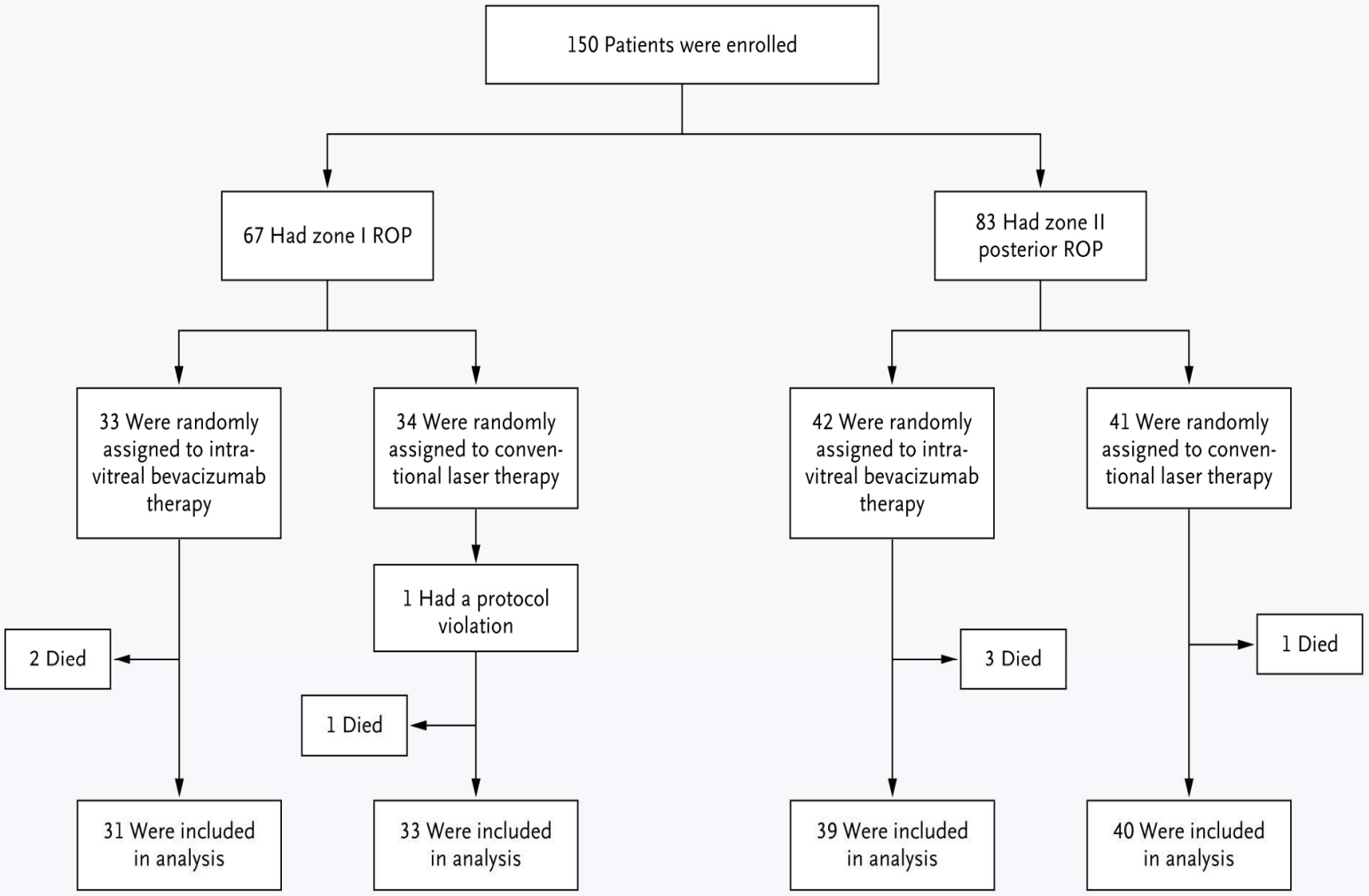
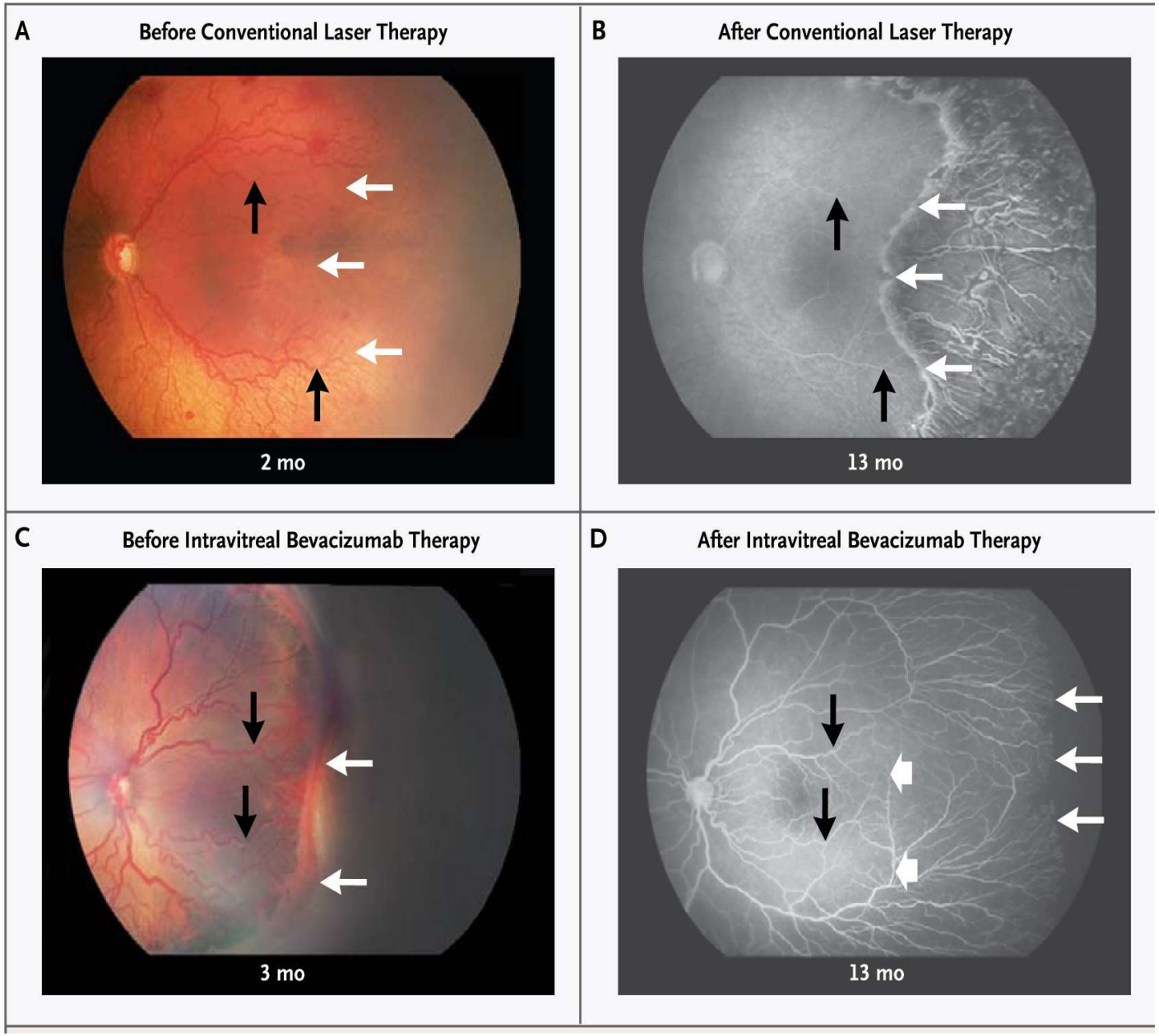


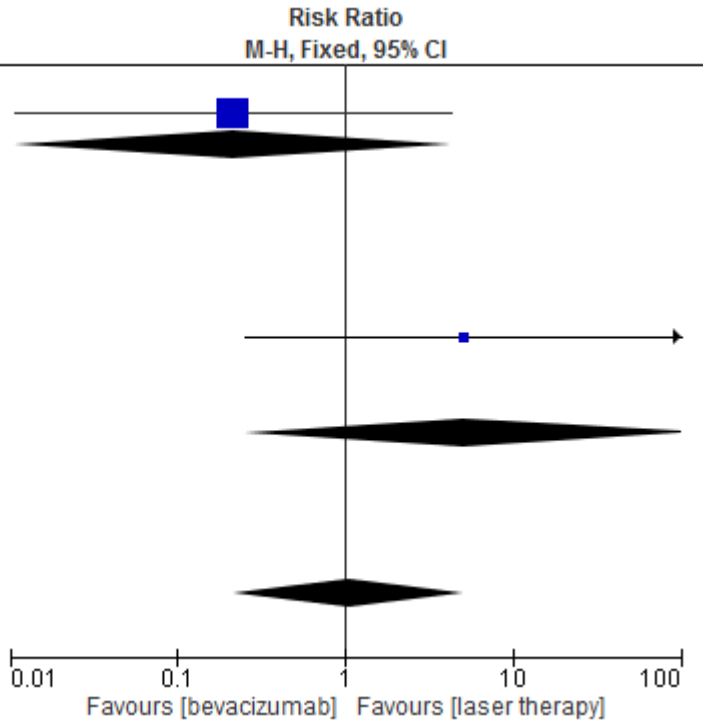
Figure 2. Enrollment, Randomization, and Follow-up of the 150 Study Infants.


A
Before Conventional Laser Therapy
2 mo
B
After Conventional Laser Therapy
13 mo
C
Before Intravitreal Bevacizumab Therapy
3 mo
D
After Intravitreal Bevacizumab Therapy
13 mo

Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity

Structural outcome: partial or complete retinal detachment

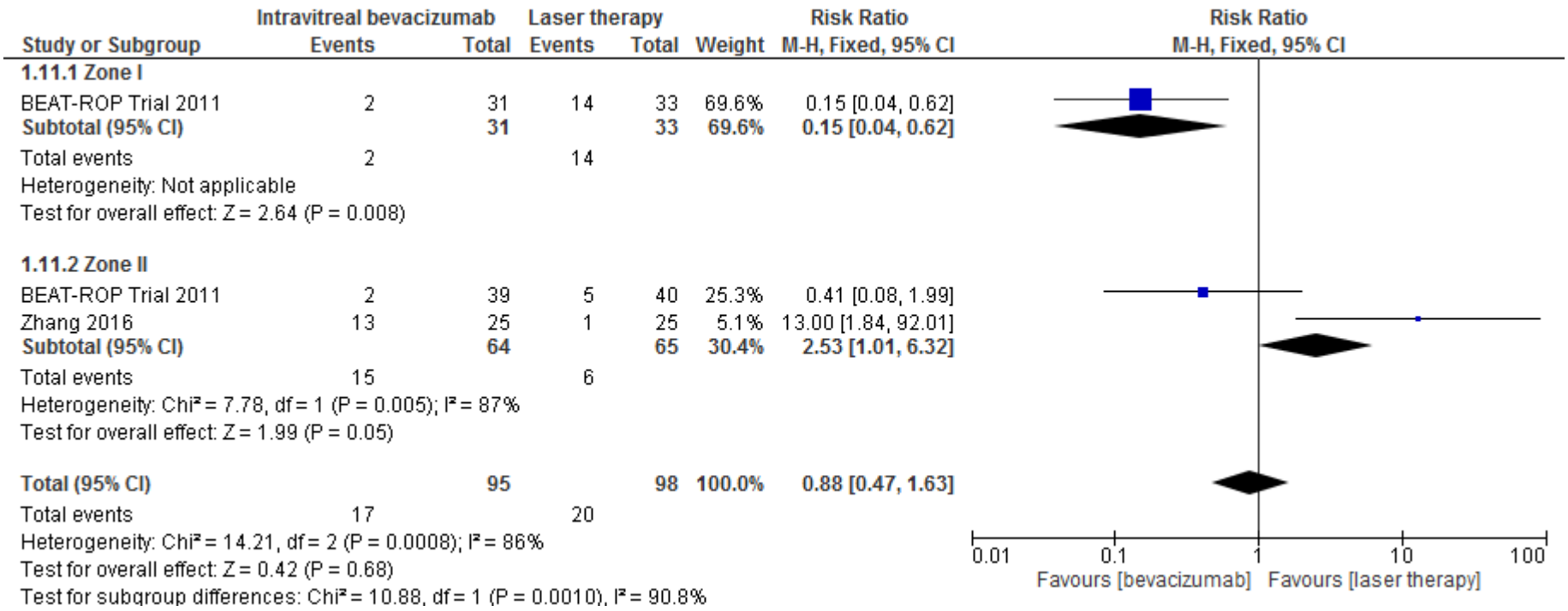
Study or Subgroup	Intravitreal bevacizumab Events	Total	Laser therapy Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Zone I						
BEAT-ROP Trial 2011	0	31	2	33	83.1%	0.21 [0.01, 4.26]
Subtotal (95% CI)		**31**		**33**	**83.1%**	**0.21 [0.01, 4.26]**
Total events	0		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.01 (P = 0.31)						
1.1.2 Zone II						
BEAT-ROP Trial 2011	2	39	0	40	16.9%	5.13 [0.25, 103.45]
Karkhaneh 2016	0	43	0	36		Not estimable
Zhang 2016	0	25	0	25		Not estimable
Subtotal (95% CI)		**107**		**101**	**16.9%**	**5.13 [0.25, 103.45]**
Total events	2		0			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.07 (P = 0.29)						
Total (95% CI)		**138**		**134**	**100.0%**	**1.04 [0.21, 5.13]**
Total events	2		2			
Heterogeneity: Chi² = 2.16, df = 1 (P = 0.14); I² = 54%						
Test for overall effect: Z = 0.05 (P = 0.96)						
Test for subgroup differences: Chi² = 2.16, df = 1 (P = 0.14), I² = 53.7%						



Sankar M Jeeva, Sankar J, Mehta M, Bhat V, Srinivasan R. Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity. Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD009734. DOI: 10.1002/14651858.CD009734.pub2.

Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity

Recurrence of ROP



Sankar M Jeeva, Sankar J, Mehta M, Bhat V, Srinivasan R. Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity. Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD009734. DOI: 10.1002/14651858.CD009734.pub2.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Data from the Canadian Neonatal Network demonstrated 3.1 times higher odds (95% CI 1.2 to 8.4) in infants (gestation less than 29 weeks) treated with bevacizumab versus laser, after adjusting for key confounders like gestation, gender, maternal education, Score for Neonatal Acute Physiology-II (SNAP-II) score, bronchopulmonary dysplasia, sepsis, and severe brain injury further underscore the importance of evaluating long-term safety outcomes following anti-VEGF therapy.

Morin and colleagues. Canadian Neonatal Network and the Canadian Neonatal Follow-Up Network Investigators. Neurodevelopmental outcomes following bevacizumab injections for retinopathy of prematurity. Pediatrics 2016;137(4):e20153218.

Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity

"Given the potential risk of systemic absorption and consequent adverse effects like cerebrovascular accidents following intravitreal anti-VEGF therapy, the lack of evidence on safety outcomes is a major concern".

Sankar and colleagues. Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity. Cochrane Database of Systematic Reviews 2016, Issue 2. Art. No.: CD009734. DOI: 10.1002/14651858.CD009734.pub2. (update pending publication December 2017)

Cochrane Neonatal

Scanning the Horizon

James Hagadorn, MD
Associate Professor of Pediatrics
University of Connecticut School of Medicine

Cochrane Neonatal

Scanning the Horizon

Emerging Evidence for Prevention and Treatment of ROP

Cochrane Neonatal

ClinicalTrials.gov

- "Retinopathy of Prematurity"
- 92 trials with ROP as primary or secondary outcome
  - Registered but not yet enrolling
  - Enrolling
  - Closed to enrollment but actively following

Cochrane Neonatal

1. Oxygen Saturation Targeting: Effects of Closed-loop Automatic Control of FiO2 in Extremely Preterm Infants

- Open treatment RCT
- Projected Enrollment: 2340, Estimated completion December 2022
- Eligible: Gestational age 23+0/7 - 27+6/7 weeks
- Intervention: closed-loop automatic control of the inspiratory fraction of oxygen vs standard care
- Outcomes: mortality; ROP and other in-hospital morbidities; 24-month outcomes

NCT03168516

Cochrane Neonatal

2. Growth Factor Biologicals: Bevacizumab, Ranibizumab, IGF-1

- 6 trials
- Intravitreal bevacizumab vs laser for severe ROP (BEAT-ROP trial) – visual acuity follow-up continues through 7 years
- Phase 3 ranibizumab vs laser for severe ROP
- Non-inferiority studies of lower dose bevacizumab intravitreal for treatment of ROP Type 1
- Observational studies of serum VEGF levels
- IGF-1/IGFBP3 Prevention of ROP - follow up
- *New data will address current safety concerns regarding anti-VEGF monoclonal Ab therapy*

Cochrane Neonatal

RAINBOW Study: Ranibizumab Compared With Laser Therapy for Treatment of ROP

- Phase 3 treatment study, Active/Not enrolling
- Randomized open label, 86 sites
- Enrollment: 220
- Eligible: Birth weight < 1500 grams with severe ROP (Zone I, stage 1+, 2+, 3 or 3+ disease, or Zone II, stage 3+ disease, or Aggressive posterior ROP)
- Intervention: intravitreal ranibizumab 0.2 mg, 0.1 mg, or laser
- Outcome: No active ROP or unfavorable structural outcome 24 weeks after starting investigational treatment; many secondary outcomes

NCT02375971

Cochrane Neonatal

Phase 1 Trial of Bevacizumab Treatment for Severe ROP

- Purpose: to find an effective dose of intravitreal bevacizumab that is lower than currently used, and can be tested in future larger studies.
- Single-group assignement, 10 sites; Enrollment: 110
- Eligible: Infants with Type 1 ROP
- Intervention: intravitreal bevacizumab in de-escalating doses
- Outcome: improvement by 4-day exam and no recurrence requiring additional treatment within 4 weeks of injection in 80% of participants at that dose.

NCT02390531

Cochrane Neonatal

3. Nutritional Supplements

- 5 trials
- DHA vs placebo for ROP prevention
- Correlation of RBC omega-3 PUFAs and subsequent ROP severity
- Arachidonic acid/DHA supplementation vs placebo for ROP prevention
- Vitamin A for ROP prevention

Cochrane Neonatal

Enteral Administration of Docosahexaenoic Acid to Prevent Retinopathy of Prematurity

- Rationale: DHA comprises 40% of the PUFAs in the brain and 60% in the retina
- Phase 2 prevention study, Mexico
- Projected enrollment: 100
- Eligible: Birth weight < 1500 grams
- Intervention: Docosahexenoic acid vs placebo enterally once daily x 14 days
- Outcome: Incidence and severity of ROP through 42-45 weeks corrected age

NCT02683317

Cochrane Neonatal

4. Erythropoietin

- 2 trials
- Influence of erythropoietin and early iron supplements on ROP prevalence and severity
- Recombinant erythropoietin for neuroprotection in very preterm infants

Cochrane Neonatal

5. Propranolol

- Rationale: beta-blockers may reduce retinal expression of VEGF and IGF-1 through blockade of beta-adrenoreceptors
- 4 trials - China, Germany, Italy
- Phase 2 studies to prevent progression of moderate ROP
- Projected enrollment 100-276
- Enteral; topical ophthalmic

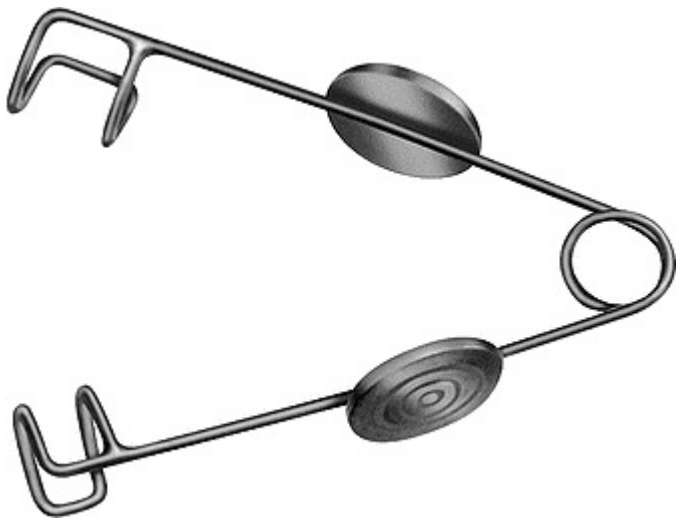
Cochrane Neonatal

Prospective Cohort Study for Propranolol Treatment in Retinopathy of Prematurity

- Phase 2 treatment study, Not yet enrolling
- Randomized masked controlled; China
- Enrollment: 100
- Eligible: Birth weight < 1500 grams with stage 1 or 2 ROP without plus
- Intervention: oral propranolol 0.25 mg/kg/day vs propranolol ophthalmic drops vs placebo (NS)
- Outcome: progression of ROP; safety; 12-month visual and developmental outcomes

NCT03038295

Cochrane Neonatal



6. Retinal Exams

- 2 trials
- RCT oral paracetamol combined with local anesthetics for pain relief during retinal exam
- Comparison of pain using two eyelid retractors

Cochrane Neonatal

7. Topical ophthalmic NSAIDs: Kerotolac, ibuprofen

- 2 trials
- Single-center RCT of kerotolac vs placebo for ROP prevention
- RCT Synergy of caffeine + ibuprofen + kerotolac for ROP prevention

Cochrane Neonatal

8. ROP As A Secondary Outcome

- Many trials
- Thyroxine
- Delivery room resuscitation with room air versus FiO2
- Prevention of BPD
- Smartphone screening for eye diseases
- Probiotics
- Feeding approaches during transfusion

Cochrane Neonatal

Summary:

- Many trials underway examining ROP as a primary or secondary outcome
- Exciting prospects for new evidence to guide prevention and treatment of ROP


EQUIPMENT
NFL

Cochrane Neonatal

Scanning the Horizon

Emerging Evidence for Prevention and Treatment of ROP

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Characteristics of infants with severe retinopathy of prematurity in countries with low, moderate, and high levels of development: implications for screening programs.

Gilbert C, Fielder A, Gordillo L, Quinn G, Semiglia R, Visintin P, Zin A; International NO-ROP Group.

Pediatrics. 2005 May;115(5):e518-25. Epub 2005 Apr 1.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

OBJECTIVE:

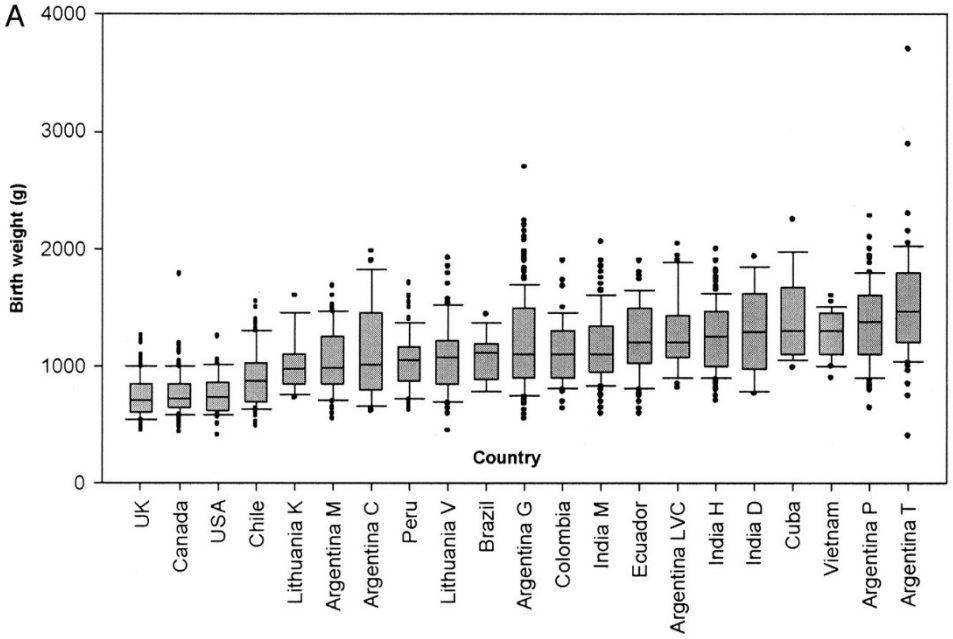
The proportion of blindness as a result of ROP varies greatly among countries depending on their level of development, being influenced by the availability of neonatal care, neonatal outcomes, and whether effective screening and treatment programs are in place.

The objective of this study was to compare characteristics of premature infants who developed severe ROP between 1996 and 2002 in highly developed countries with less developed countries.

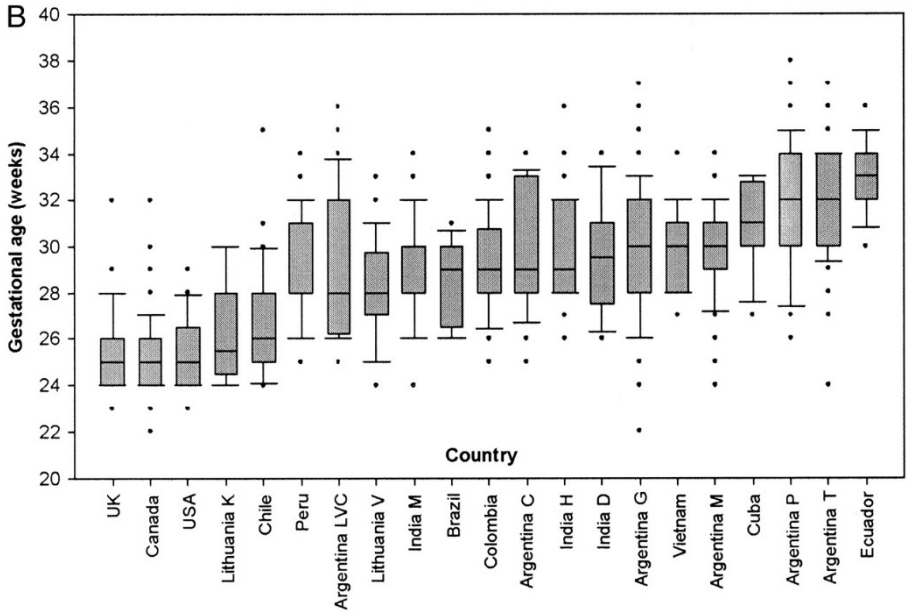
METHODS:

This was an observational study. A questionnaire was completed by ophthalmologists in countries with low, moderate, and high development rankings (3 highly developed countries and from 10 less well-developed countries) who screen for ROP in which they supplied birth weights and gestational ages (GAs) of infants who were treated for threshold ROP or identified with more advanced stages of the disease. Birth weights and GAs of infants with severe ROP were measured.

Gilbert and colleagues. Pediatrics. 2005 May;115(5):e518-25. Epub 2005 Apr 1.



Box plots of birth weights of infants reported with severe ROP from 13 countries with varying levels of development.



Box plots of gestational ages of infants reported with severe ROP from 13 countries with varying levels of development.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

CONCLUSIONS:

These findings suggest that larger, more mature infants are developing severe ROP in countries with low/moderate levels of development compared with highly developed countries. ROP screening programs need to use criteria that are appropriate for their local population.

Gilbert and colleagues. Pediatrics. 2005 May;115(5):e518-25. Epub 2005 Apr 1.

RETINOPATHY OF PREMATURITY

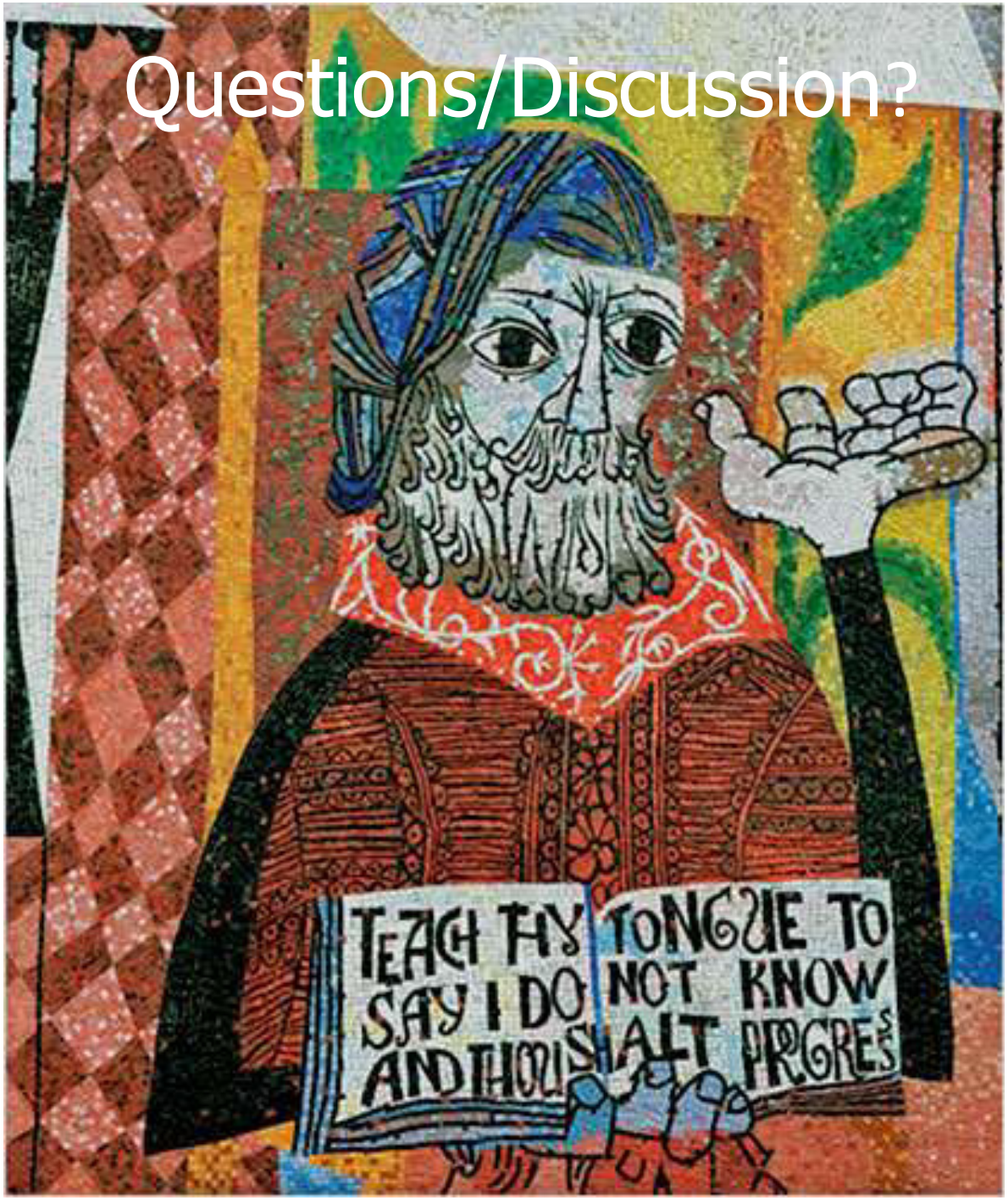
Limited ability to prevent Retinopathy of Prematurity

Effective: Appropriate Oxygen Restriction and Monitoring
Ineffective: Vitamin E, Superoxide dismutase, Light reduction
Jury still out: Vitamin A, Inositol, B blockers

Treatment of pre-threshold ROP

Effective: Retinal ablation surgery
Ineffective: Supplemental oxygen in evolving ROP
Jury still out: Anti VEGF Therapy

Questions/Discussion?



Housekeeping details!

CME credit?

https://neonatal.cochrane.org/december-2017-continuing-medical-education-credit-and-nursing-contact-hour-credit

Next web seminar?

Making the GRADE: Understanding the strength of the evidence

Late winter 2018