



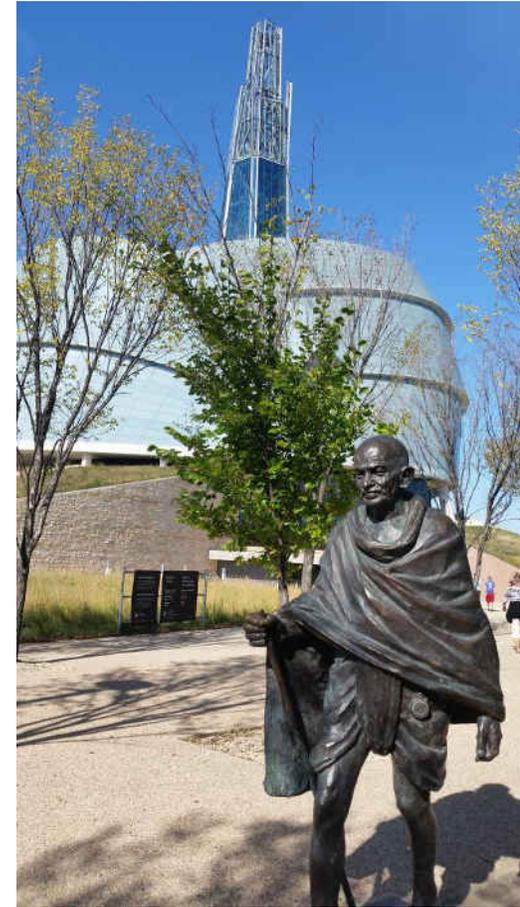
# How Research has changed my practice in the Past five years

Ganesh Srinivasan MD DM FAAP

Director, Neonatal- Perinatal Medicine Residency Program

University of Manitoba

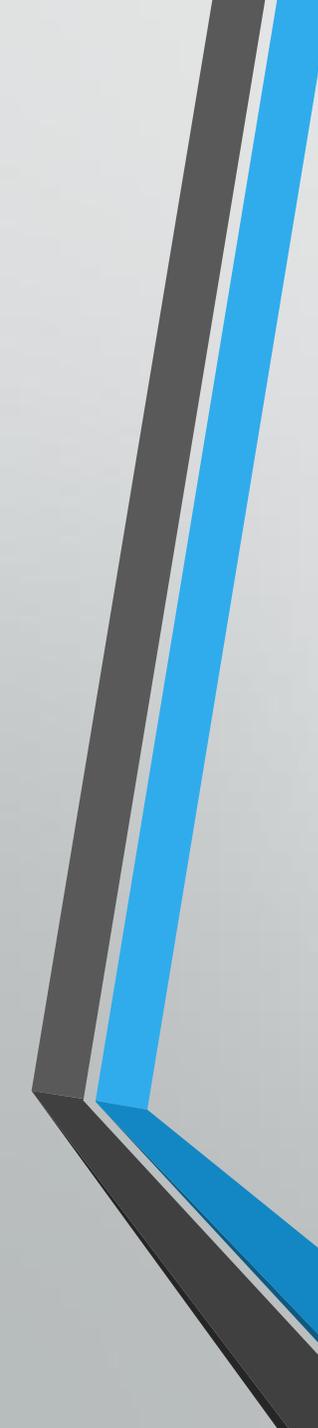
EXPLORER INNOVATOR PIONEER ADVENTURER VISIONARY TRAILBLAZER



No Conflicts to Disclose: “ Truth is God”- M.K Gandhi



UNIVERSITY  
OF MANITOBA

- 
- Edge of Viability
  - Delayed cord clamping
  - Oxygen- Resuscitation
  - Oxygen during NICU stay – low or high
  - CPAP vs Intubation and surfactant
  - Caffeine
  - Antibiotic use and abuse
  - Retinopathy of Prematurity
  - PDA ligation ( Not!)
  - Hypothermia for HIE
  - Neuromonitoring

Less is More

# Edge of Viability

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Between-Hospital Variation in Treatment and Outcomes in Extremely Preterm Infants

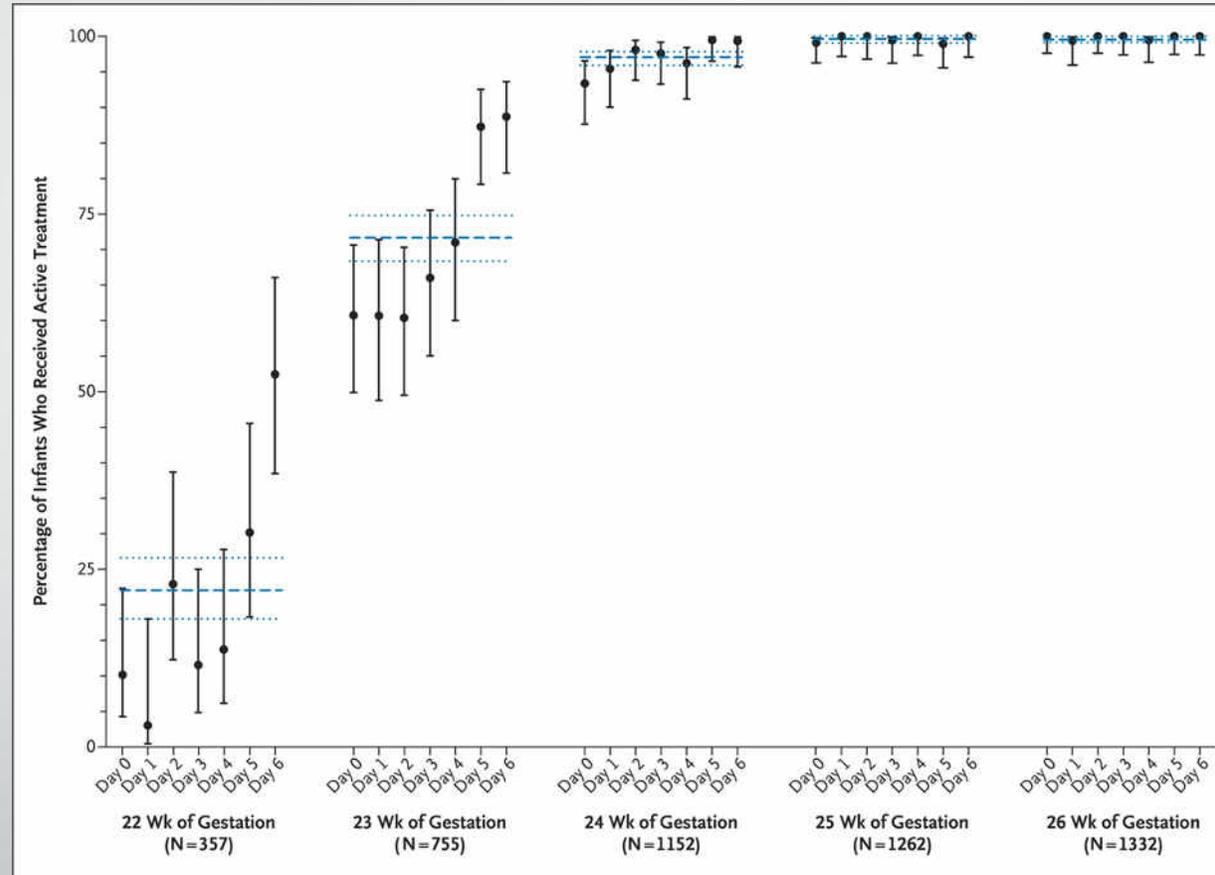
Matthew A. Rysavy, B.S., Lei Li, Ph.D., Edward F. Bell, M.D., Abhik Das, Ph.D., Susan R. Hintz, M.D., Barbara J. Stoll, M.D., Betty R. Vohr, M.D., Waldemar A. Carlo, M.D., Seetha Shankaran, M.D., Michele C. Walsh, M.D., Jon E. Tyson, M.D., M.P.H., C. Michael Cotten, M.D., M.H.S., P. Brian Smith, M.D., M.P.H., M.H.S., Jeffrey C. Murray, M.D., Tarah T. Colaizy, M.D., M.P.H., Jane E. Brumbaugh, M.D., and Rosemary D. Higgins, M.D., for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network

N Engl J Med  
Volume 372(19):1801-1811  
May 7, 2015



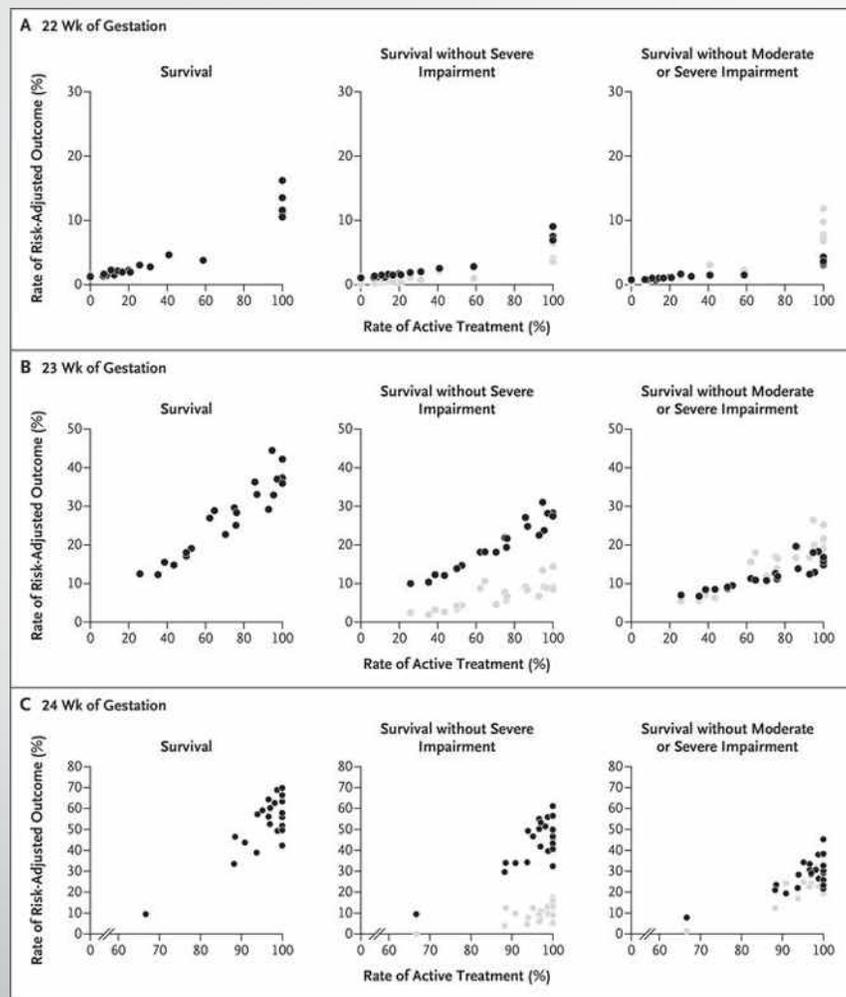
The NEW ENGLAND  
JOURNAL of MEDICINE

# Rates of Active Treatment by Gestational Age at Birth



Rysavy MA et al. N Engl J Med 2015;372:1801-1811

## Hospital Rates of Risk-Adjusted Outcomes and Active Treatment by Gestational Age at Birth



Rysavy MA et al. *N Engl J Med* 2015;372:1801-1811



The NEW ENGLAND  
JOURNAL of MEDICINE

## Edge of Viability

- Differences in hospital practices regarding the initiation of active treatment in infants born at 22, 23, or 24 weeks of gestation explain some of the between-hospital variation in survival and survival without impairment among such patients.

# 2013 Canadian Neonatal Network

## Gestational age specific mortality or significant morbidity (six morbidities)

GA	Number of neonates	Number survived (%)	Number of neonates discharged home directly from network sites	Number (%) without any of the six morbidities	Number (%) with any one morbidity prior to discharge	Number (%) with any two morbidities prior to discharge	Number (%) with any three morbidities prior to discharge	Number (%) with any four morbidities prior to discharge	Number (%) with any five morbidities prior to discharge	Number (%) with all six morbidities prior to discharge
<24	92	43 (47)	16	1 (6)	4 (25)	4 (25)	3 (19)	2 (13)	2 (13)	0
24	197	133 (68)	56	7 (13)	19 (34)	17 (30)	10 (18)	3 (5)	0	0
25	247	195 (79)	76	15 (20)	26 (34)	18 (24)	13 (17)	4 (5)	0	0
26	267	228 (85)	92	29 (32)	37 (40)	17 (18)	9 (10)	0	0	0

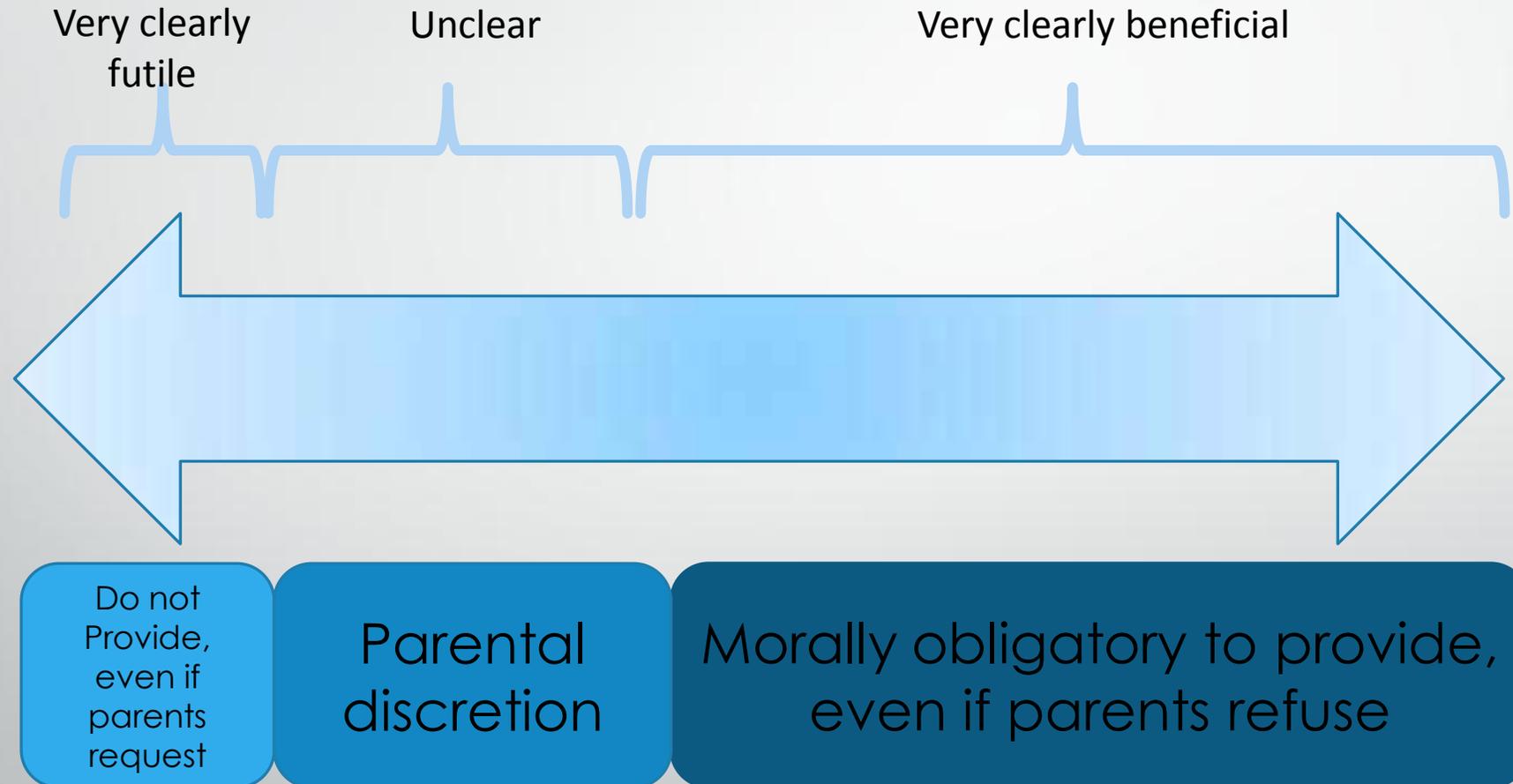
Morbidities were counted as score of one for each of the following

- i. IVH grade 3 or 4 or PVL
- ii. Stage 3 or higher ROP
- iii. Oxygen use at 36 weeks or at discharge if earlier
- iv. Culture proven early onset or late onset sepsis
- v. Stage 2 or 3 NEC
- vi. PDA requiring surgical ligation

# In Winnipeg

Site	FY11-12	FY12-13	FY13-14	FY14-15	FY15-16
HSC					
23 weeks	1/10 (10%)	0/4	0/8	0/7	-
24 weeks	1/5 (20%)	2/5 (40%)	2/6(33%)	1/3 (33%)	3/4 (75%)
St. B					
23 weeks	2/2	1/2 (50%)	0	1/1	3/5 (60%)
24 weeks	0	1/2 (50%)	1/3 (66%)	2/4 (50%)	3/5 (60%)

# Deciding to Forgo LST





## Meet Mac

One of the youngest babies ever born at St. Boniface Hospital



Mac Gross, nine weeks old, cuddles with his mom, Tiffany Gross.

**BY HOLLI MONCRIEFF**  
Winnipeg Health Region  
Wave, May / June 2015

**READ MORE**

- [Miracle babies](#)
- [About kangaroo care](#)

Tiffany Gross lies back on her anti-gravity chair and gently wraps her arms around the tiny infant lying on her chest.

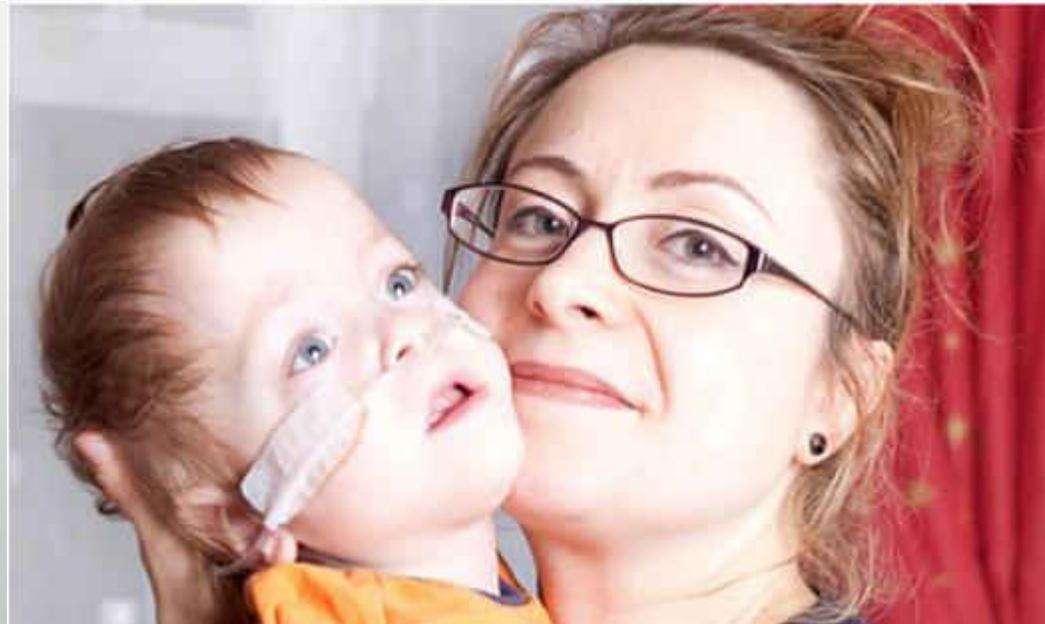
Her son, Mac, was prematurely born on February 9 at 22 weeks and six days gestation - about four months before term. Weighing in at just 630 grams (21 ounces), Mac is the youngest surviving premature baby born at St. Boniface Hospital.

**Premature  
birth**

The Observer

'Nathan was born at 23 weeks. If I'd known then what I do now, I'd have wanted him to die in my arms'

Alexia Pearce adores her 'gorgeous' three-year-old son, yet she is aware that his life - a life blighted by cerebral palsy and chronic lung disease - is unlikely to last long into his teens. In this moving account, she asks: are we always right to save premature babies?



## HEALTH

Presented by 

**TRENDING** [Alan Kurdi](#) | [Recession](#) | [Election](#) | [Blue Jays](#) | [Donald Trump](#) | [CitizenSparks](#)

### Canadian pediatricians recommend letting 22-week-old preemies die. Should doctors try to save the tiny newborns?



**TOM BLACKWELL** | May 29, 2015 1:57 PM ET  
[More from Tom Blackwell](#) | [@tomblackwellNP](#)



# Delayed Cord Clamping or Milking In ELBW

## REVIEW

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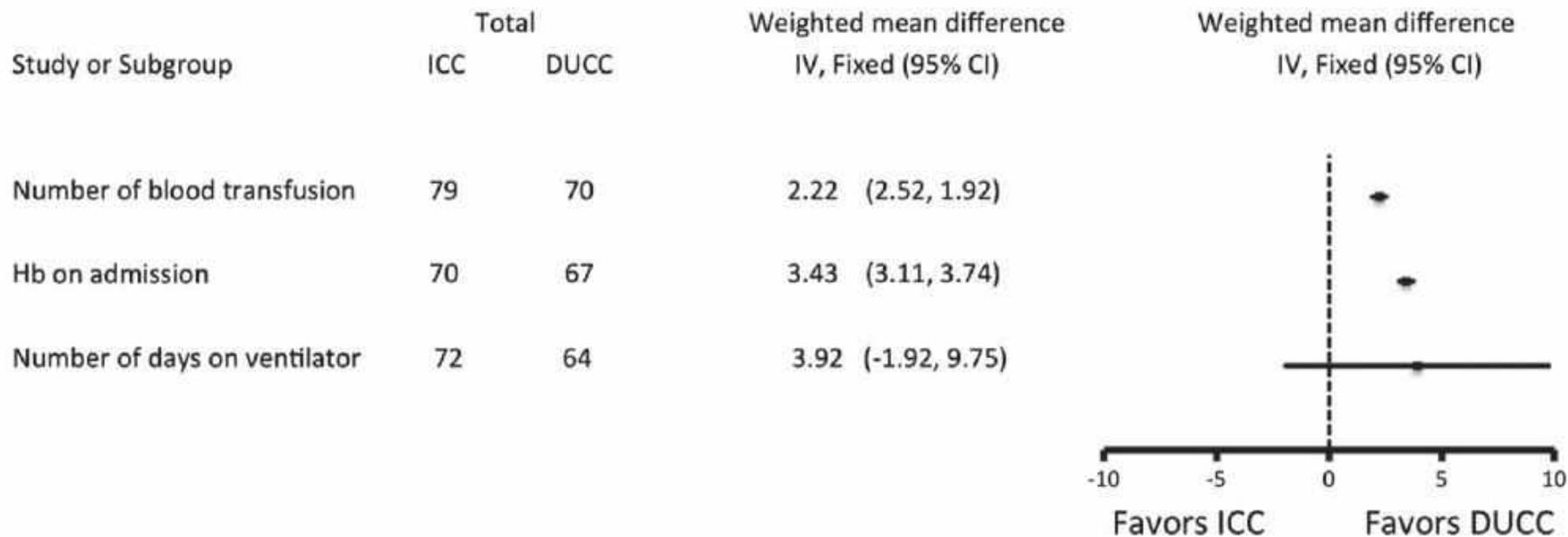
### **Effects of placental transfusion in extremely low birthweight infants: meta-analysis of long- and short-term outcomes**

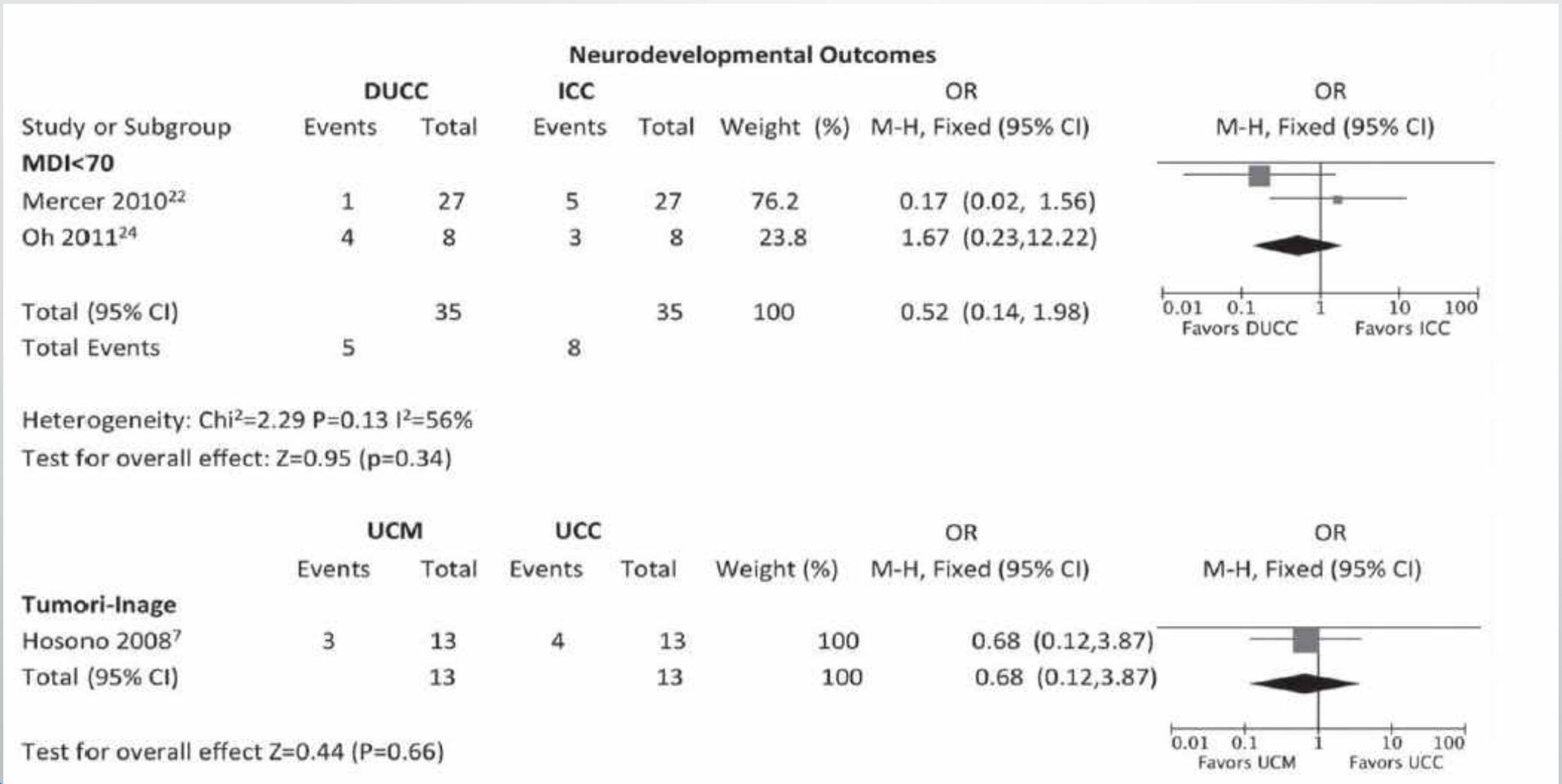
*Sarvin Ghavam,<sup>1</sup> Dushyant Batra,<sup>2</sup> Judith Mercer,<sup>3,4</sup> Amir Kugelman,<sup>5</sup> Shigeharu Hosono,<sup>6</sup>  
William Oh<sup>4</sup>, Heike Rabe,<sup>7</sup> and Haresh Kirpalani<sup>1,8</sup>*

**TABLE 1. Short-term outcomes of umbilical transfusion strategies**

Outcome	Number of infants	Mean difference	95% CI	p value for overall effect
Hb on admission	137	3.42	3.11 to 3.74	<0.001
RBC transfusion requirement	149	-2.22	-2.52 to -1.92	<0.001
Admission blood pressure	113	4.9	4.22 to 5.58	<0.001
Days of mechanical ventilation	136	-3.92	-9.75 to 1.92	0.15
		OR	95% CI	
IVH	196	0.56	0.29 to 1.29	0.08
Episodes of late onset sepsis	154	0.39	0.18 to 0.81	0.01

**Short Term Outcomes**





# 2012 WHO guidelines on basic newborn resuscitation

- In newly born term or preterm babies who do not require positive-pressure ventilation, the cord should not be clamped earlier than 1 min after birth (*strong recommendation*).
- When newly born term or preterm babies require positive-pressure ventilation, the cord should be clamped and cut to allow effective ventilation to be performed (*conditional recommendation*).
- Newly born babies who do not breathe spontaneously after thorough drying should be stimulated by rubbing the back 2–3 times before clamping the cord and initiating positive-pressure ventilation (*conditional recommendation*).

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**EDITORIAL**

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**Delayed Cord Clamping and Umbilical Cord Milking at Birth**

SIDDARTH RAMJI

*From the Department of Neonatology, Maulana Azad Medical College, New Delhi, India. siddarthramji@gmail.com*

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INDIAN PEDIATRICS

749

VOLUME 52—SEPTEMBER 15, 2015

**Effect of Delayed Cord Clamping on Neurodevelopment at 4 Years of Age: A Randomized Clinical Trial**

Ola Andersson, MD, PhD<sup>1</sup>; Barbro Lindquist, PhD<sup>2</sup>;  
Magnus Lindgren, PhD<sup>3</sup>; Karin Stjernqvist, PhD<sup>3</sup>; Magnus Domellöf, MD,  
PhD<sup>4</sup>; Lena Hellström-Westas, MD, PhD<sup>1</sup>

JAMA Pediatr. 2015;169(7):631-638. doi:10.1001/jamapediatrics.2015.0358

# Oxygen in the Delivery room



“Oxygen is a dangerous drug”- Dr. S F Irani (1994 KEM, Mumbai, NICU rounds)



ELSEVIER

Contents lists available at ScienceDirect

Resuscitation

journal homepage: [www.elsevier.com/locate/resuscitation](http://www.elsevier.com/locate/resuscitation)



European Resuscitation Council Guidelines for Resuscitation 2015  
Section 7. Resuscitation and support of transition of babies at birth

Jonathan Wyllie<sup>a,\*</sup>, Jos Bruinenberg<sup>b</sup>, Charles Christoph Roehr<sup>d,e</sup>, Mario Rüdiger<sup>f</sup>,  
Daniele Trevisanuto<sup>c</sup>, Berndt Uriesberger<sup>g</sup>

<sup>a</sup> Department of Neonatology, The James Cook University Hospital, Middlesbrough, UK

<sup>b</sup> Department of Paediatrics, Sint Elisabeth Hospital, Tilburg, The Netherlands

<sup>c</sup> Department of Women and Children's Health, Padua University, Azienda Ospedaliera di Padova, Padua, Italy

<sup>d</sup> Department of Neonatology, Charité Universitätsmedizin, Berlin, Berlin, Germany

<sup>e</sup> Newborn Services, John Radcliffe Hospital, Oxford University Hospitals, Oxford, UK

<sup>f</sup> Department of Neonatology, Medizinische Fakultät Carl Gustav Carus, TU Dresden, Germany

<sup>g</sup> Division of Neonatology, Medical University Graz, Graz, Austria



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Part 7: Neonatal resuscitation  
2015 International Consensus on Cardiopulmonary Resuscitation and  
Emergency Cardiovascular Care Science with Treatment  
Recommendations<sup>☆,☆☆</sup>

Jonathan Wyllie (Co-Chair)<sup>\*1</sup>, Jeffrey M. Perlman (Co-Chair)<sup>1</sup>, John Kattwinkel,  
Myra H. Wyckoff, Khalid Aziz, Ruth Guinsburg, Han-Suk Kim, Helen G. Liley,  
Lindsay Mildenhall, Wendy M. Simon, Edgardo Szyld, Masanori Tamura,  
Sithembiso Velaphi, on behalf of the Neonatal Resuscitation Chapter Collaborators<sup>2</sup>

Resuscitate Full term neonates with Room air FiO<sub>2</sub> 0.21 and  
Preterm <35 wks 0.21 to 0.30

**Neonatology**

**Systematic Review and Meta-Analysis**

Neonatology 2014;105:55–63

DOI: [10.1159/000356561](https://doi.org/10.1159/000356561)

Received: August 12, 2013

Accepted after revision: October 8, 2013

Published online: November 15, 2013

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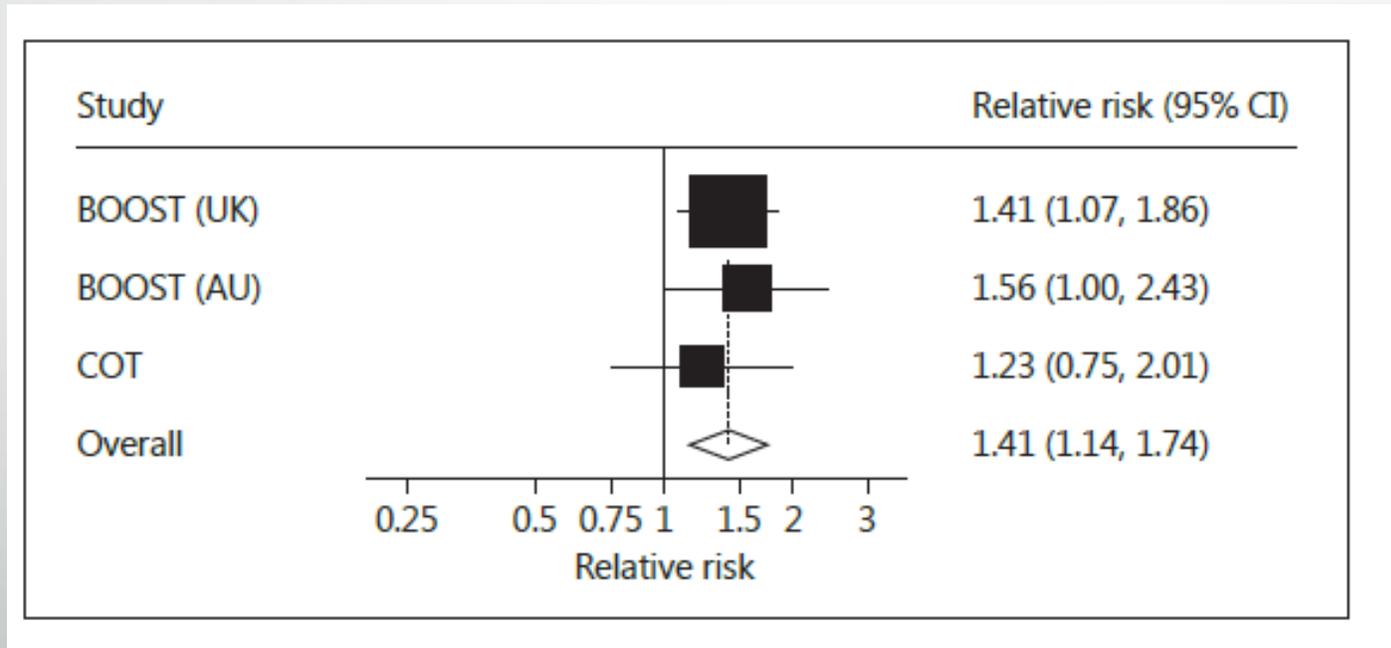
# **Optimal Oxygenation of Extremely Low Birth Weight Infants: A Meta-Analysis and Systematic Review of the Oxygen Saturation Target Studies**

Ola Didrik Saugstad<sup>a</sup> Dagfinn Aune<sup>b, c</sup>

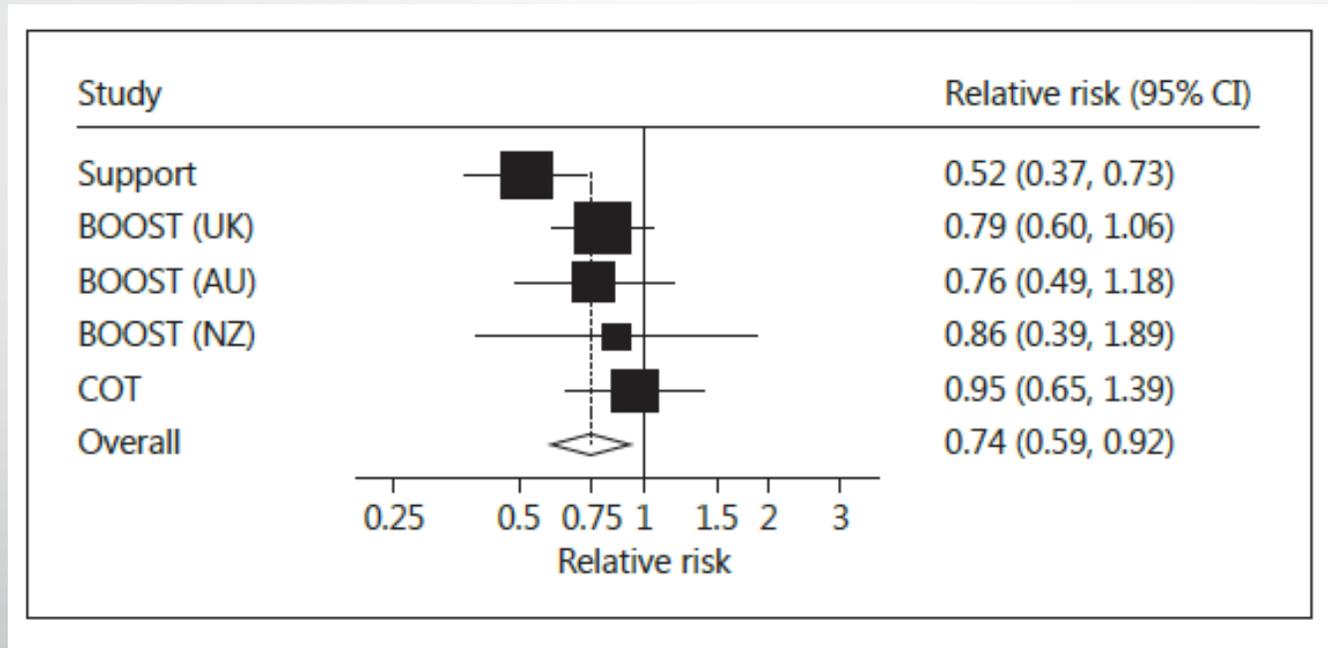
<sup>a</sup>Department of Pediatric Research, Oslo University Hospital, University of Oslo, Oslo, and <sup>b</sup>Department of Public Health and General Practice, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway; <sup>c</sup>Department of Epidemiology and Biostatistics, School of Public Health, Imperial College, London, UK

Dr. Haresh Kirpalani kindly revised the manuscript.

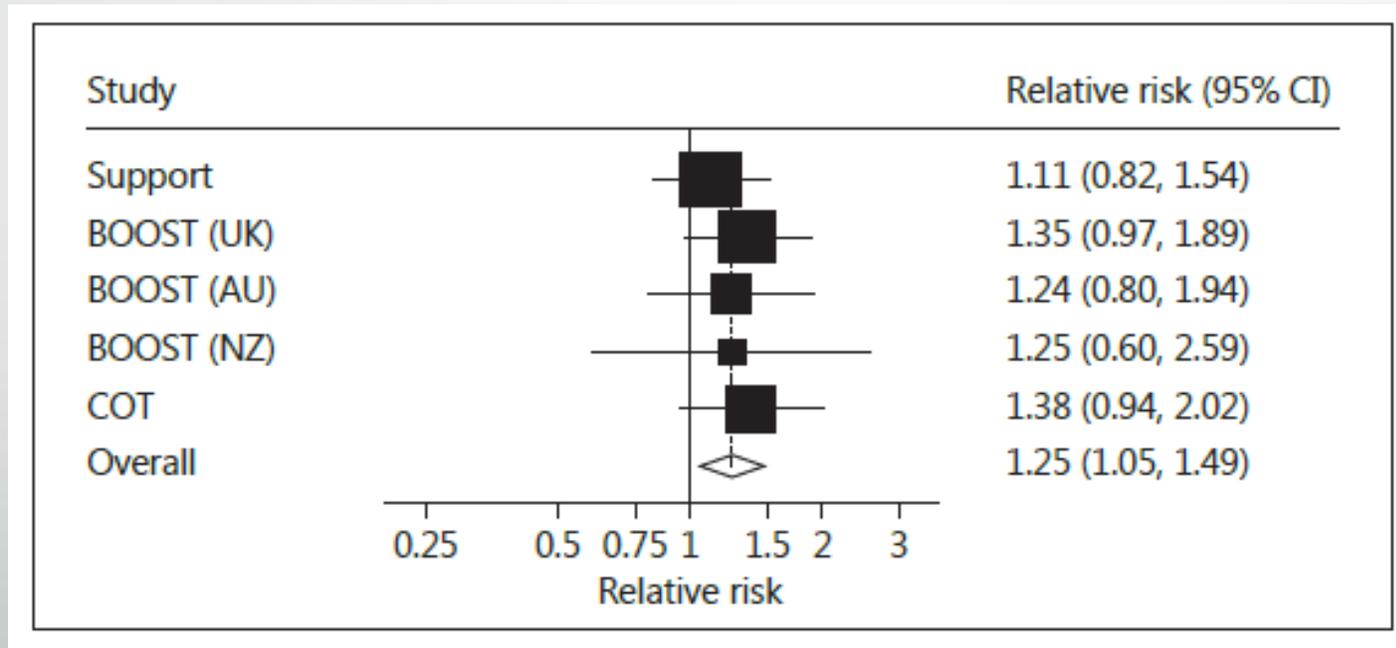
# Mortality



# Retinopathy of Prematurity



# NEC



# Use of NCPAP in delivery room and Non Invasive Ventilation

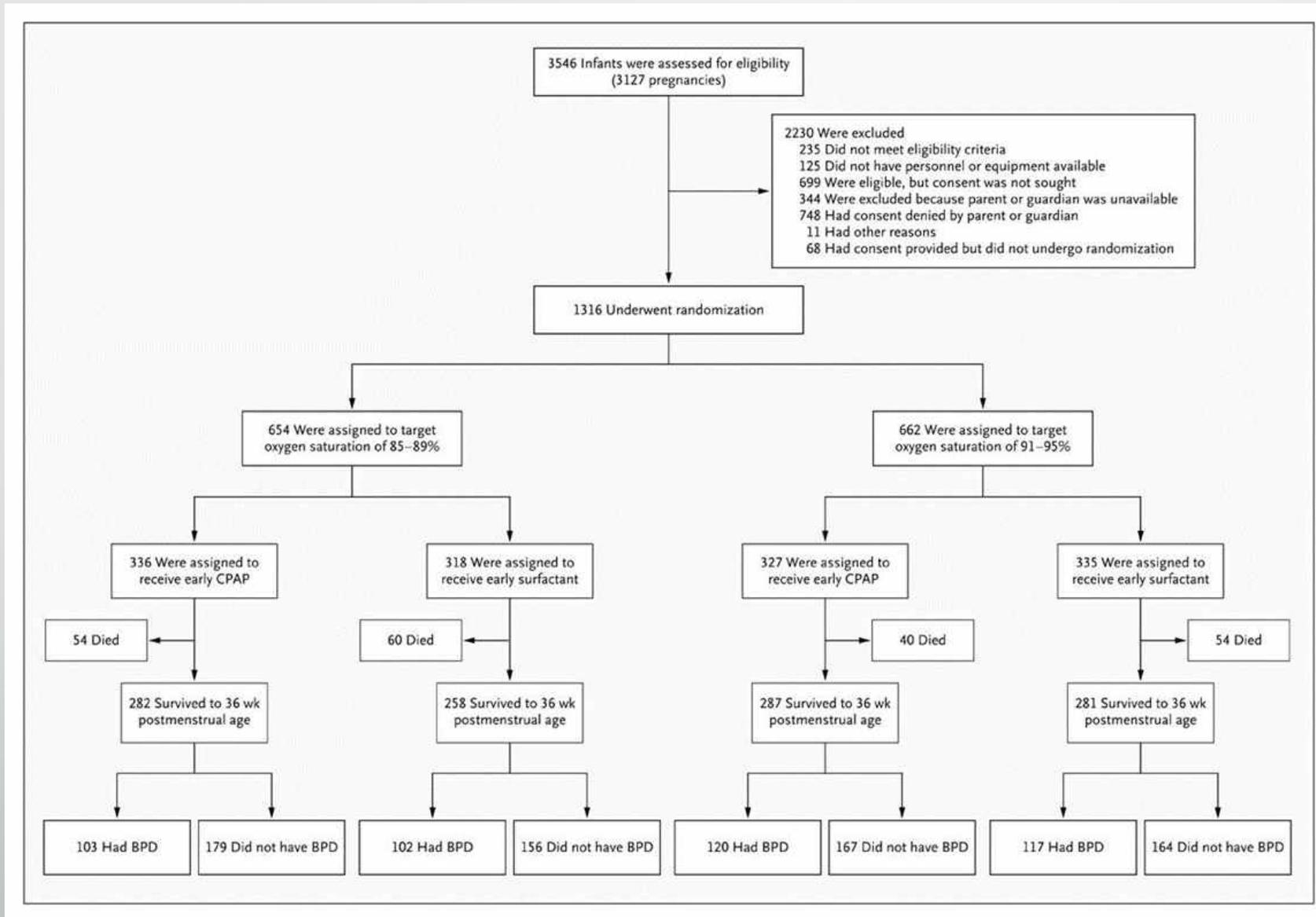
SUPPORT Study Group of the Eunice Kennedy Shriver  
NICHD Neonatal Research Network. N Engl J Med  
2010;362:1970-1979



The NEW ENGLAND  
JOURNAL of MEDICINE

# Study overview

- In this part of a randomized, 2-by-2 factorial trial involving extremely preterm infants, use of intubation and surfactant treatment (within 1 hour after birth) was compared with initiation of continuous positive airway pressure (CPAP) in the delivery room and subsequent use of a protocol-driven limited ventilation strategy
- The rate of death or bronchopulmonary dysplasia (the primary outcome) did not differ significantly between the groups; the CPAP group required intubation less frequently and for fewer days than did the surfactant group
- These results support consideration of CPAP as an alternative to intubation and surfactant in preterm infants



**Table 3. Selected Prespecified Outcomes.\***

Outcome	CPAP (N = 663)	Surfactant (N = 653)	Relative Risk with CPAP (95% CI)	Difference in Means (95% CI)	Adjusted P Value
BPD or death by 36 wk of postmenstrual age — no. (%)					
Physiological definition of BPD†	317 (47.8)	333 (51.0)	0.95 (0.85 to 1.05)		0.30
BPD defined by need for supplemental oxygen	323 (48.7)	353 (54.1)	0.91 (0.83 to 1.01)		0.07
BPD by 36 wk of postmenstrual age — no./total no. (%)					
Physiological definition of BPD†	223/569 (39.2)	219/539 (40.6)	0.99 (0.87 to 1.14)		0.92
BPD defined by need for supplemental oxygen	229/569 (40.2)	239/539 (44.3)	0.94 (0.82 to 1.06)		0.32
Death by 36 wk of postmenstrual age — no. (%)	94 (14.2)	114 (17.5)	0.81 (0.63 to 1.03)		0.09
Need for supplemental oxygen — no. of days‡					0.12
Adjusted mean	62.2±1.6	65.3±1.6		-3.1 (-7.1 to 0.8)	
Unadjusted median	52	56			
Interquartile range	20 to 86	27 to 91			
Need for mechanical ventilation — no. of days‡§					0.03
Adjusted mean	24.8±1.0	27.7±1.1		-3.0 (-5.6 to -0.3)	
Unadjusted median	10	13			
Interquartile range	2 to 32	2 to 36			
Survival without need for high-frequency or conventional ventilation at 7 days — no./total no. (%)	362/655 (55.3)	318/652 (48.8)	1.14 (1.03 to 1.25)		0.01
Any air leak in first 14 days — no. (%)	45 (6.8)	48 (7.4)	0.89 (0.6 to 1.32)		0.56
Necrotizing enterocolitis requiring medical or surgical treatment — no./total no. (%)	83/654 (12.7)	63/636 (9.9)	1.25 (0.92 to 1.71)		0.15
Intraventricular hemorrhage grade 3 or 4 — no./total no. (%)¶	92/642 (14.3)	72/628 (11.5)	1.26 (0.94 to 1.68)		0.12
Postnatal corticosteroid therapy for BPD — no./total no. (%)	47/649 (7.2)	83/631 (13.2)	0.57 (0.41 to 0.78)		<0.001
Severe retinopathy of prematurity among survivors — no./total no. (%)	67/511 (13.1)	65/473 (13.7)	0.94 (0.69 to 1.28)		0.71

\* Plus-minus values are means ±SD. BPD denotes bronchopulmonary dysplasia, CI confidence interval, and CPAP continuous positive airway pressure.

† The physiological definition of BPD includes, as a criterion, the receipt of more than 30% supplemental oxygen at 36 weeks, the need for positive-pressure support, or in the case of infants requiring less than 30% oxygen, the need for any supplemental oxygen at 36 weeks after an attempt at withdrawal of supplemental oxygen.<sup>16,17</sup>

‡ Data are for 1098 infants who survived to discharge, transfer, or 120 days; the maximum follow-up was 120 days.

§ This variable includes high-frequency ventilation and conventional ventilation.

¶ There are four grades of intraventricular hemorrhage; higher grades indicate more severe bleeding.



Published in final edited form as:

*J Pediatr.* 2014 August ; 165(2): 240–249.e4. doi:10.1016/j.jpeds.2014.02.054.

## **Respiratory Outcomes of the Surfactant Positive Pressure and Oximetry Randomized Trial**

Timothy P. Stevens, MD MPH<sup>1</sup>, Neil N. Finer, MD<sup>2</sup>, Waldemar A. Carlo, MD<sup>3</sup>, Peter G. Szilagyi, MD<sup>1</sup>, Dale L. Phelps, MD<sup>1</sup>, Michele C. Walsh, MD MS<sup>4</sup>, Marie G. Gantz, PhD<sup>5</sup>, Abbot R. Lupton, MD<sup>6</sup>, Bradley A. Yoder, MD<sup>7</sup>, Roger G. Faix, MD<sup>7</sup>, Jamie E. Newman, PhD, MPH<sup>5</sup>, Abhik Das, PhD<sup>8</sup>, Barbara T. Do, MSPH<sup>5</sup>, Kurt Schibler, MD<sup>9</sup>, Wade Rich, RRT<sup>2</sup>, Nancy S. Newman, RN<sup>4</sup>, Richard A. Ehrenkranz, MD<sup>10</sup>, Myriam Peralta-Carcelen, MD MPH<sup>3</sup>, Betty R. Vohr, MD<sup>6</sup>, Deanne E. Wilson-Costello, MD<sup>4</sup>, Kimberly Yolton, PhD<sup>9</sup>, Roy J. Heyne, MD<sup>11</sup>, Patricia W. Evans, MD<sup>12</sup>, Yvonne E. Vaucher, MD MPH<sup>2</sup>, Ira Adams-Chapman, MD<sup>13</sup>, Elisabeth C. McGowan, MD<sup>14</sup>, Anna Bodnar, MD<sup>7</sup>, Athina Pappas, MD<sup>15</sup>, Susan R. Hintz, MD MS Epi<sup>16</sup>, Michael J. Acarregui, MD<sup>17</sup>, Janell Fuller, MD<sup>18</sup>, Ricki F. Goldstein, MD<sup>19</sup>, Charles R. Bauer, MD<sup>20</sup>, T. Michael O'Shea, MD MPH<sup>21</sup>, Gary J. Myers, MD<sup>1</sup>, and Rosemary D. Higgins, MD<sup>22</sup> on behalf of the SUPPORT Study Group of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Neonatal Research Network\*

# Antibiotic Overuse in the NICU

## ORIGINAL STUDIES

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### Antibiotic Use in Neonatal Intensive Care Units and Adherence With Centers for Disease Control and Prevention 12 Step Campaign to Prevent Antimicrobial Resistance

*Sameer J. Patel, MD,\*† Adebayo Oshodi, MD,‡§ Priya Prasad, MPH,¶|| Patricia Delamora, MD,\*\*  
Elaine Larson, PhD,††† Theoklis Zaoutis, MD, MSCE,¶|| David A. Paul, MD,‡§  
and Lisa Saiman, MD, MPH\*†††*

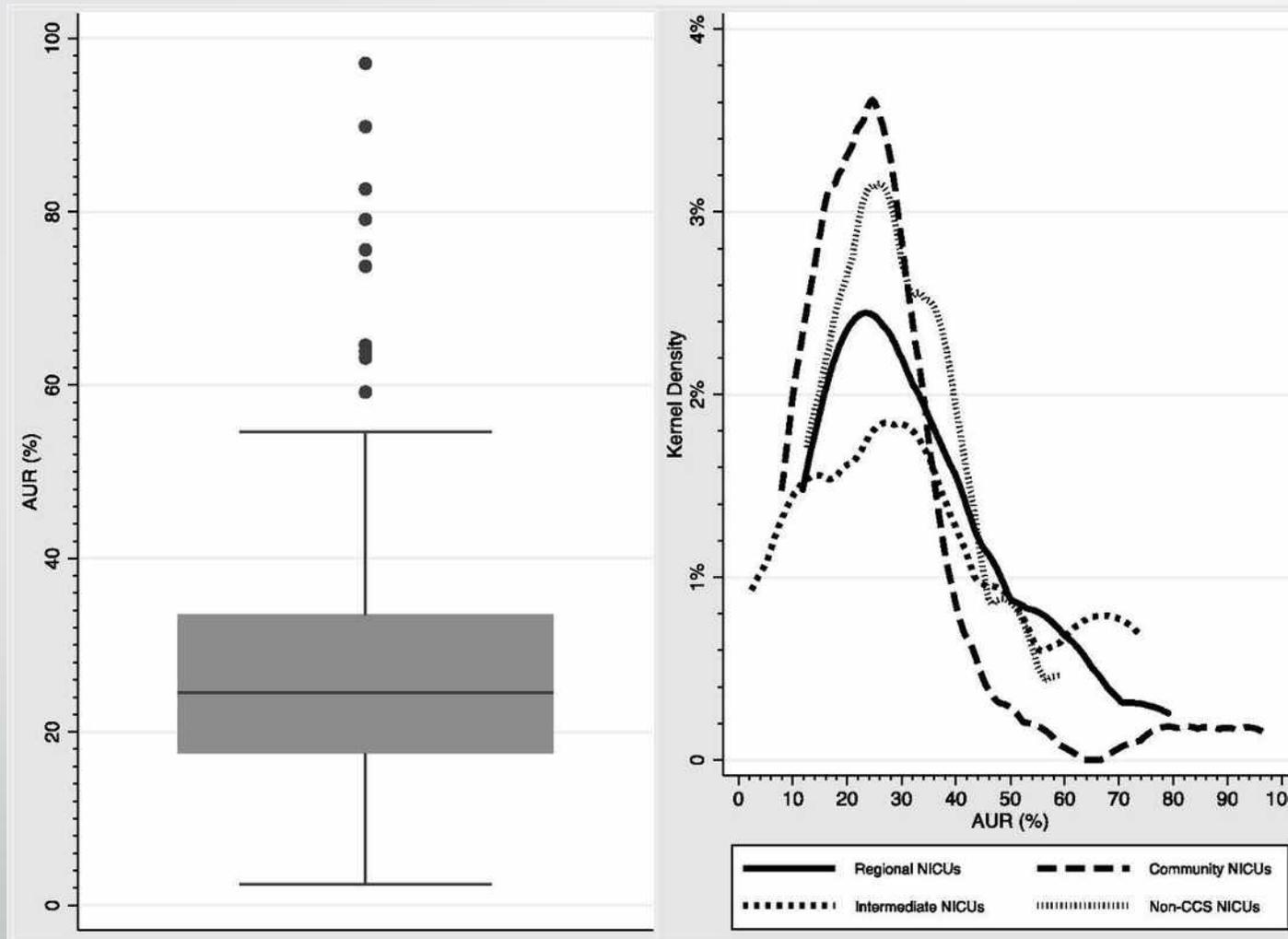
# Neonatal Intensive Care Unit Antibiotic Use

Joseph Schulman, MD, MS<sup>a</sup>, Robert J. Dimand, MD<sup>a</sup>, Henry C. Lee, MD<sup>b,c</sup>, Grace V. Duenas, MPH<sup>b,c</sup>, Mihoko V. Bennett, PhD<sup>b,c</sup>,  
Jeffrey B. Gould, MD, MPH<sup>b,c</sup>

[www.pediatrics.org/cgi/doi/10.1542/peds.2014-3409](http://www.pediatrics.org/cgi/doi/10.1542/peds.2014-3409)

Forty- fold variation in NICU antibiotic prescribing practice across 127 NICUs  
with similar burdens of proven infection, NEC, surgical volume, and mortality!

# Range of AUR values and distribution of AUR values by level of care.



Joseph Schulman et al. Pediatrics 2015;135:826-833

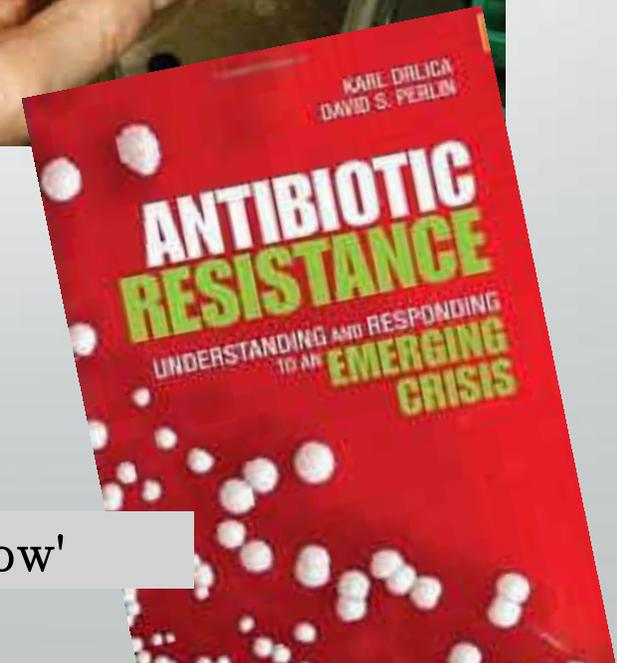
Antibiotic resistance now 'a public health problem of global proportions,' researcher warns



Superbug New Delhi-Metallo-1 spreading worldwide

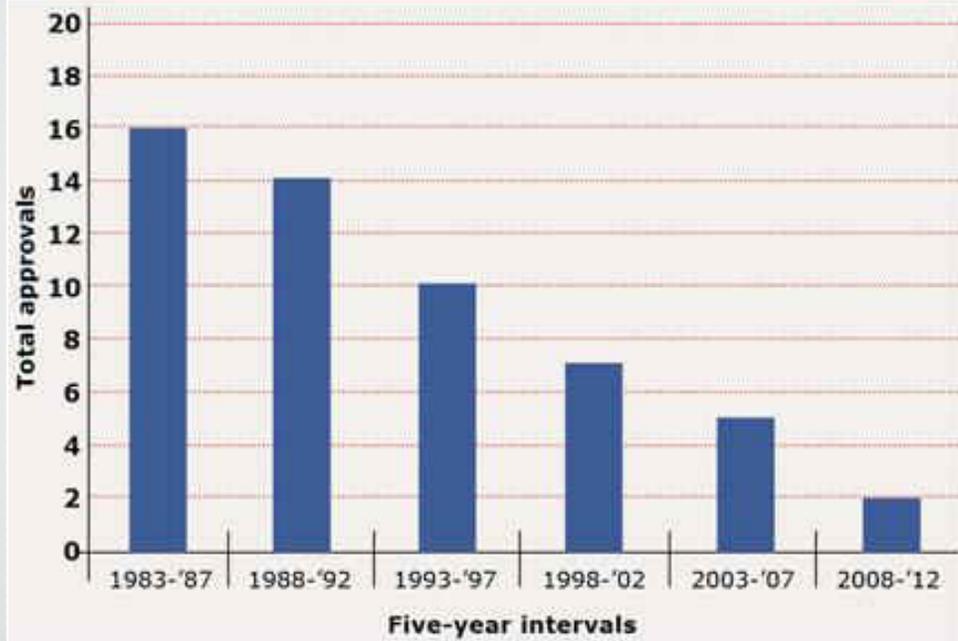
London, Aug 11 (PTI)

Scientists have warned that a new superbug, called New Delhi-Metallo-1, which is resistant to antibiotics, has reached Britain and could spread worldwide as nothing is being developed to combat it.



Antibiotic progress on superbugs called 'alarmingly slow'

## New systemic antibacterial agents approved by the U.S. Food and Drug Administration



Source: 10 x '20 Progress Report (Clinical Infectious Diseases)

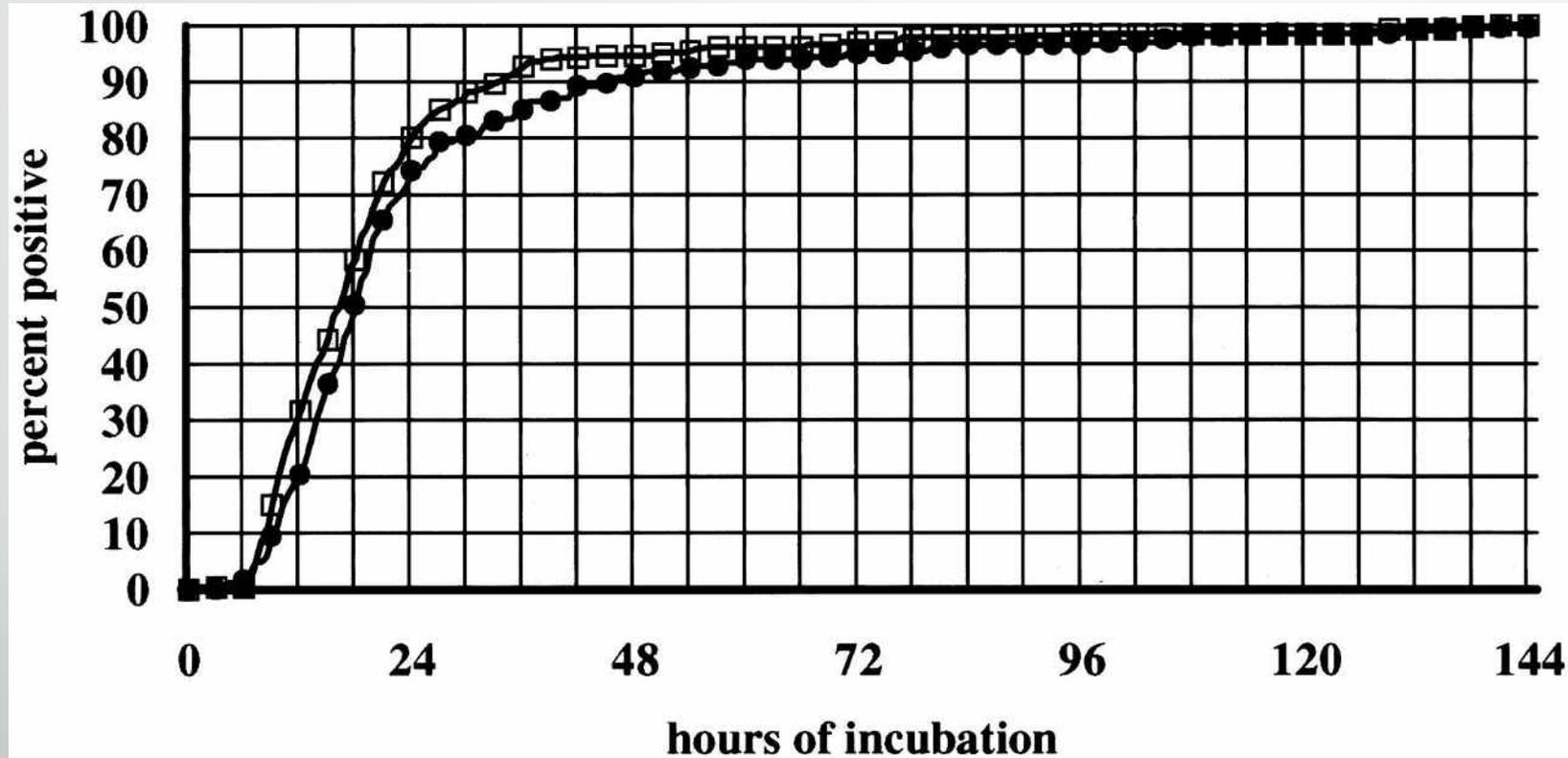
# Prolongation of Empiric Antibiotic Course and later sepsis

Study (number of patients)	Group 1	Group 2	RR for LOS
Shah et al 2013 (216)	≥4 days	<4 days	2.1 (1.2-3.7)
Ghany et al 2012 (207) <sup>a</sup>	≥5 days	<5 days	1.27 (1.12-1.44) <sup>b</sup>
Kuppala et al 2011 (365)	≥5 days	<5 days	2.45 (1.28-4.67)
Cotton et al 2009 (4039)	≥4 days	<4 days	1.21 (1.03-1.42)

<sup>a</sup>received ampicillin and gentamicin

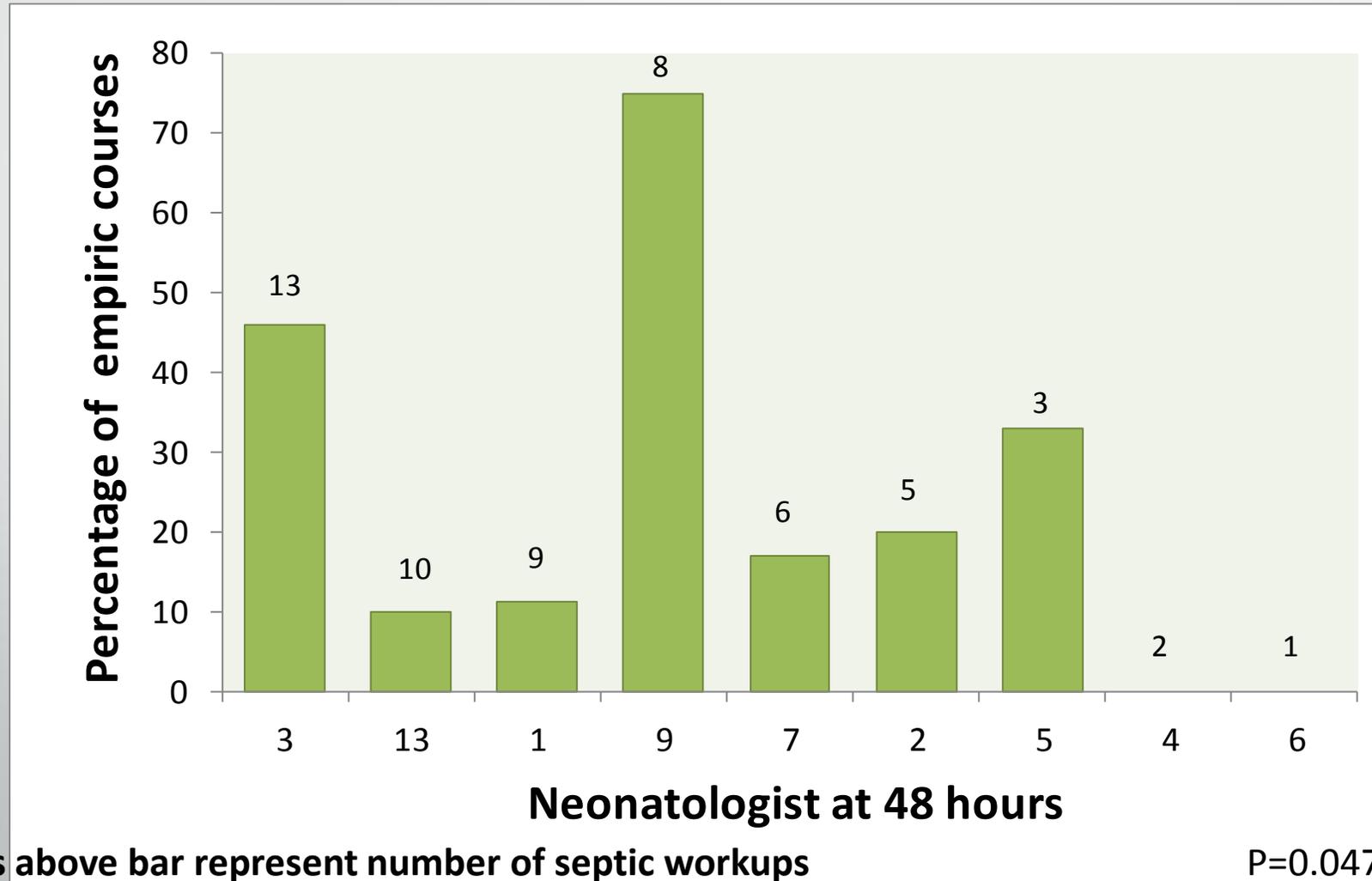
<sup>b</sup>risk per day of antibiotic

Comparison of time to detection of pretreatment (□) positive blood cultures and posttreatment (○) positive blood culture results.



Garcia-Prats J A et al. Pediatrics 2000;105:523-527

# Prolonged Empiric Antibiotics in Culture Negative Infants < 29 weeks (>48 hours)



# Retinopathy of Prematurity

- Screening : Identify the at-risk population
  - ▶ birth weight < 1500g
  - ▶ gestational age < 31/40





# Retinopathy of Prematurity

*The* NEW ENGLAND  
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ESTABLISHED IN 1812

FEBRUARY 17, 2011

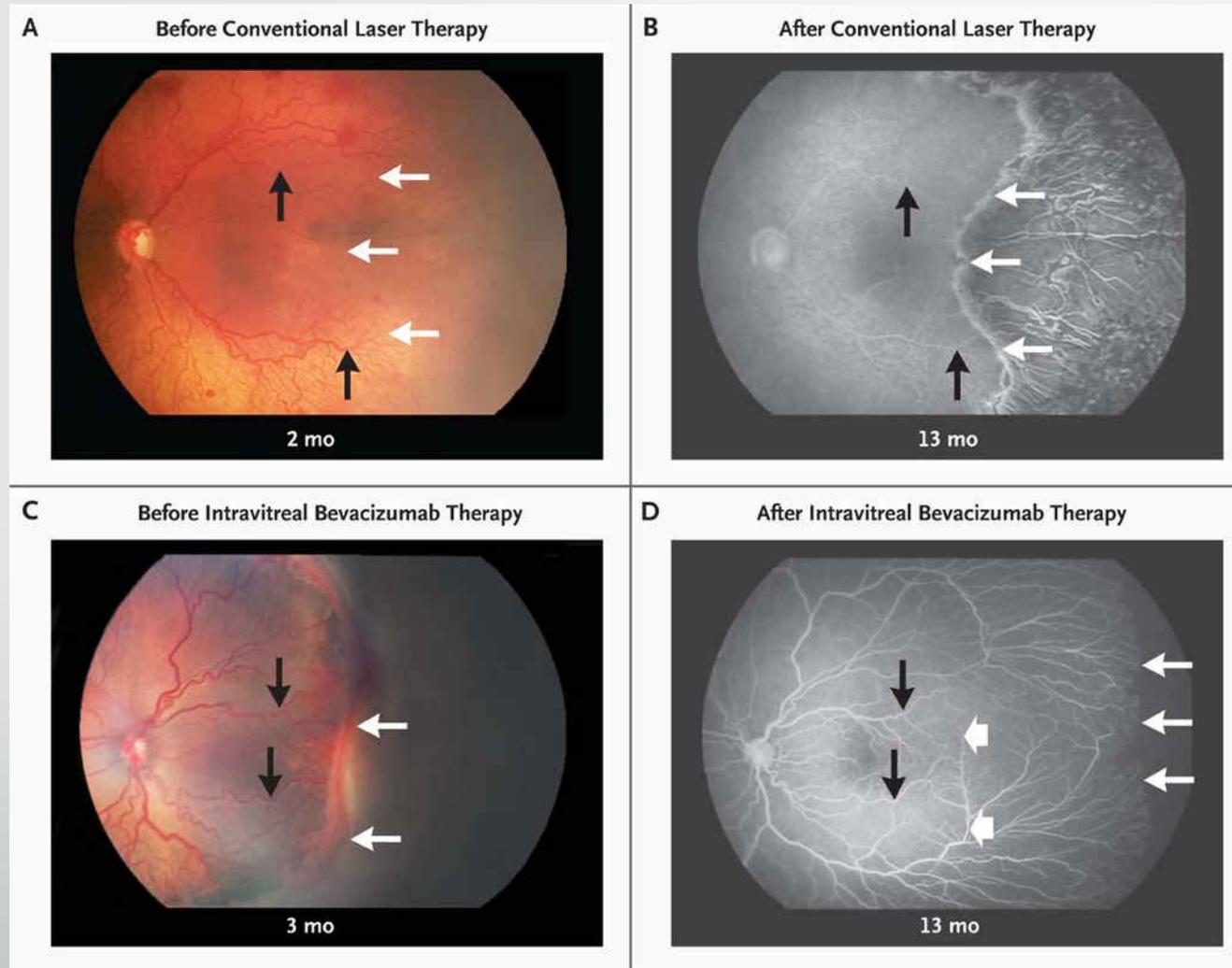
VOL. 364 NO. 7

## Efficacy of Intravitreal Bevacizumab for Stage 3+ Retinopathy of Prematurity

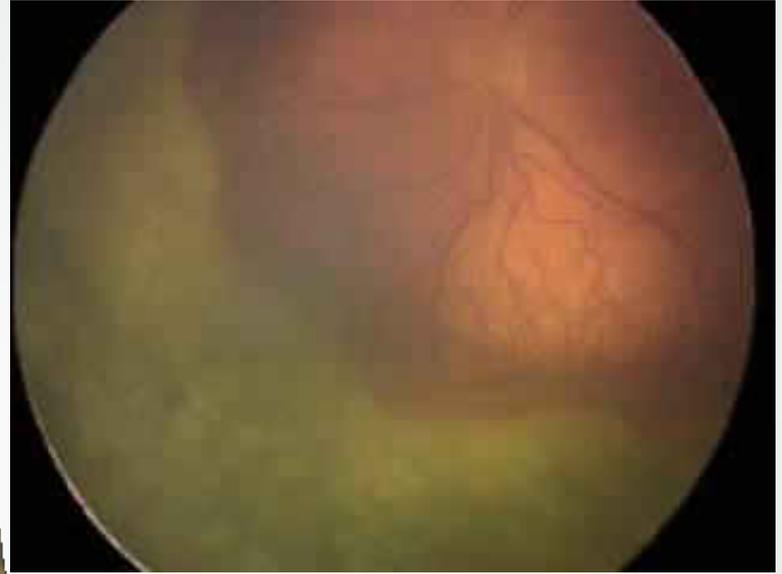
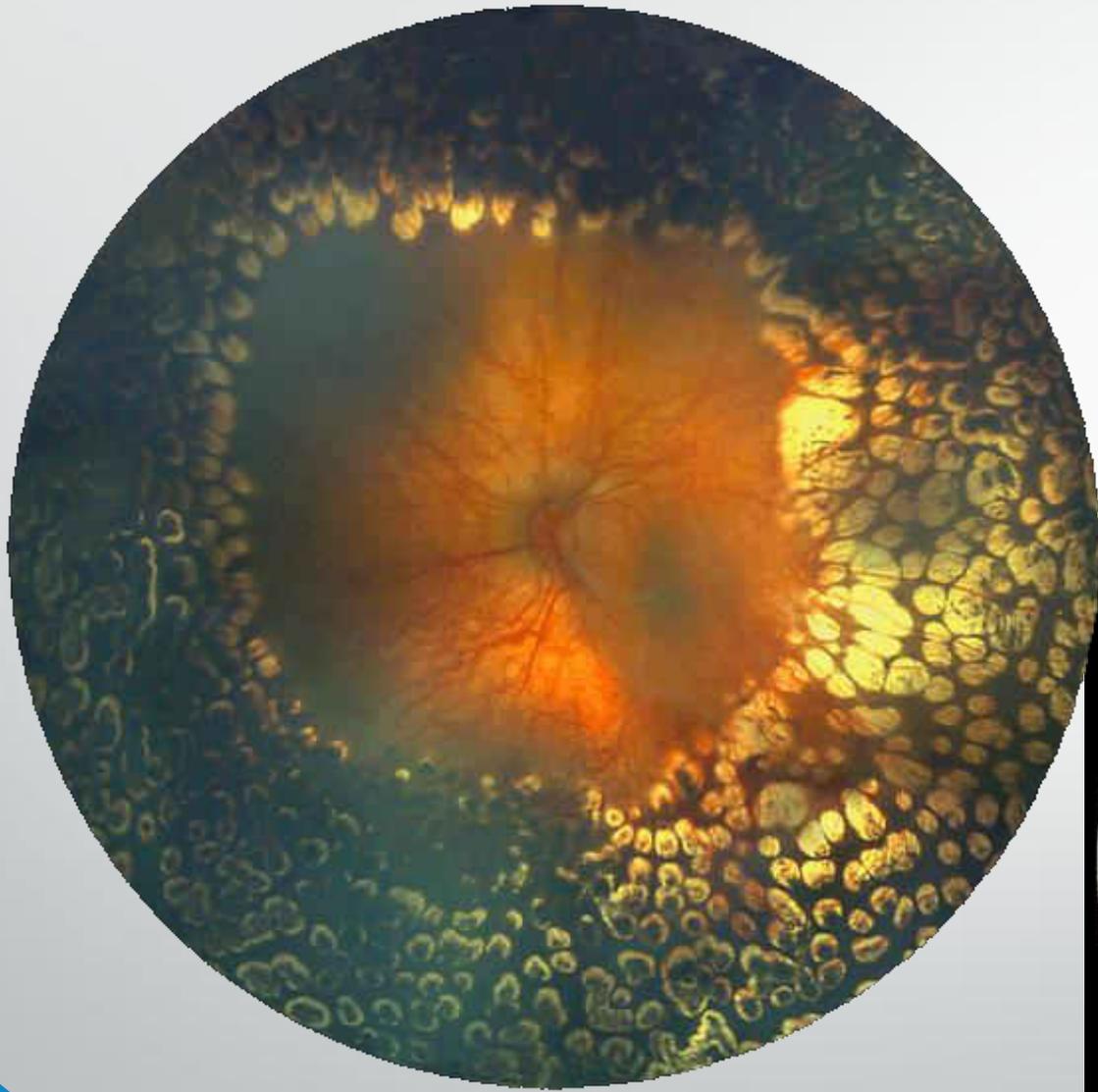
Helen A. Mintz-Hittner, M.D., Kathleen A. Kennedy, M.D., M.P.H., and Alice Z. Chuang, Ph.D.,  
for the BEAT-ROP Cooperative Group\*

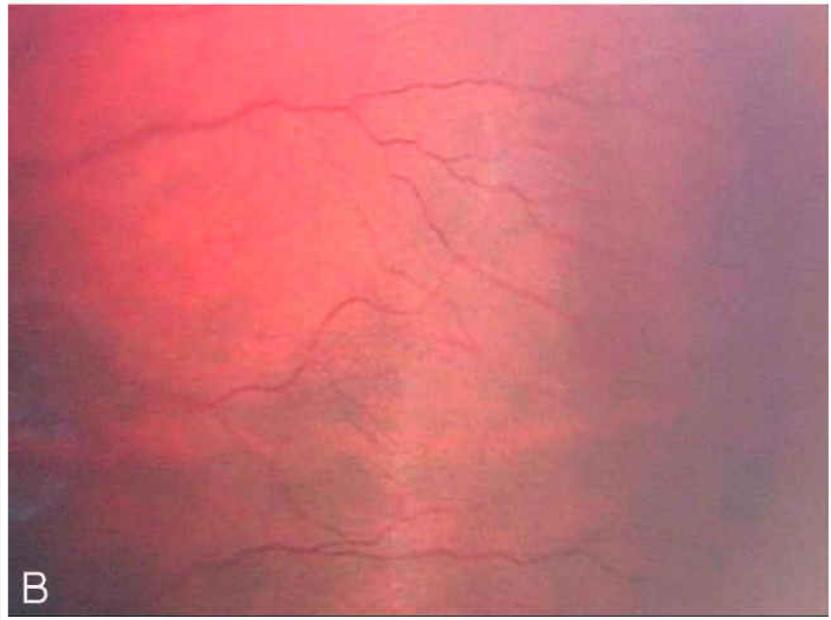
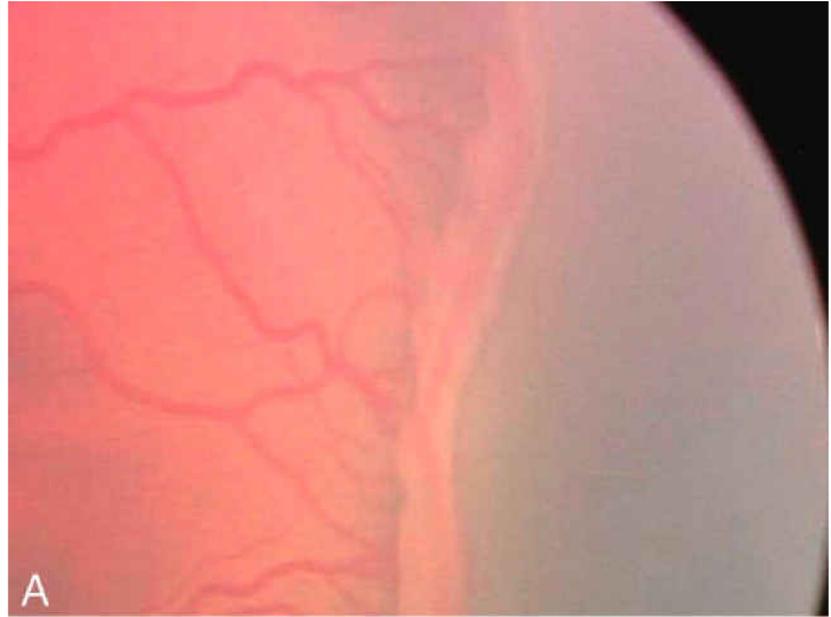
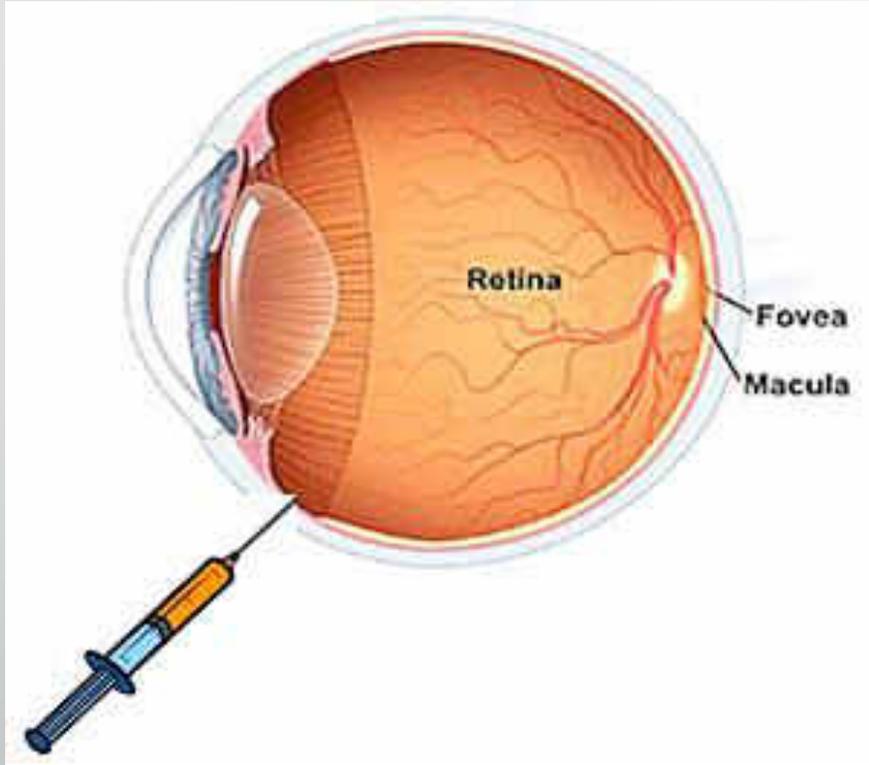
N ENGL J MED 364:7 NEJM.ORG FEBRUARY 17, 2011

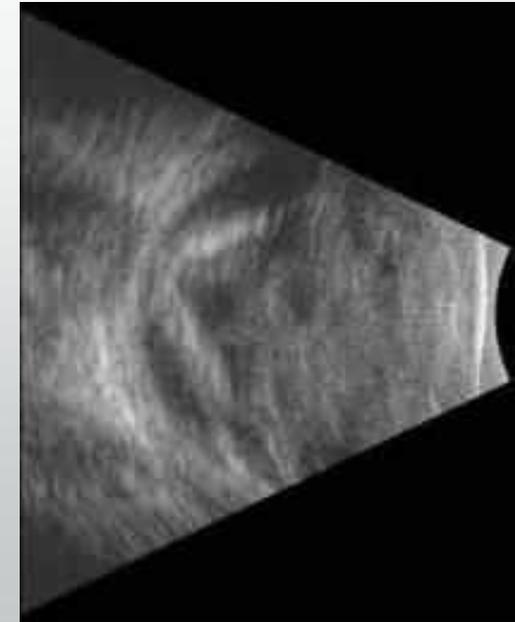
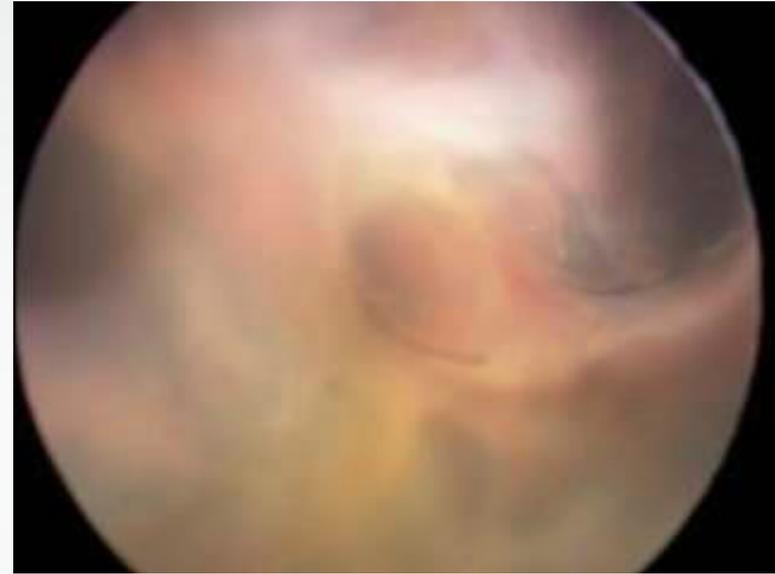
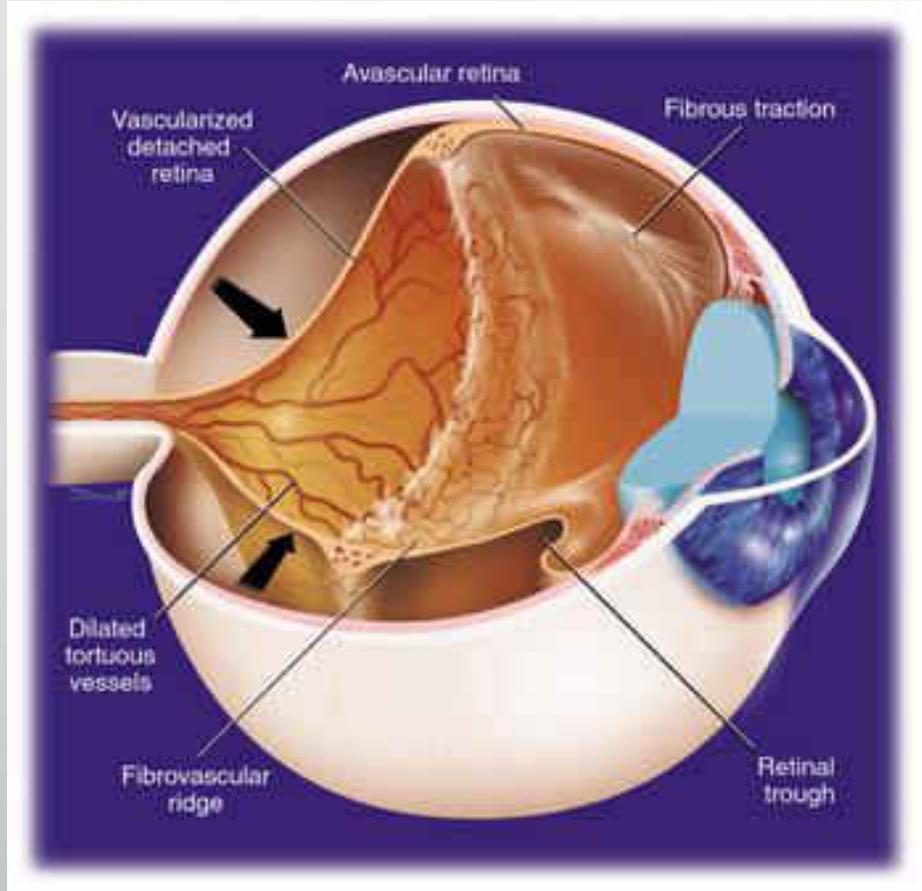
## Fundus Photographs and Fluorescein Angiograms of Retinas in Study Infants with Stage 3+ Retinopathy of Prematurity in Zone I, before and after Treatment.



Mintz-Hittner HA et al. N Engl J Med 2011;364:603-615





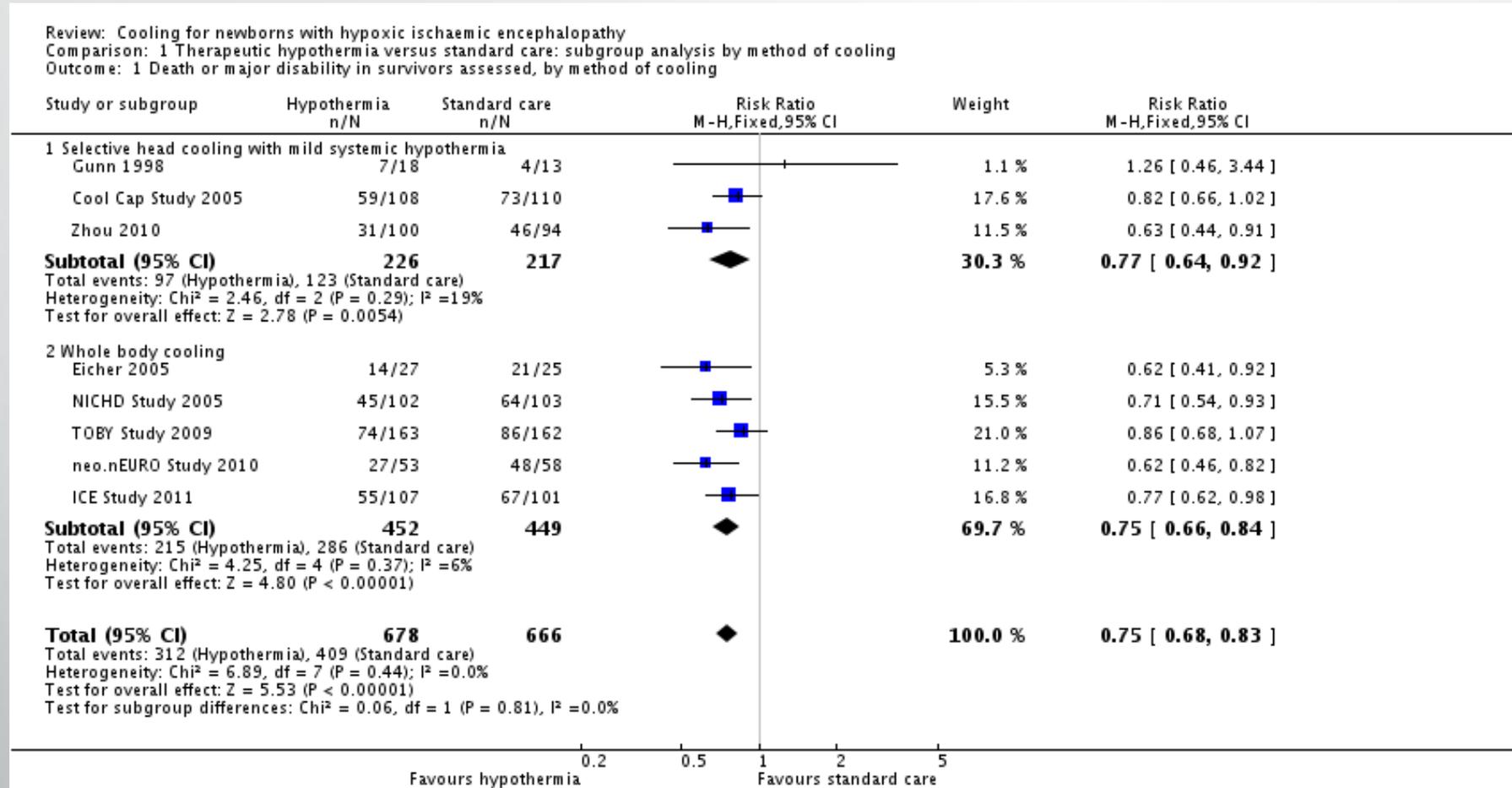




Research translates to Practice ever so slowly



# Therapeutic Hypothermia for HIE



Cooling for newborns with hypoxic ischaemic encephalopathy.  
 Jacobs SE<sup>1</sup>, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG.

## NIRS in HIE

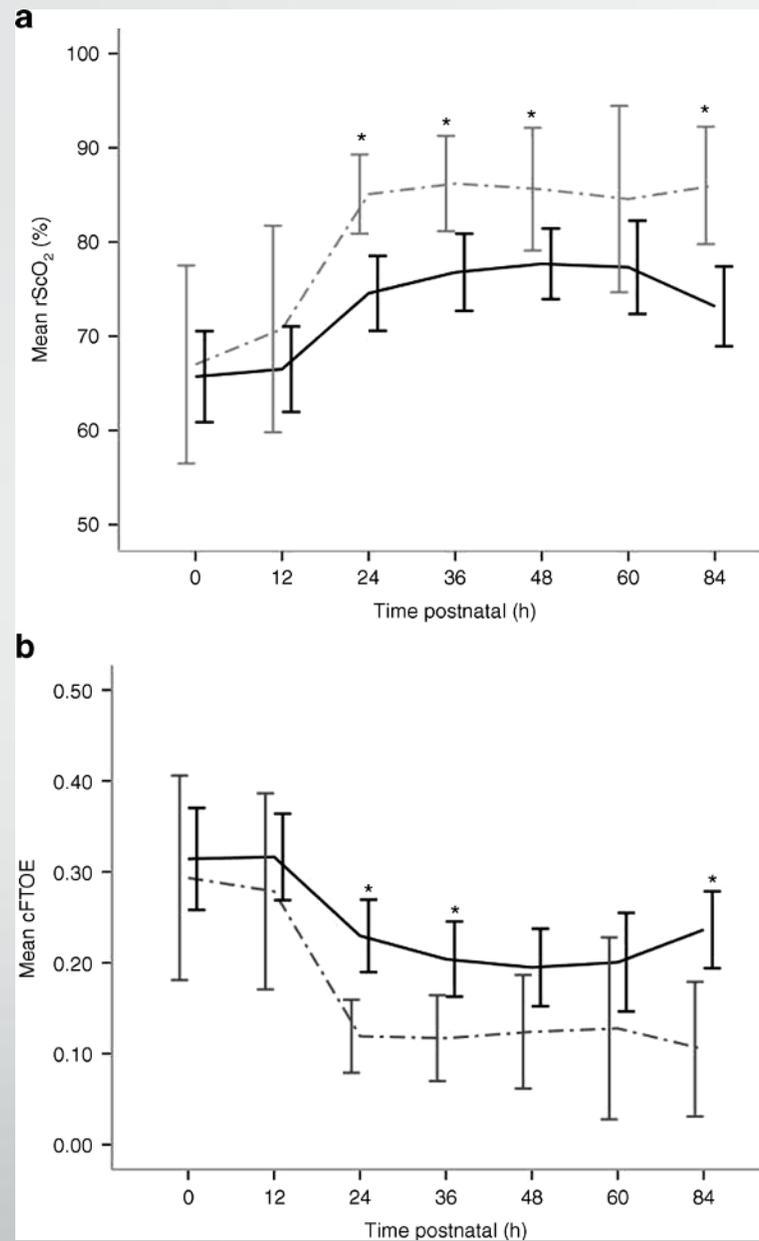


Figure 1

# Is near-infrared spectroscopy clinically useful in the preterm infant?

Cristine Sortica da Costa,<sup>1</sup> Gorm Greisen,<sup>2</sup> Topun Austin<sup>1</sup>



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Review

## Near-infrared spectroscopy: Applications in neonates

Beena G. Sood <sup>a, b, \*</sup>, Kathleen McLaughlin <sup>b</sup>, Josef Cortez <sup>c</sup>

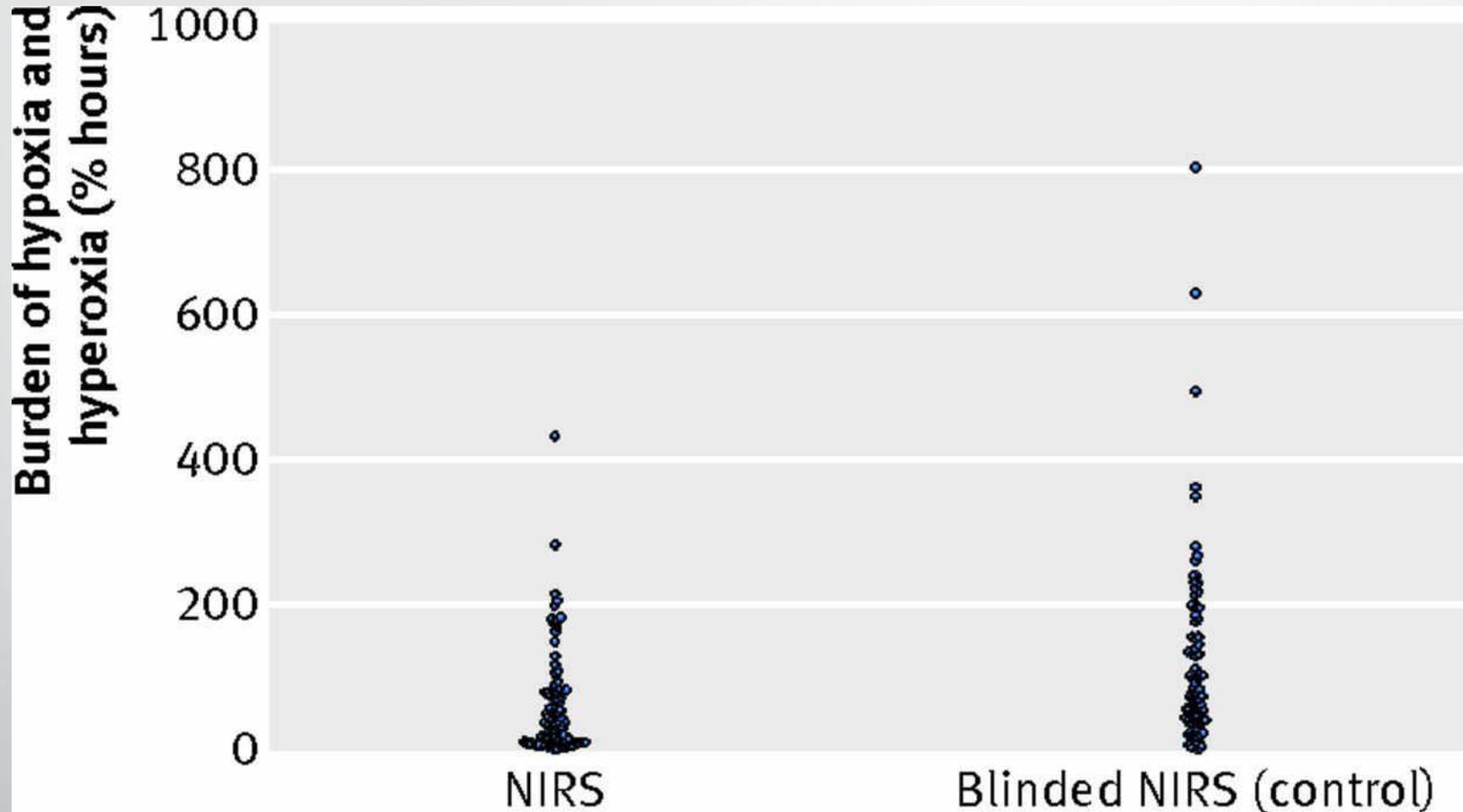


<sup>a</sup> Division of Neonatal-Perinatal Medicine, Department of Pediatrics, Wayne State University, Children's Hospital of Michigan, Detroit, MI, USA

<sup>b</sup> Hutzel Women's Hospital, Detroit, MI, USA

<sup>c</sup> Division of Neonatology, Department of Pediatrics, University of Florida Health Jacksonville, Jacksonville, FL, USA

## Burden of hypoxia and hyperoxia by treatment group . SafeBoos



Simon Hyttel-Sorensen et al. BMJ 2015;350:bmj.g7635

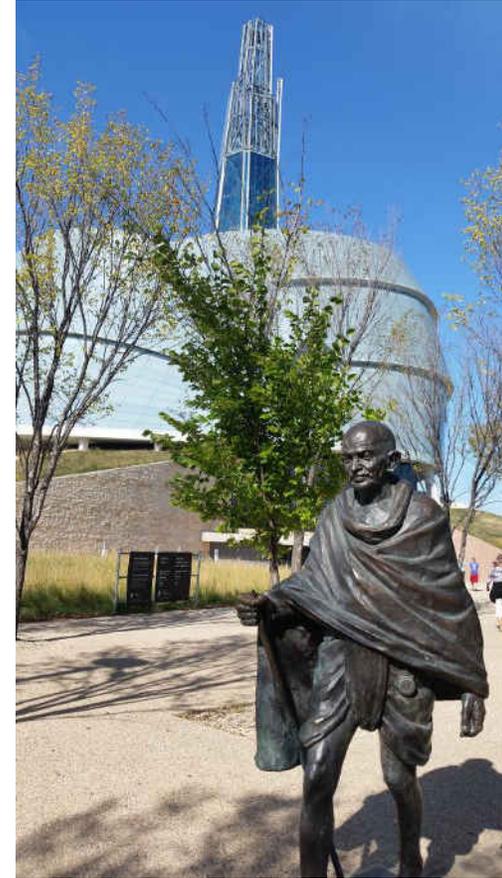


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# How has research changed your practice?

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