

Desafios Actuales en Neonatologia



- ⌘ Situacion Mundial de la Sobrevivencia Neonatal
- ⌘ Avances en Chile en sobrevivencia Neonatal
- ⌘ Como podemos seguir avanzando
- ⌘ Practicas basadas en la evidencia

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LSHTM U of London

Sobrevivencia Neonatal a Nivel Global



- ⌘ Este año morirán 4 millones de niños ante de cumplir un mes de vida. Esto es alrededor de 400 niños en la próxima hora
- ⌘ Solo el 1 % de estas muertes ocurren en los países con ingreso de sobre US 10.000 per capita
- ⌘ Un tercio de las muertes ocurren en el primer día de vida.
- ⌘ Gran número de estas muertes son evitables con medidas simples

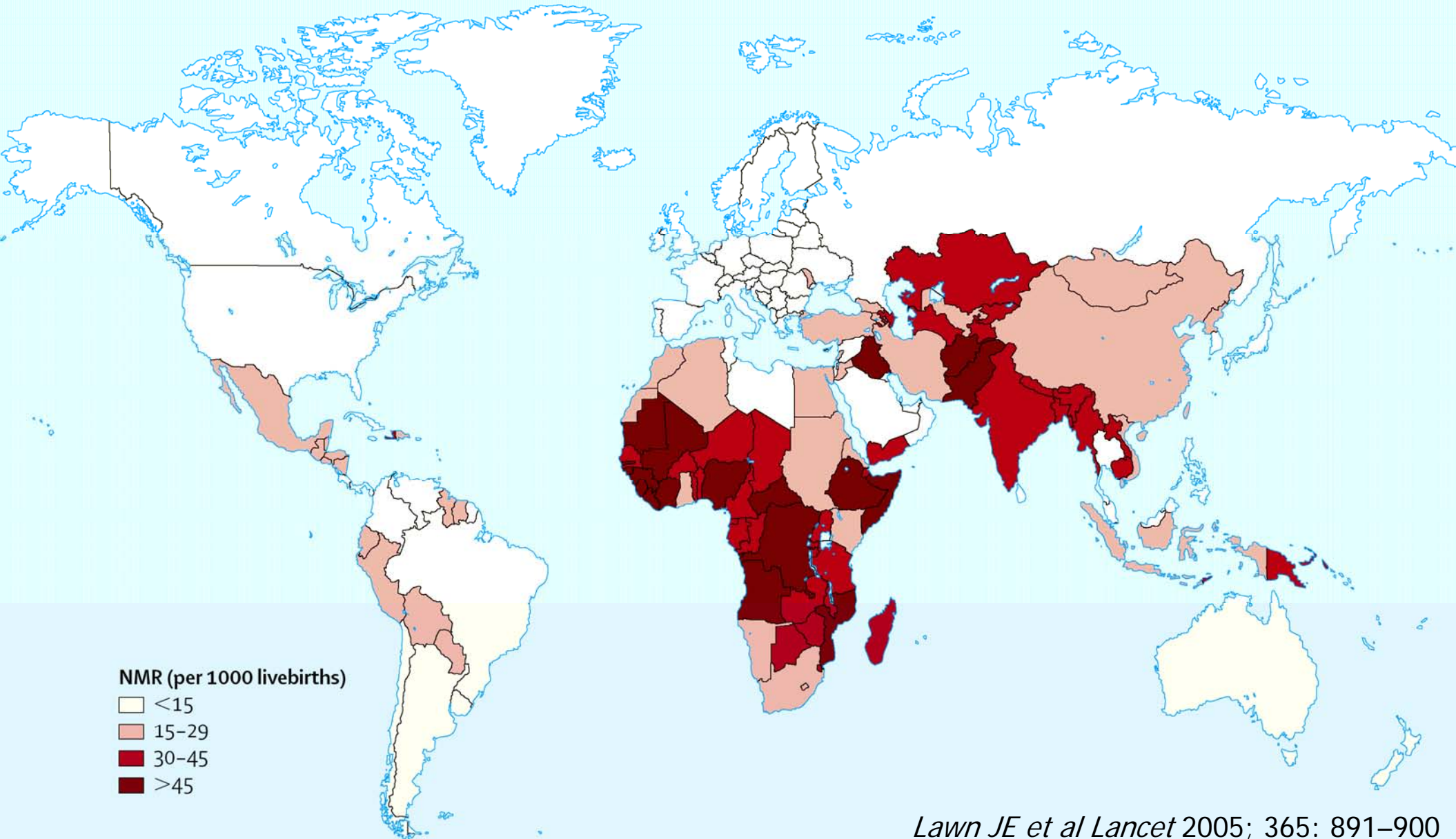
4 million neonatal deaths occur every year

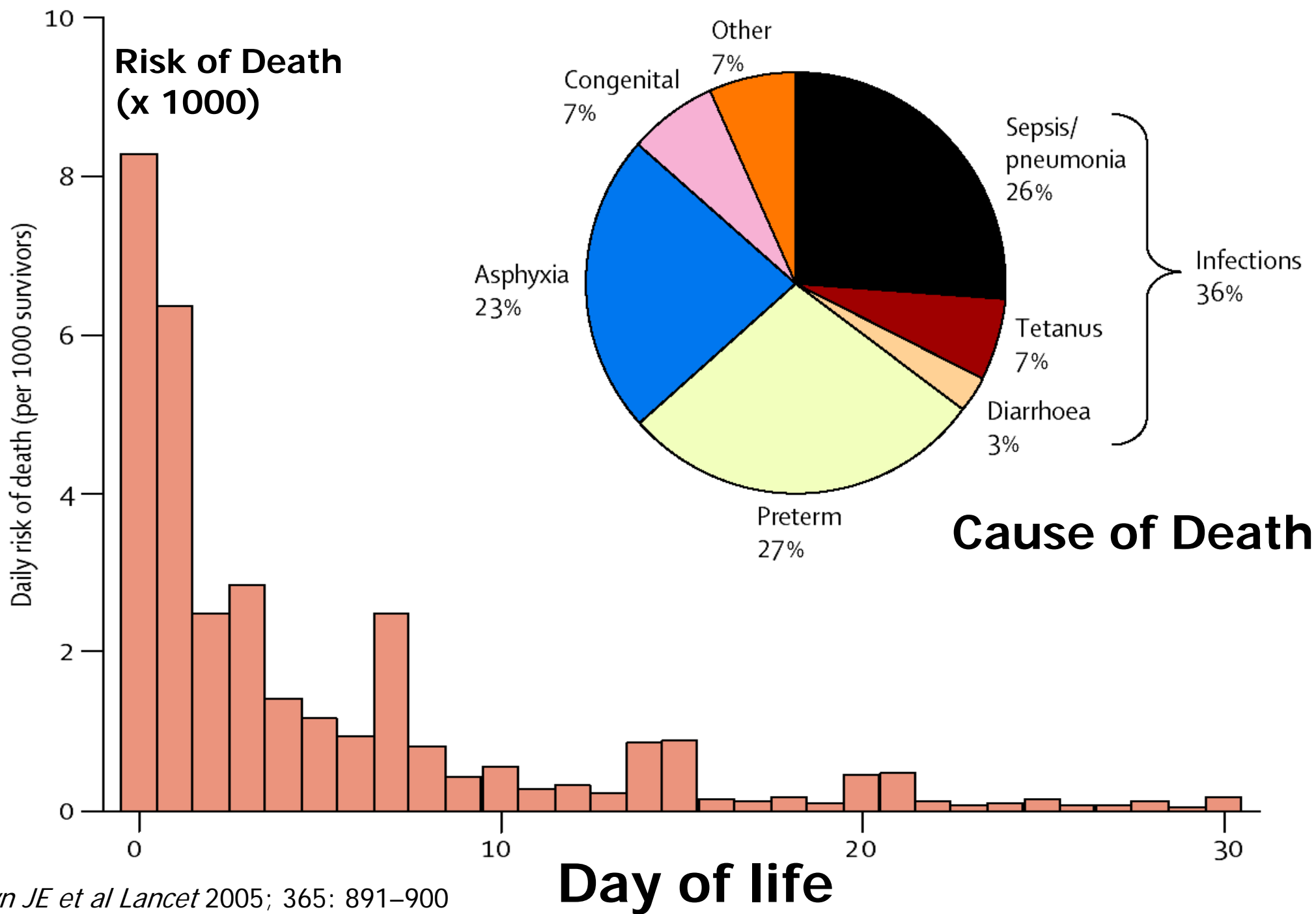
Lawn JE et al Lancet 2005; 365: 891–900

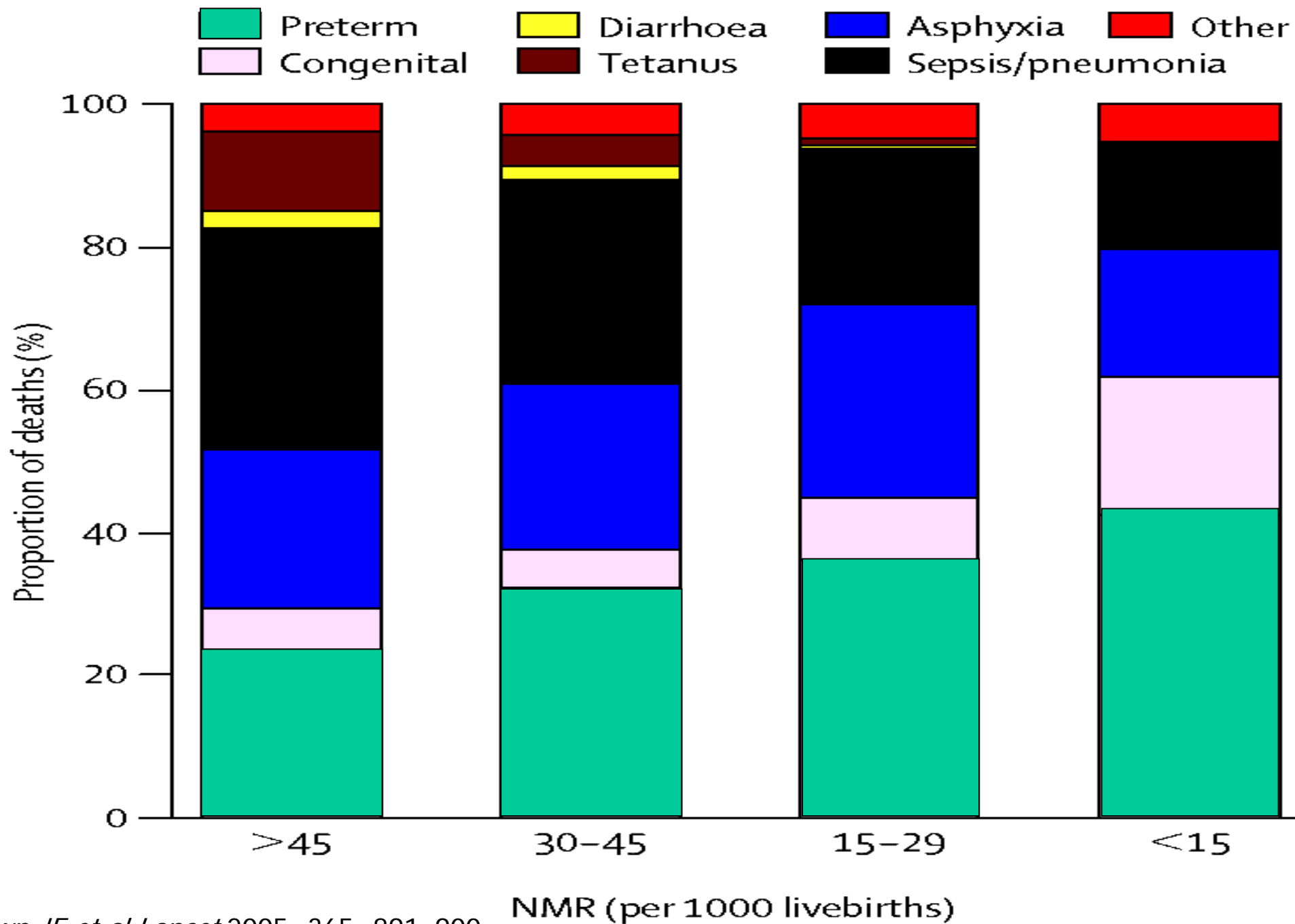
Why?

- The major direct causes of neonatal deaths are infections (36%), preterm birth (28%), asphyxia (23%)
- Cause of death varies with level of neonatal mortality. 60–80% of neonatal deaths arise in low birthweight
- Reduction of mortality among moderately preterm and term IUGR is feasible without complex technology.
- Maternal complications, especially during childbirth, carry a high risk of neonatal death.
- Elimination of mortality gap between richest/poorest developing countries could avert 0.75 million deaths.

Mortalidad Neonatal a nivel Global (x 1000)







Life-cycle factors

Lawn JE et al Lancet 2005; 365: 891–900

Maternal age (years) 1.1–2.3

<18 1.3–2.0

>35

Maternal size

Height <150 cm 1.3–4.8

Prepregnancy weight <47 kg 1.1–2.4

Parity

Primigravida 1.3–2.2

Parity >6 1.4–1.5

Poor obstetric history (previous perinatal death or instrumental delivery) 1.6–3.5

Antenatal factors

Lawn JE et al Lancet 2005; 365: 891–900

Multiple pregnancy	2.0–6.8
Hypertensive disorders	
Pre-eclampsia	1.7–3.7
Eclampsia	2.9–13.7
Bleeding per vagina after 8th month	3.4–5.7
Maternal jaundice	2.0–7.9
Maternal anaemia (PCV <0.21)	1.9–4.2
Maternal anaemia (PCV <33%)	NS in 4 studies
Maternal malaria (blood test positive)	2.2–3.5†
Syphilis (perinatal death)	1.7–5.8
HIV (infant death)	7.2

Intrapartum factors

Lawn JE et al Lancet 2005; 365: 891–900

Malpresentation

Breech 6.4–14.7

Other 8.3–33.5

Obstructed labour/dystocia 6.7–84.9

Prolonged second stage 2.6–4.8

Maternal fever during labour ($>38^{\circ}\text{C}$) 9.7–10.2

Rupture of membranes >24 h 1.8–6.7

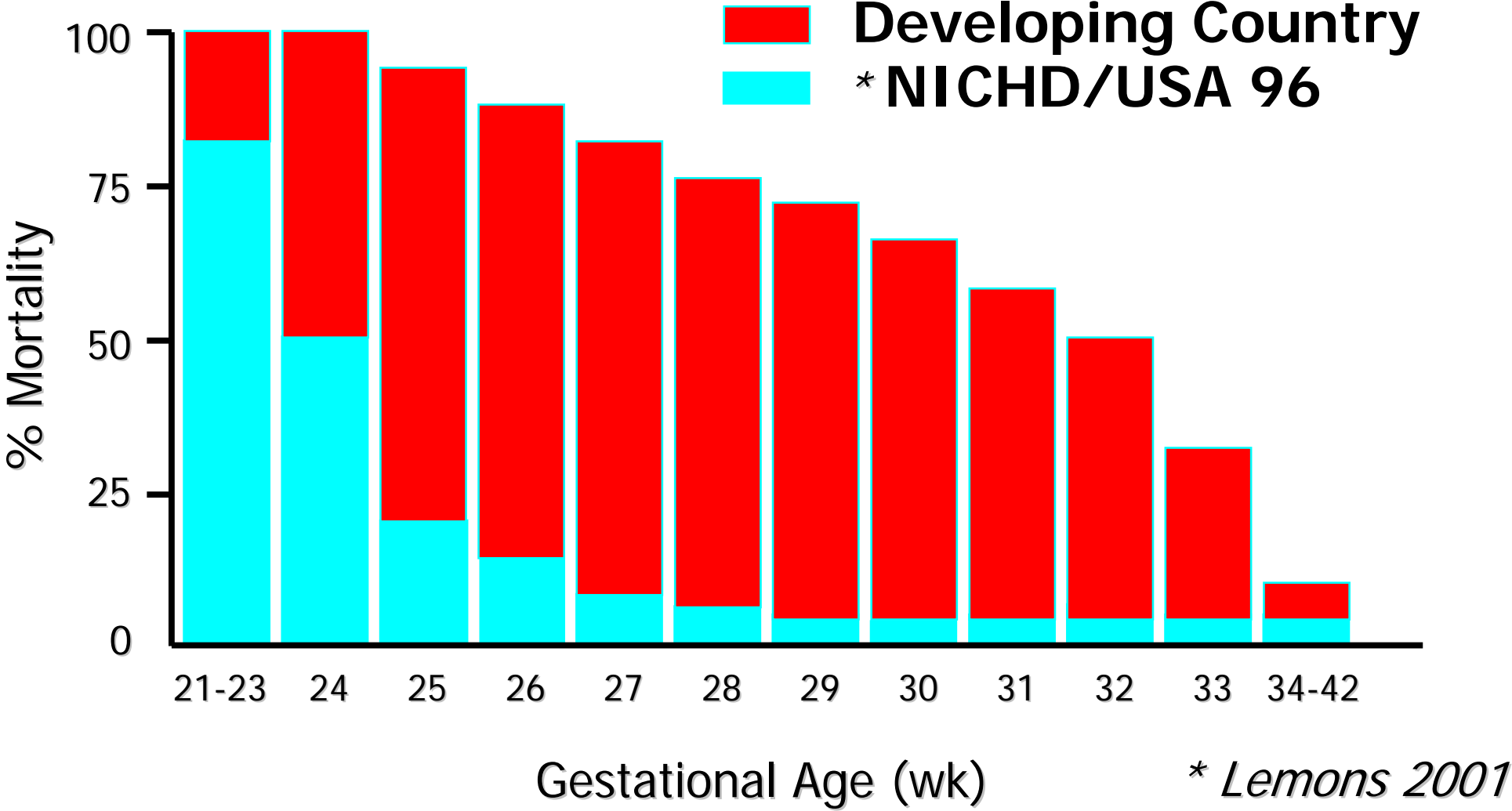
Meconium staining of liquor 11.5

Low Birth Weight

A close-up photograph of a newborn baby with a very thin, frail appearance, being held gently in the hands of an elderly person. The baby's skin is pale and appears delicate. The elderly person's hands are wrinkled and weathered, showing signs of age. The baby is wrapped in a yellow and red cloth. The background is a blue fabric.

45% of Bangladeshi infants
Weigh less than 2.5 Kg
The highest of any country

Neonatal Mortality by Gestational Age

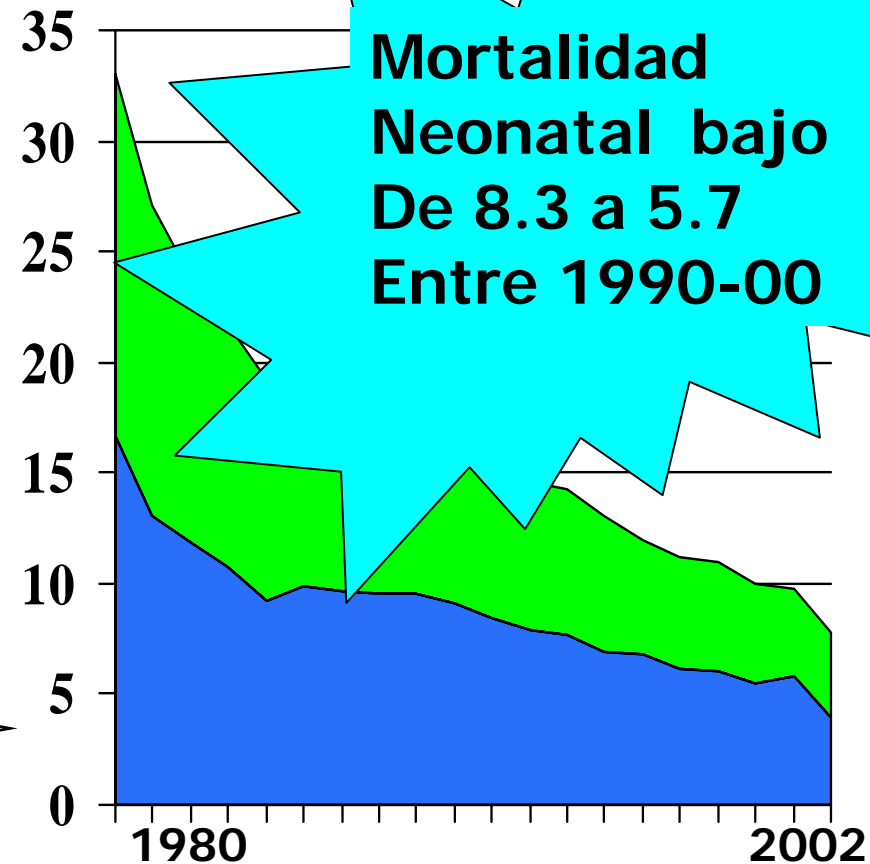
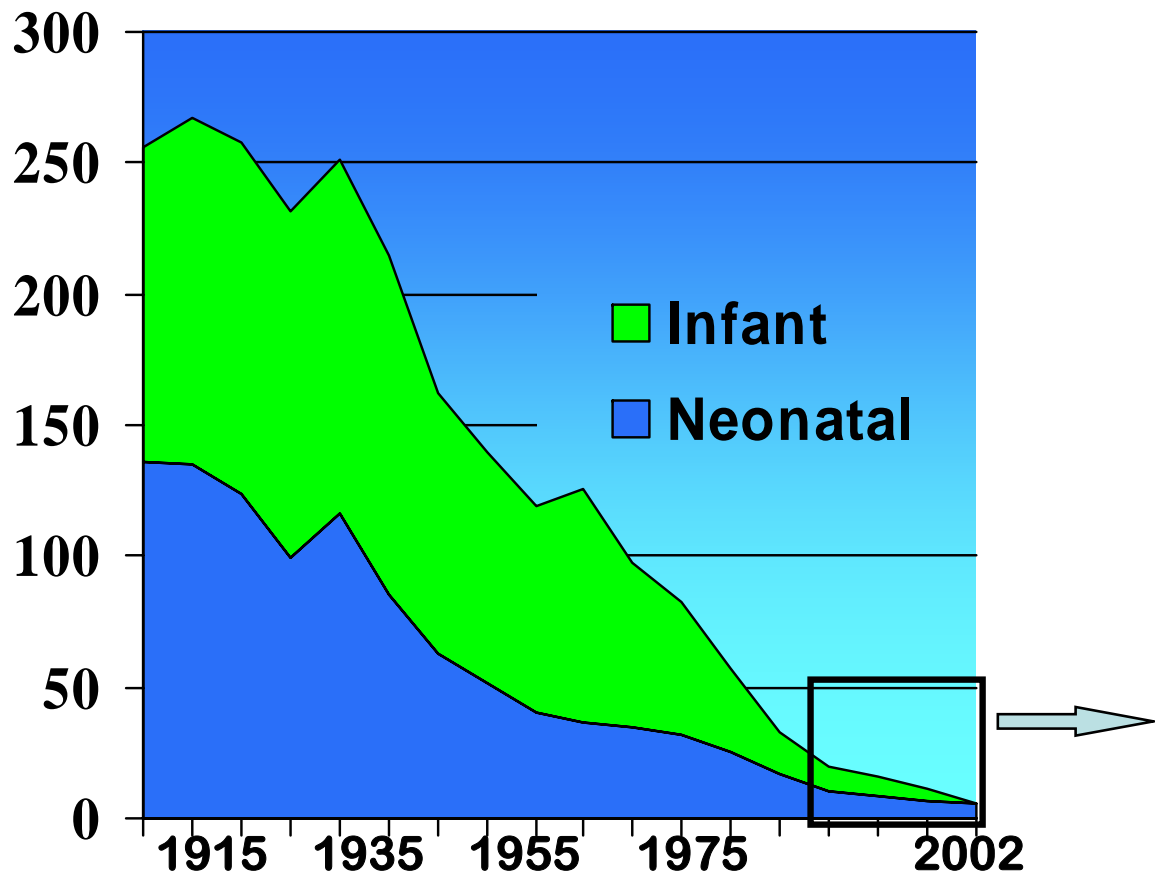


Avances en Chile en sobrevida Neonatal

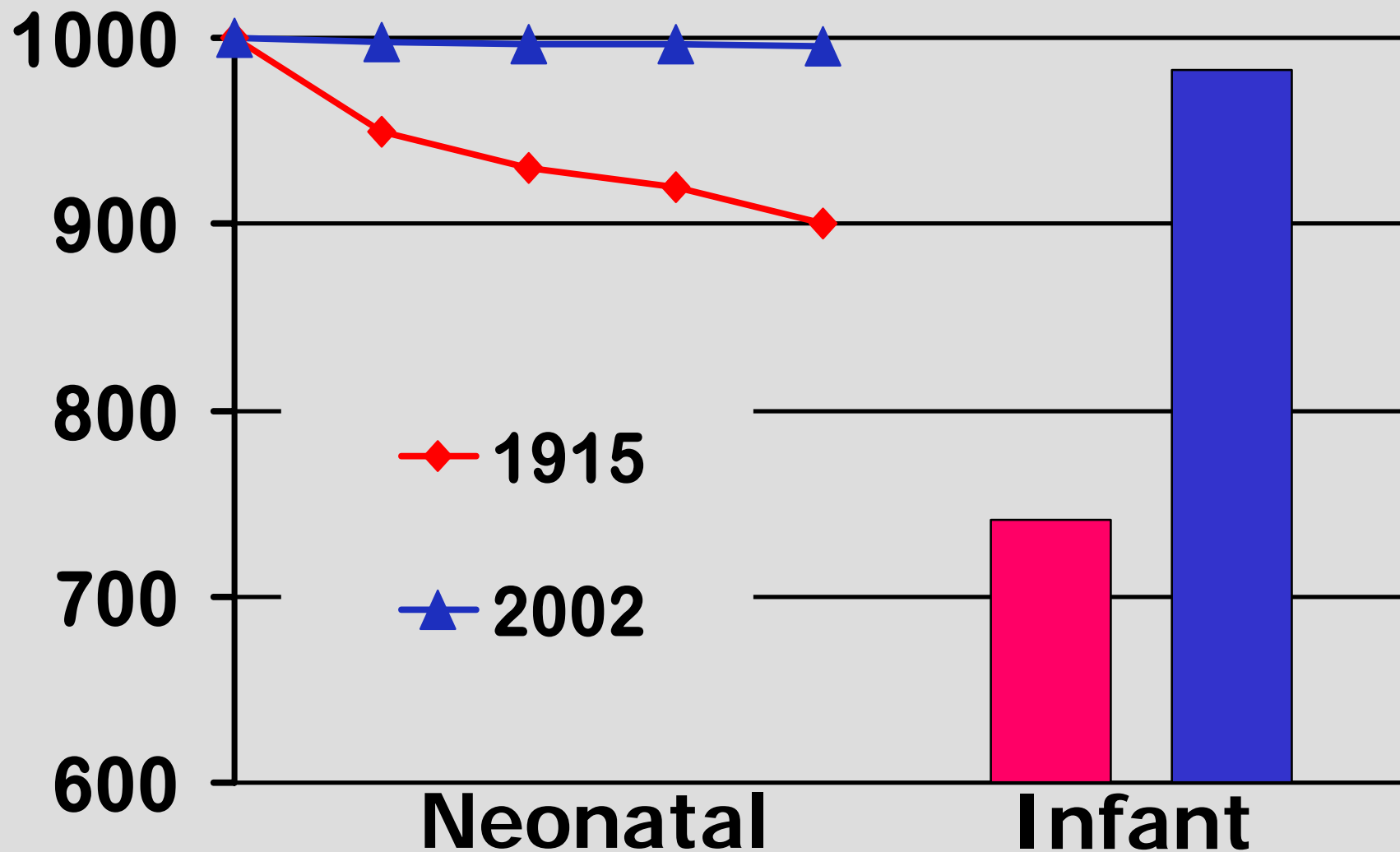


- ⌘ Chile ha progresado notablemente en disminuir las muertes neonatales
- ⌘ Gran parte del progreso en Chile se debió al aumento de la cobertura del parto hospitalario, mejor cuidado obstétrico y neonatal, y al mejor peso al nacer.
- ⌘ El avance en los últimos 20 años se debe en parte al mejor cuidado intensivo neonatal.

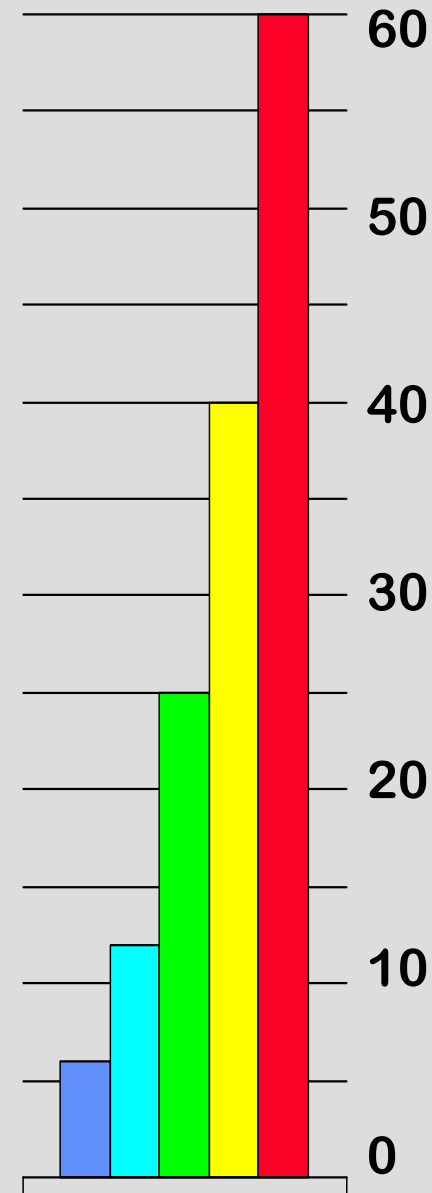
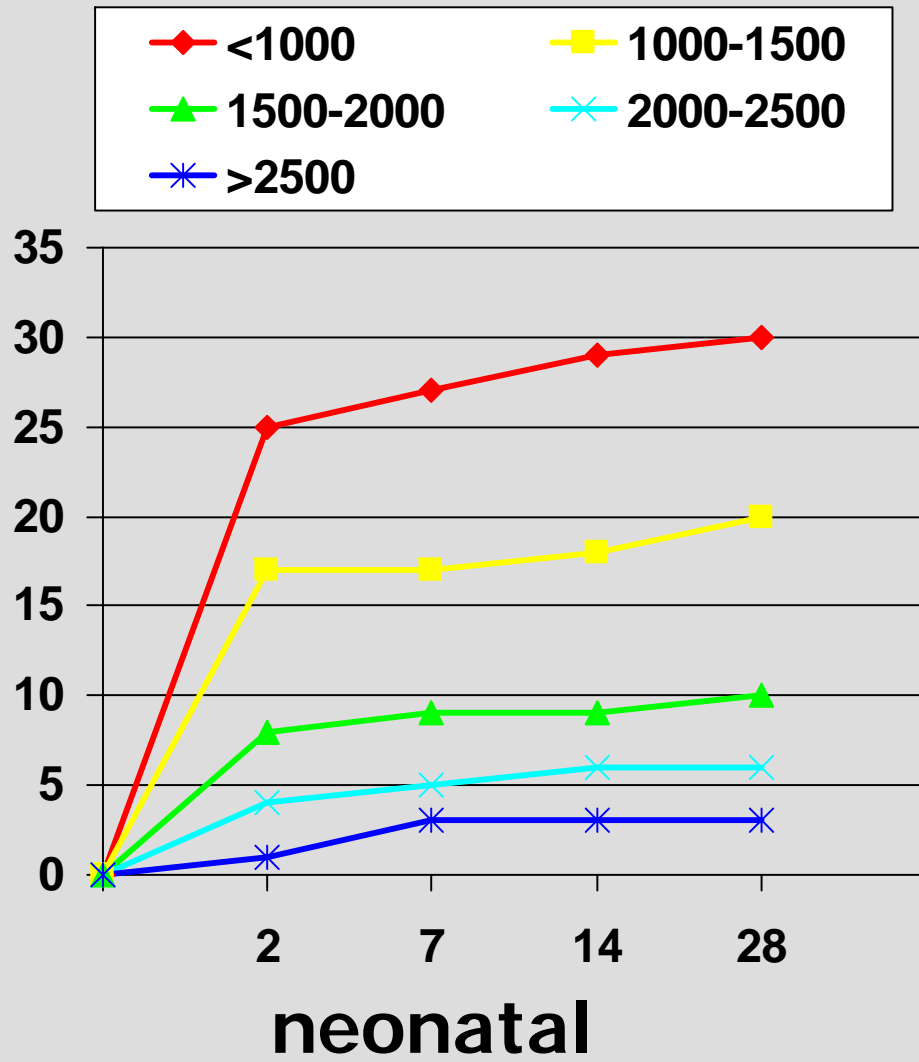
Neonatal and Infant Mortality (x 1000 births) Chile 1915-2002



Child Survival Chile 1915-02



Mortalidad neonatal e infantil por grupos de peso



infantil

Chilean
Ministry of
Health
Report

Desafios Actuales en Neonatologia



- ⌘ Pending issues (CLD, Brain/retina, NEC, Sepsis)
- ⌘ Survival and long term consequences of BW < 600 g
- ⌘ Improve quality of neonatal care and health care delivery systems
- ⌘ Costs, cost effectiveness and reimbursement of care

A newborn baby is lying in a hospital bed, appearing unwell. The baby's face is pale and they have a slightly open mouth. There are several medical tubes and wires connected to the baby's chest and head. The background shows a typical hospital room setting with a white bedsheet and some medical equipment.

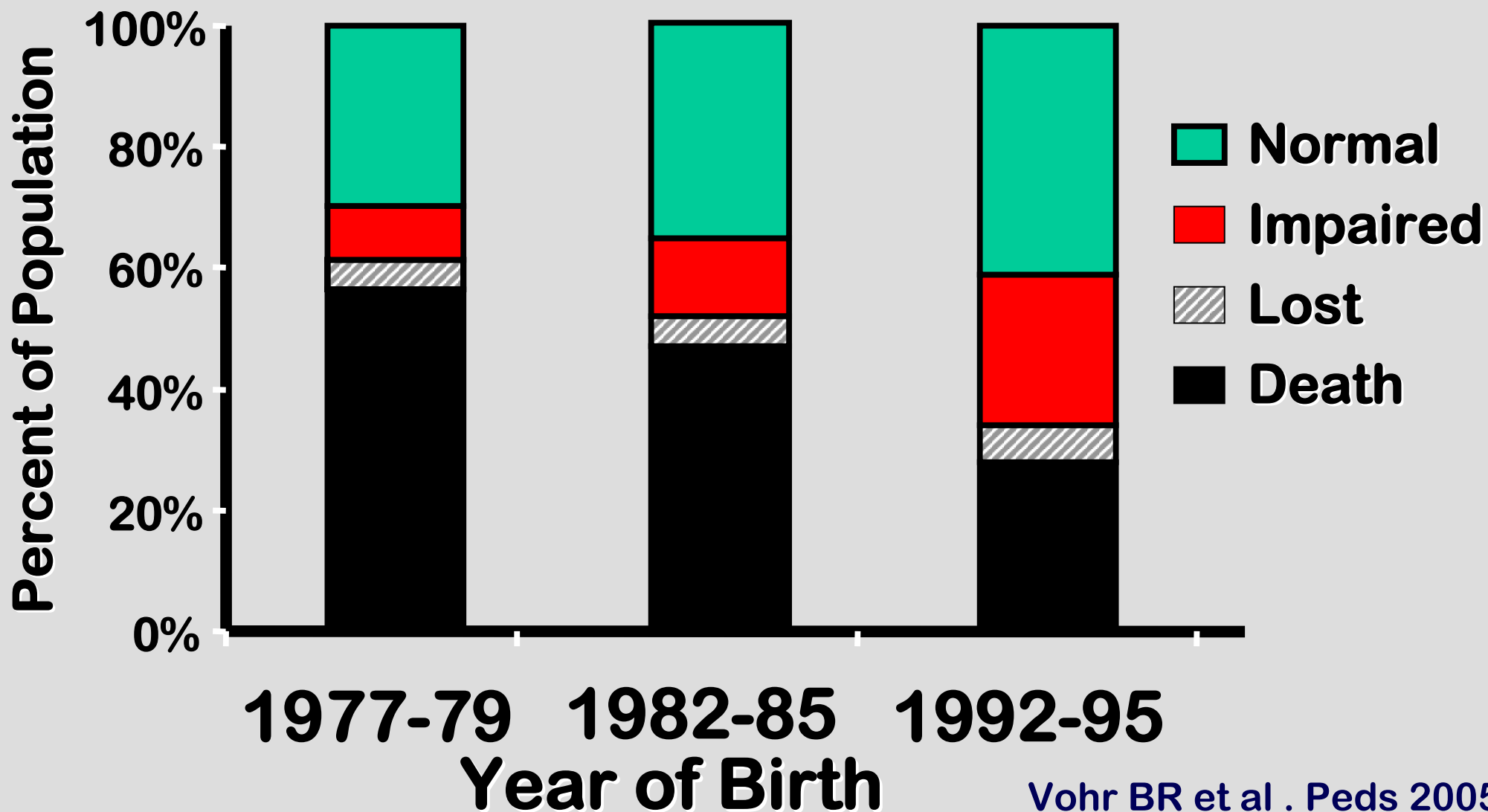
Brain/retina

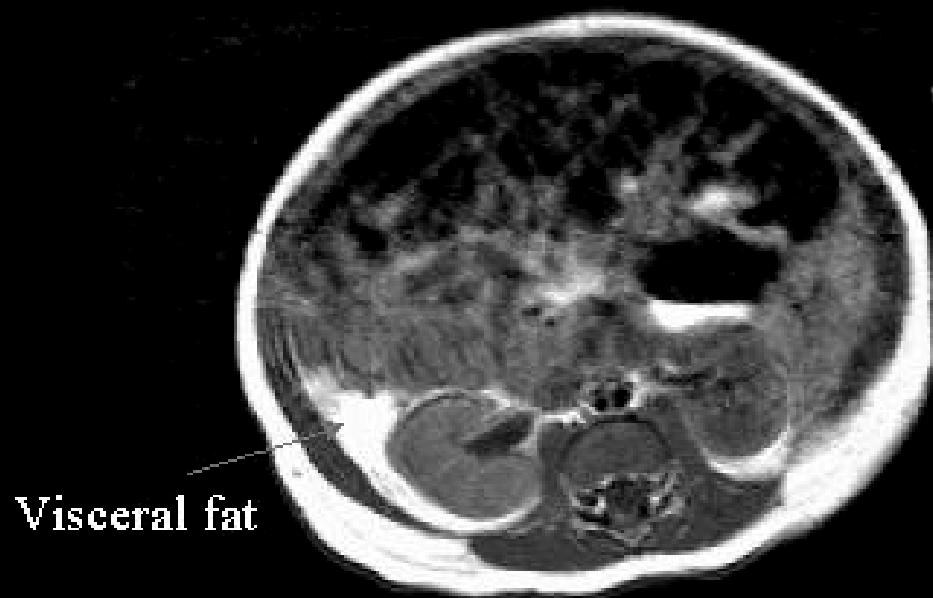
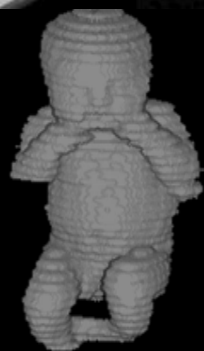
CLD

Sepsis

NEC

Two Year Outcome of Very Low Birth Weight Infants (< 1000 gm) USA





Fetal Infants: The Fate of 4172 Infants With Birth Weights of 401 to 500 Grams—The Vermont Oxford Network Experience (1996–2000)

- 17% survived until discharge, 2186 (52%) died in the DR and 1986 48% were admitted to a NICU.
- Infants who survived the DR and went to NICU were more likely to be female (58% vs 49%), to be SGA (56% vs 11%), to be Rx with prenatal steroids (61% vs 12%) and born by cesarean section (55% vs 5%).
- 36 % of NICU admissions survived to discharge GA of 690 NICU survivors was 25.3 ± 2 weeks, survivors experienced significant morbidity in the NICU.



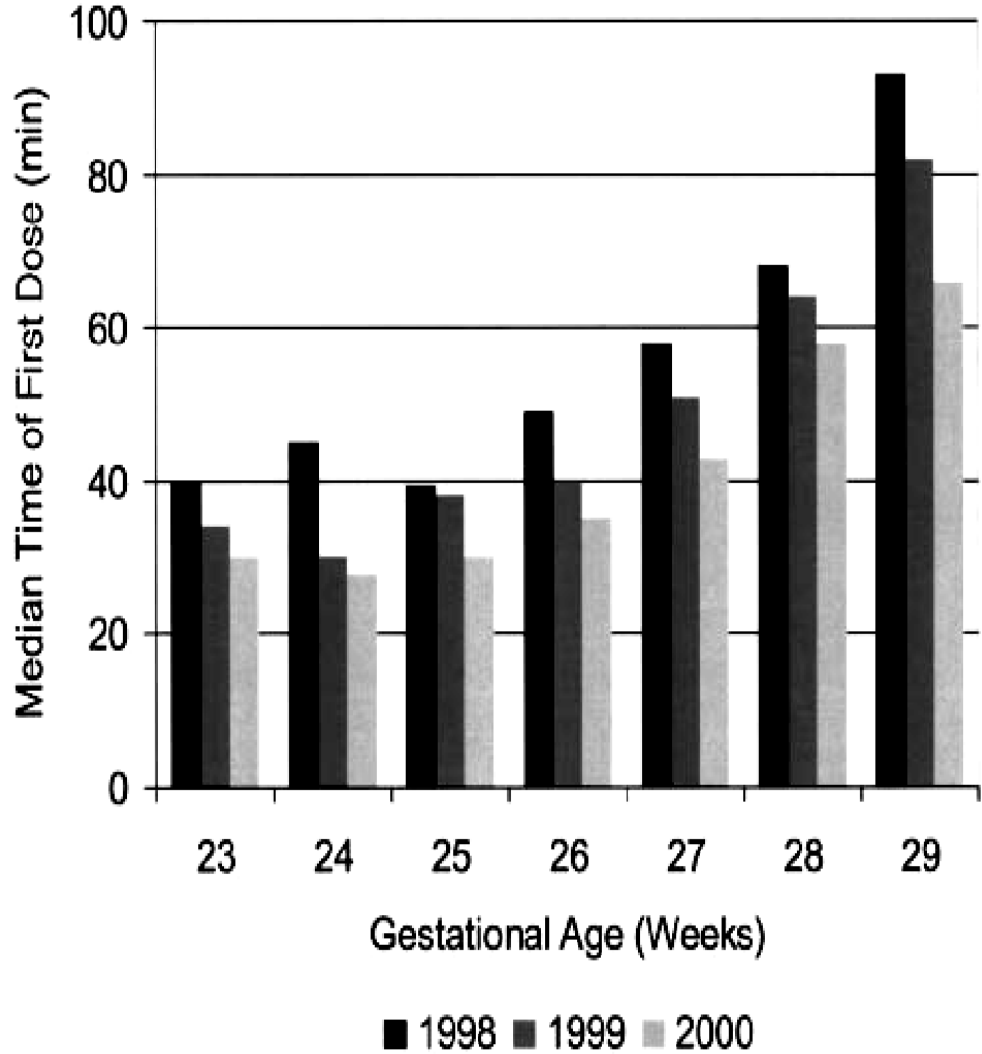
“These infants are not “miracle babies.” We are neither miracle workers nor “techno crazies”. We are in a difficult position. We need a new approach. If we don’t, we will be asking the same questions 10 years from now”. Jerold F. Lucey

Timing of Initial Surfactant Treatment for Infants 23 to 29 Weeks' Gestation: Is Routine Practice Evidence Based?

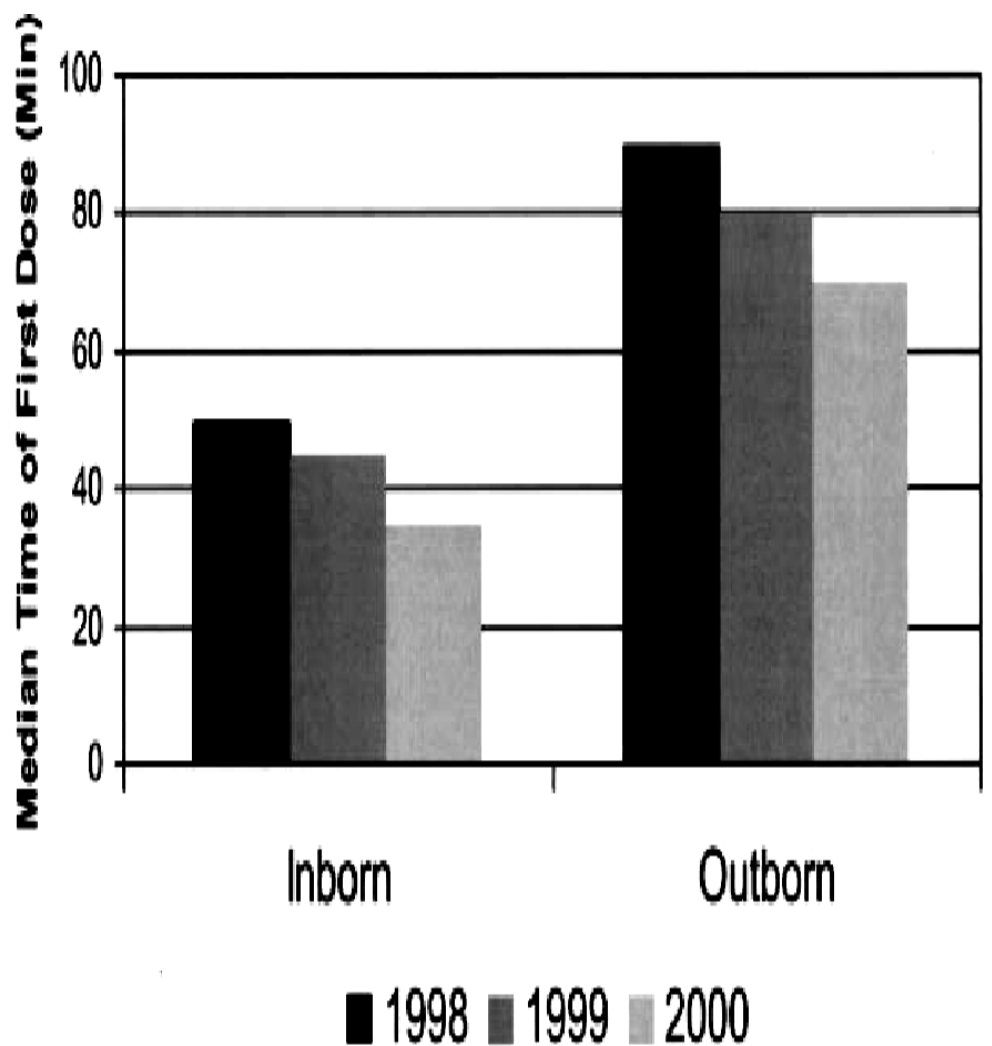
Objective. To describe the timing of initial surfactant treatment for high-risk preterm infants in routine practice and compare these findings with evidence from RCT and published guidelines.

Methods. Vermont Oxford Network Database for infants born from 1998 to 2000, BW 401-1500 g and GA 23-29 wks were analyzed to determine the time after birth at which the initial dose of surfactant was administered. Multivariate models adjusting for clustering of cases within hospitals identified factors associated with surfactant use and its timing.

Time (min) for first dose of surfactant by gestational age and year of birth

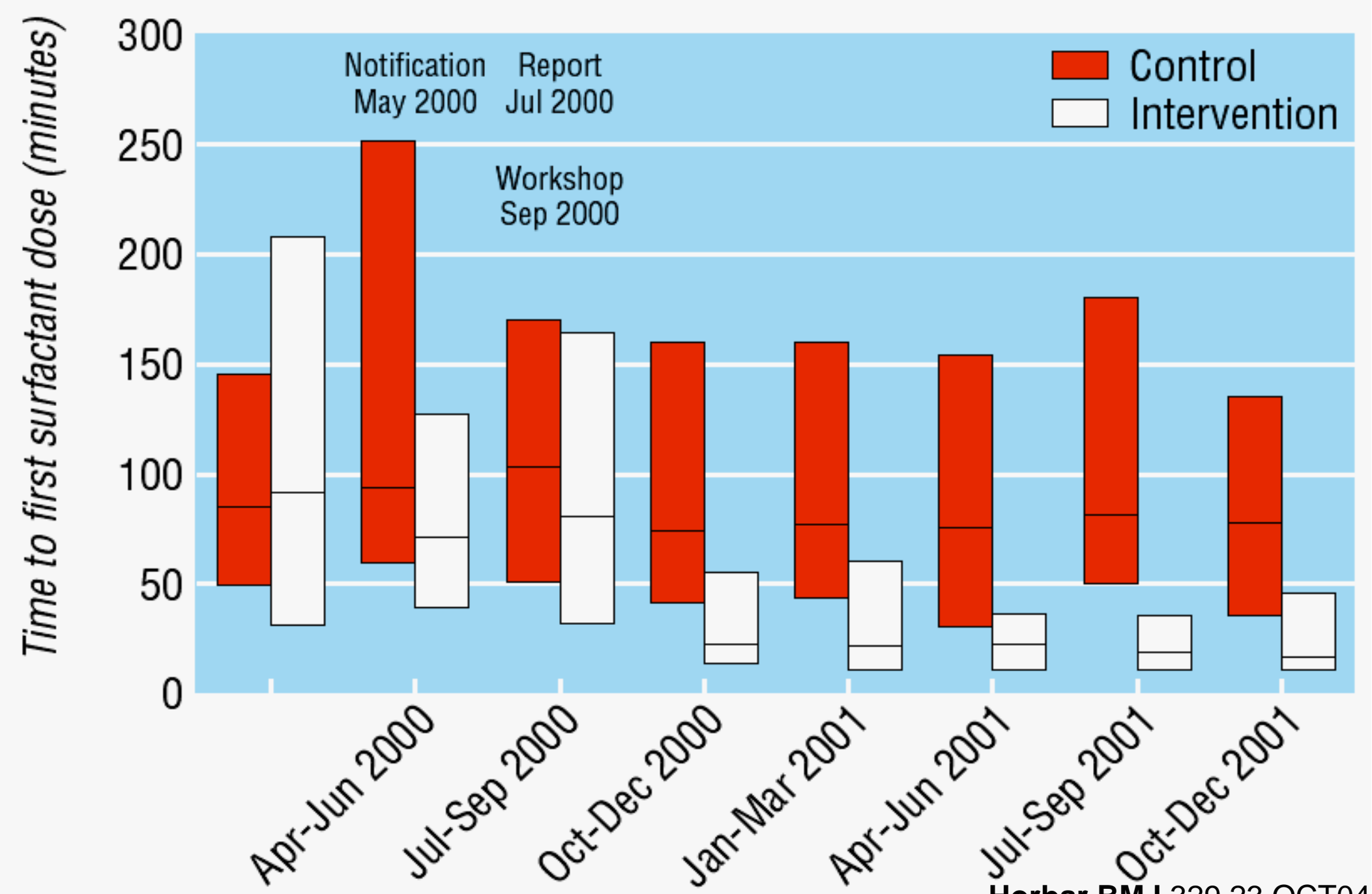


Time (min) for first dose of surfactant by place & year of birth



Meta-analysis of 8 trials of prophylactic surfactant

- Administration of natural surfactant extract leads to a significant reduction in the **risk of pneumothorax** (typical relative risk: 0.62; [95% CI: 0.42-0.89]; typical risk reduction: 2% [95% CI 4% to 1%])
- Significant reduction in the **risk of mortality** (typical relative risk: 0.61; [95% CI: 0.48-0.77]; typical risk reduction: 5%; [95% CI: 7% to 2%]).
- Because of the greater risk of RDS and mortality with decreasing gestational age, the benefits of prophylactic surfactant administration are most pronounced in infants of < 30 weeks' gestation.



What is already known on this topic

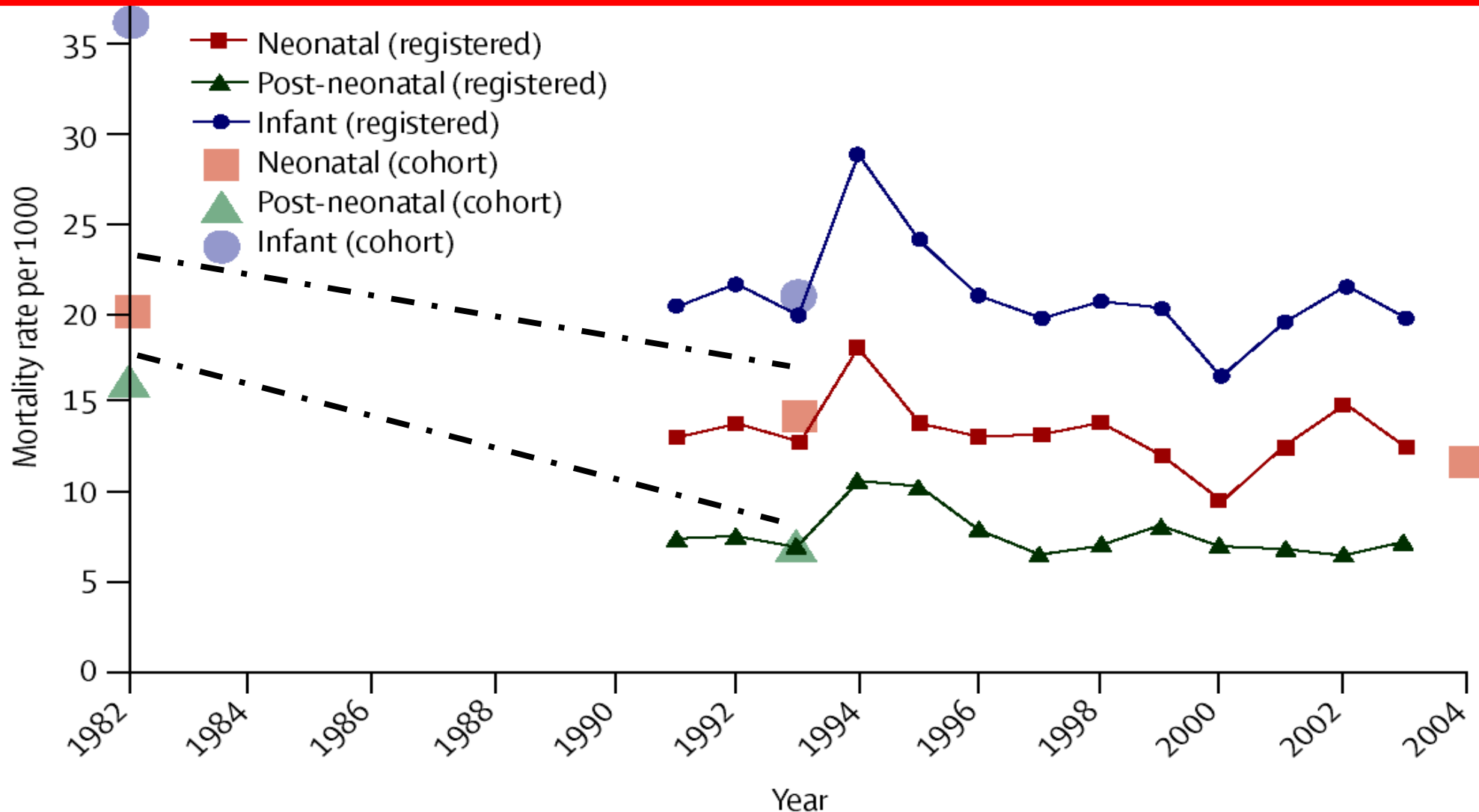
Quality improvement collaborative interventions encourage evidence based practices as used in various healthcare settings

What this study adds:

A multifaceted collaborative quality improvement intervention based on four key habits (***change, evidence based practice, systems thinking, & collaborative learning***) was used to promote evidence based surfactant therapy for preterm infants

- It produced significant changes in the timing of surfactant use and a 37% increase in surfactant treatment in the delivery room.
- It did not result in changes in mortality or Pneumothorax. however power to detect these may have been low.

The challenge of reducing neonatal mortality in middle-income countries: findings from three Brazilian birth cohorts in 1982, 1993, and 2004



Neonatal Mortality by Birth Weight and Gestational Age

	Birth cohort (year)			p*
	1982	1993	2004 (Jan–Jul)	
Birthweight (g)				0.0001
<1500	44 (688)	28 (609)	13 (382)	
1500–2499	37 (79)	20 (43)	5 (23)	
≥2500	34 (6)	17 (4)	6 (3)	
Unknown	3 (600)	10 (588)	4 (667)	
Gestational age (weeks)				0.0001
<34	24 (490)	17 (153)	12 (145)	
34–36	8 (33)	5 (13)	5 (19)	
≥37	35 (8)	19 (5)	6 (3)	
Unknown	51 (41)	34 (55)	5 (17)	
Total	118 (20)	75 (14)	28 (12)	

Data are number of deaths (rate per 1000 in category). * χ^2 test for heterogeneity.

maternal characteristics show lower risk for neonatal death	Birth cohort (year)			p
	1982	1993	2004 (Jan–Jul)	
Number of livebirths	5914	5249	2403	
Height (cm)				
Mean (SD)	156.4 (6.0)	159.8 (6.8)	160.9 (6.9)	0.0001*
<150	637 (11.0%)	239 (4.6%)	69 (3.9%)	0.0001*
Pre-gestational weight (kg)				
Mean (SD)	55.7 (9.6)	58.2 (10.5)	60.8 (12.1)	0.0001*
<49	1168 (23.1%)	805 (15.7%)	256 (11.4%)	0.0001*
Schooling (years)				
Mean (SD)	6.5 (4.2)	6.7 (3.6)	8.0 (3.5)	0.0001*
0	327 (5.5%)	130 (2.5%)	29 (1.2%)	0.0001*
≥9	1493 (25.3%)	1350 (25.8%)	1021 (42.8%)	0.0001*
Birth interval (months)				
Mean (SD)	44.9 (34.1)	58.5 (41.3)	66.7 (46.9)	0.0001*
<24	1123 (30.6%)	587 (19.2%)	193 (16.0%)	0.0001*
Antenatal care				
≥1 attendances	5589 (94.9%)	4987 (95.2%)	2276 (98.6%)	0.0001*
Antenatal care started in first trimester	1124 (61.5%)	3579 (72.3%)	1739 (74.2%)	0.0001*
Mean (SD) number of antenatal visits	6.6 (3.2)	7.7 (3.7)	8.3 (3.3)	0.0001*

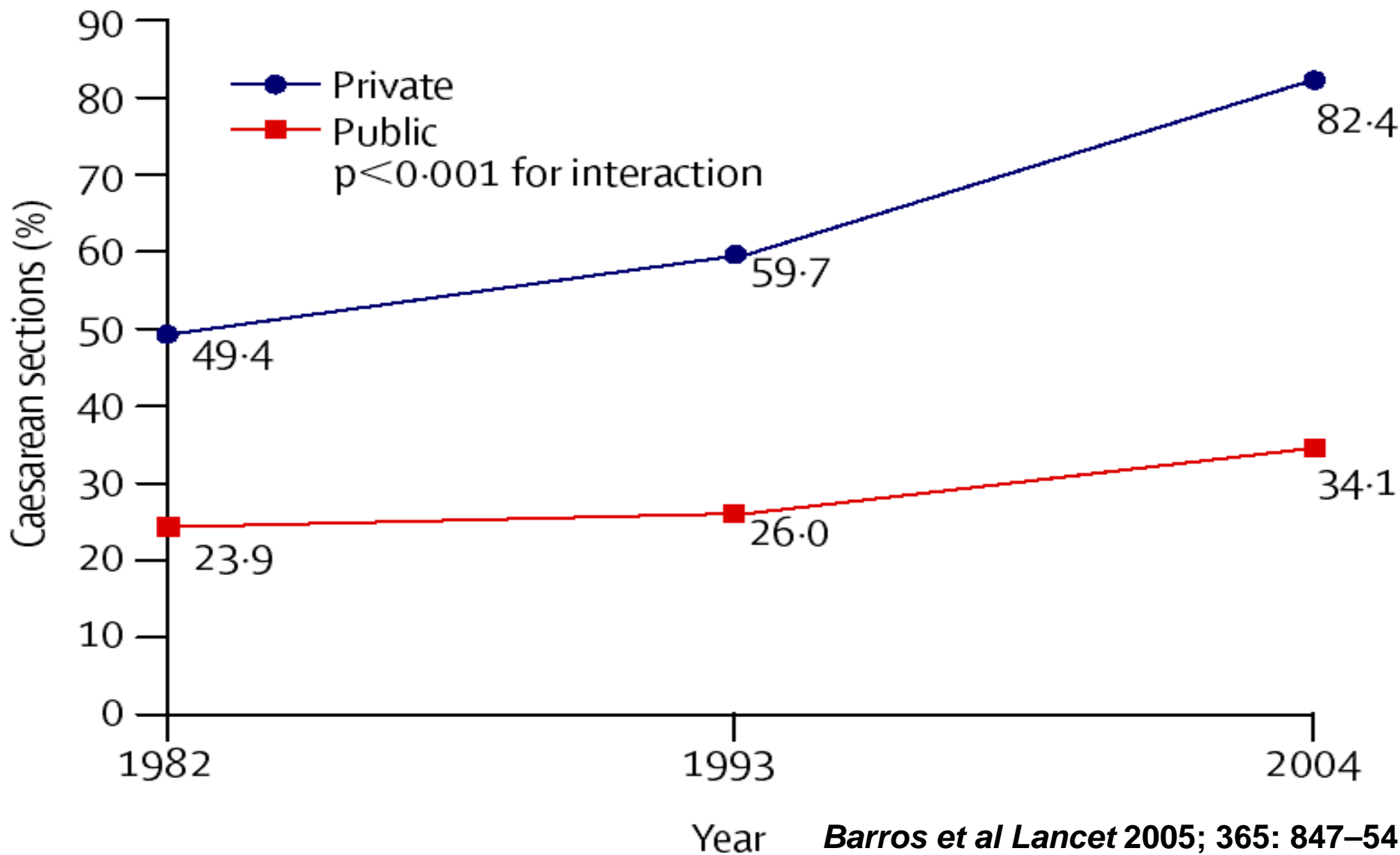
Perinatal outcomes

	1982	1993	2004 (Jan-Jul)	
Number of livebirths	5914	5249	2403	
Type of payment				0.0001*
Private care or private insurance	867 (14.7%)	708 (13.5%)	454 (18.9%)	
Government insurance	5047 (85.3%)	4541 (86.5%)	1946 (81.1%)	
Caesarean sections	1632 (27.6%)	1602 (30.5%)	1039 (43.2%)	0.0001*
Gestational age (weeks)†				0.0001
<34	49 (1.1%)	111 (2.4%)	83 (3.9%)	
34-36	245 (5.3%)	387 (8.4%)	259 (12.3%)	
37-38	1038 (22.3%)	933 (20.1%)	574 (26.3%)	
≥39	3333 (71.4%)	3197 (69.1%)	1196 (57.5%)	
Missing or implausible data	1249 (21.1%)	621 (11.8%)	291 (12.1%)	0.0001
Pre-term births (<37 weeks)	294 (6.3%)	498 (10.8%)	342 (16.2%)	0.0001*
Birthweight (g)				
Mean (SD)	3187 (565)	3157 (549)	3140 (554)	0.0001*
<1500	64 (1.1%)	46 (0.9%)	34 (1.4%)	0.10
<2500	534 (9.0%)	510 (9.8%)	248 (10.4%)	0.05*
>3500	1620 (27.4%)	1283 (24.5%)	572 (23.9%)	0.0001*
Small for gestational age	1014 (21.7%)	1117 (24.2%)	394 (18.7%)	0.001
Unknown	5	17	6	
Deaths (mortality rates per 1000 births)				
Late fetal (total births)	97 (16.1)	55 (10.4)	24 (9.9)	0.005*
Neonatal (livebirths)	118 (20.0)	75 (14.3)	28 (11.7)	0.003*
Postneonatal (livebirths)	92 (15.6)	36 (6.8)	n/a	0.0001

% Preterm & LBW 82-04 by type of delivery

	Preterm births		Low birthweight		Mean (SD) birthweight (g)	
	Vaginal	Caesarean	Vaginal	Caesarean	Vaginal	Caesarean
1982	206/3292 (6.3%)	88/1373 (6.4%)	390/4281 (9.1%)	144/1628 (8.9%)	3173 (554)	3226 (591)
1993	328/3189 (10.3%)	170/1439 (11.8%)	354/3635 (9.7%)	156/1597 (9.8%)	3135 (528)	3207 (592)
2004	188/1183 (15.9%)	154/929 (16.6%)	124/1362 (9.1%)	124/1035 (12.0%)	3123 (519)	3161 (597)
p	0.0001*	0.0001*	0.60	0.01*	0.001*	0.002*

% Cesarean Section Private vs Public Care



The challenge of reducing neonatal mortality in middle-income countries: findings from three Brazilian birth cohorts in 1982, 1993, and 2004

Barros et al Lancet 2005; 365: 847–54

Fernando C Barros, Cesar G Victora, Aluisio J D Barros, Ina S Santos, Elaine Albernaz, Alicia Matijasevich, Marlos R Domingues, Iândora K T Scowitz, Pedro C Hallal, Mariângela F Silveira, J Patrick Vaughan

Despite improvements in maternal risk characteristics, preterm births increased from 6.3% in 1982 to 16.2% in 2004, with a 47 g reduction in mean birth weight. Antenatal visits in 2004 was 8.3 per woman, but quality of care was inadequate.

Rate of caesarean sections increased greatly, from 28% in 1982 to 43% in 2004, reaching 374 of 456 of all private deliveries in 2004. Higher rates of preterm births seemed to result from CS caesarean sections or inductions.

Newborn care improved, GA specific mortality rates fell by about 50% since 1982. As a result, neonatal mortality rates remain stable since 1990, despite higher rates of preterm deliveries

Prácticas basadas en la evidencia



- ⌘ Como definir grados de calidad de la evidencia
- ⌘ Importancia de las revisiones sistemáticas
- ⌘ Estudios Colaborativos Randomizados ¿única manera?
- ⌘ Como podemos seguir avanzando

Grados de Calidad de la Evidencia:

- I Revisión sistemática de todos los estudios relevantes de calidad
- II Basado por lo menos en un estudio clínico controlado randomizado PCCR
- III-1 Varios estudios controlados no-randomizados
- III-2 Estudios de cohortes o caso-control bien diseñados
- III-3 Múltiples estudios de cambios en el tiempo
- IV Opinión de autoridades respetables, basado en experiencia clínica, estudios descriptivos, informes de grupos técnicos.

Que lo que es una revisión sistemática?

- ⌘ Se distingue de otras revisiones por el rigor metodológico que asegurar que los resultados y conclusiones son **lo mas cercano posible a la verdad.**
- ⌘ Los **métodos son definidos a priori** en forma explicita y están documentados en un protocolo.
- ⌘ Se presentan los detalles de métodos y las conclusiones de forma tal que **otros puedan juzgar la calidad**
- ⌘ Puede ser '**replicado**' por cualquier evaluador usando los mismos métodos.

Ventajas de una revisión sistemática:

- ⌘ Combina diversas poblaciones, tipo de intervenciones y efectos – son mas generalizables
- ⌘ Puede evaluar si los efectos de una intervención son diferentes según la definición de la enfermedad y para posibles sub grupos de la población estudiada.
- ⌘ Por tener un número mayor de sujetos tienen mayor significancia y robustez (evitan errores).
- ⌘ Permiten definir con mayor precisión la magnitud del efecto observado

National Institute of Child
Health & Human Development



www.nichd.nih.gov/cochrane/cochrane.htm

Alphabetical listing of systematic reviews

[A](#) [B](#) [C](#) [D](#) [E](#) [F](#) [G](#) [H](#) [I](#) [J](#) [K](#) [L](#) [M](#) [N](#) [O](#) [P](#) [Q](#) [R](#) [S](#) [T](#) [U](#) [V](#) [W](#) [X](#) [Y](#) [Z](#)

A

- [Aerosolized diuretics in preterm infants with \(or developing\) chronic lung disease](#)

B

www.nichd.nih.gov/cochrane/cochrane.htm

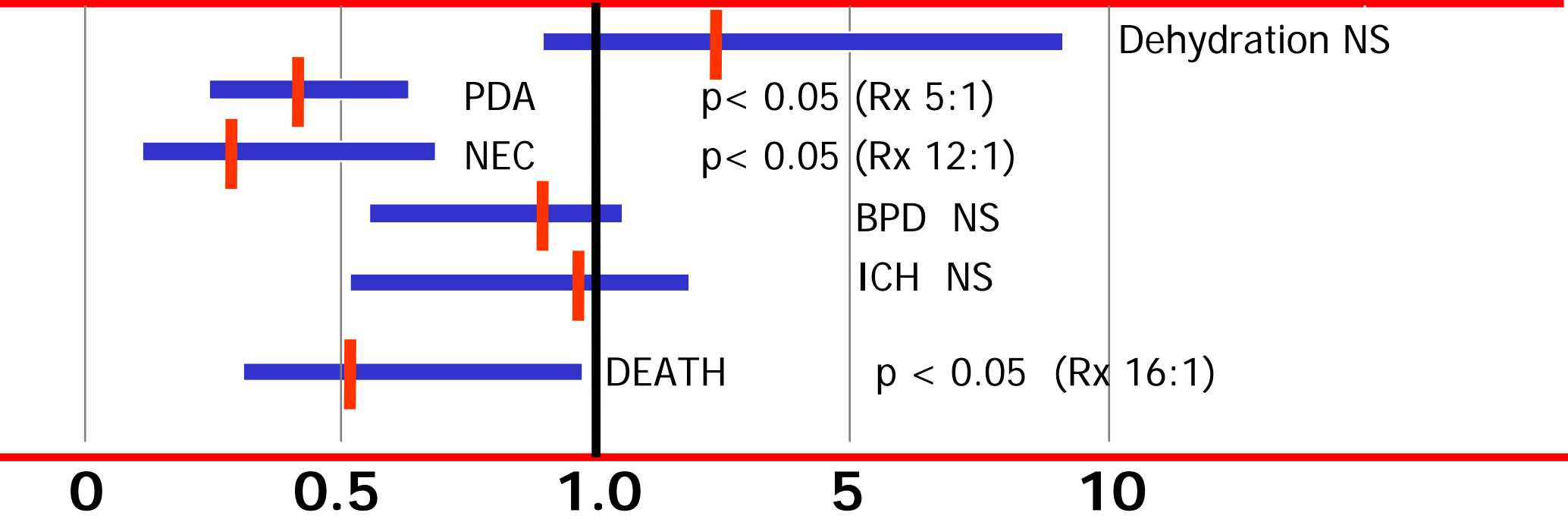
National Institute of Child
Health & Human Development



Restricted versus Liberal Water Supply in LBW

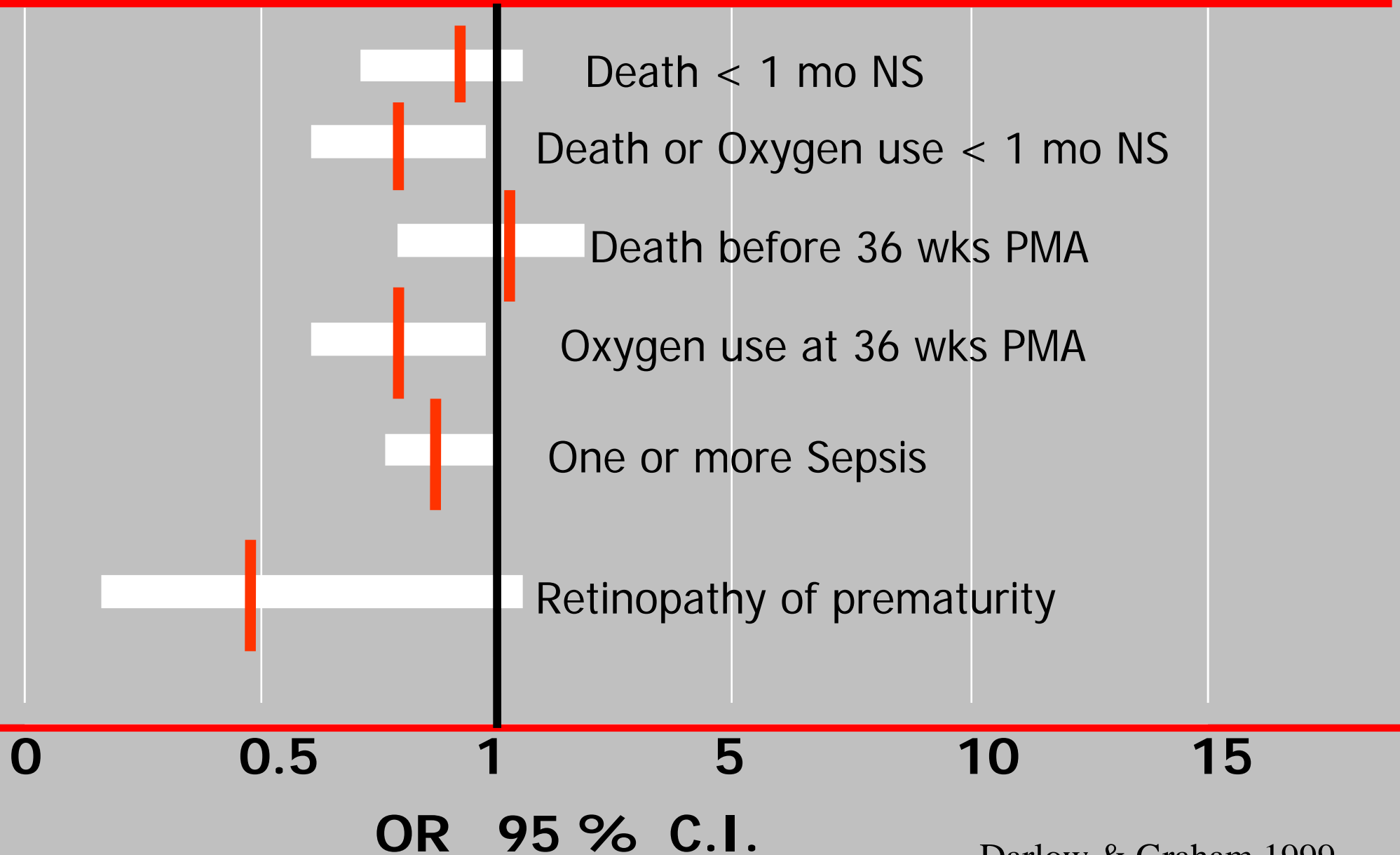
Restricted versus liberal water intake (4 studies total)

	n studies	n participants	Mean (95 % confidence interval)	
Weight loss (%)	3	326	1.94 (0.82 - 3.07)	WMD
Dehydration	2	258	2.43 (0.71 - 8.28)	RR
Patent ductus arteriosus	3	358	0.40 (0.26 - 0.63)	RR
Necrotizing Enterocolitis	3	358	0.30 (0.13 - 0.71)	RR
Bronchopulmonary dysplasia	3	358	0.80 (0.56 - 1.14)	RR
Intracranial hemorrhage	2	188	0.94 (0.52 - 1.72)	RR
Death	4	414	0.52 (0.28 - 0.96)	RR

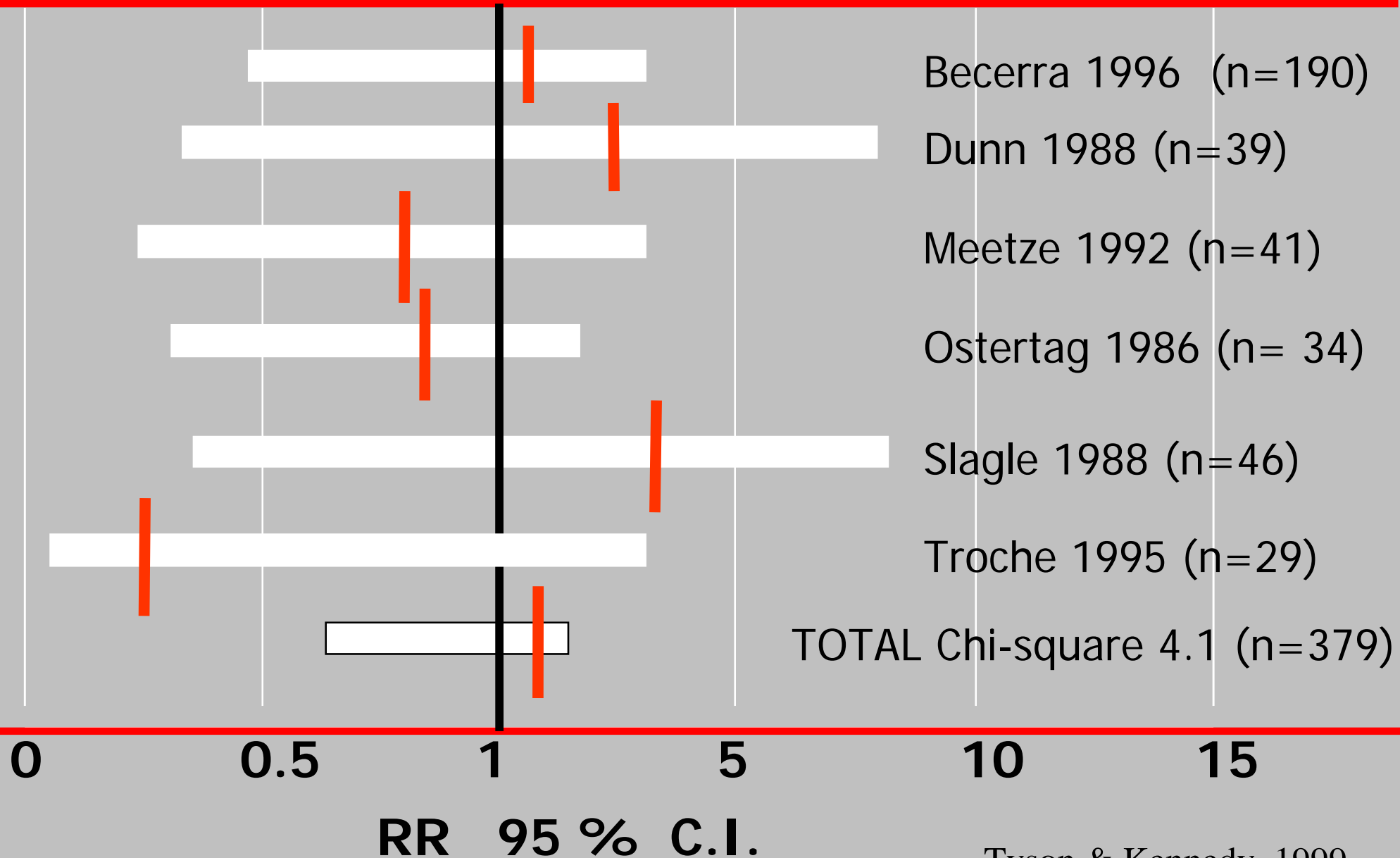


Relative Risk 95 % confidence interval

Vit A supplement to prevent morbidity in VLBW



Minimal Enteral Nutrition and NEC in VLBW

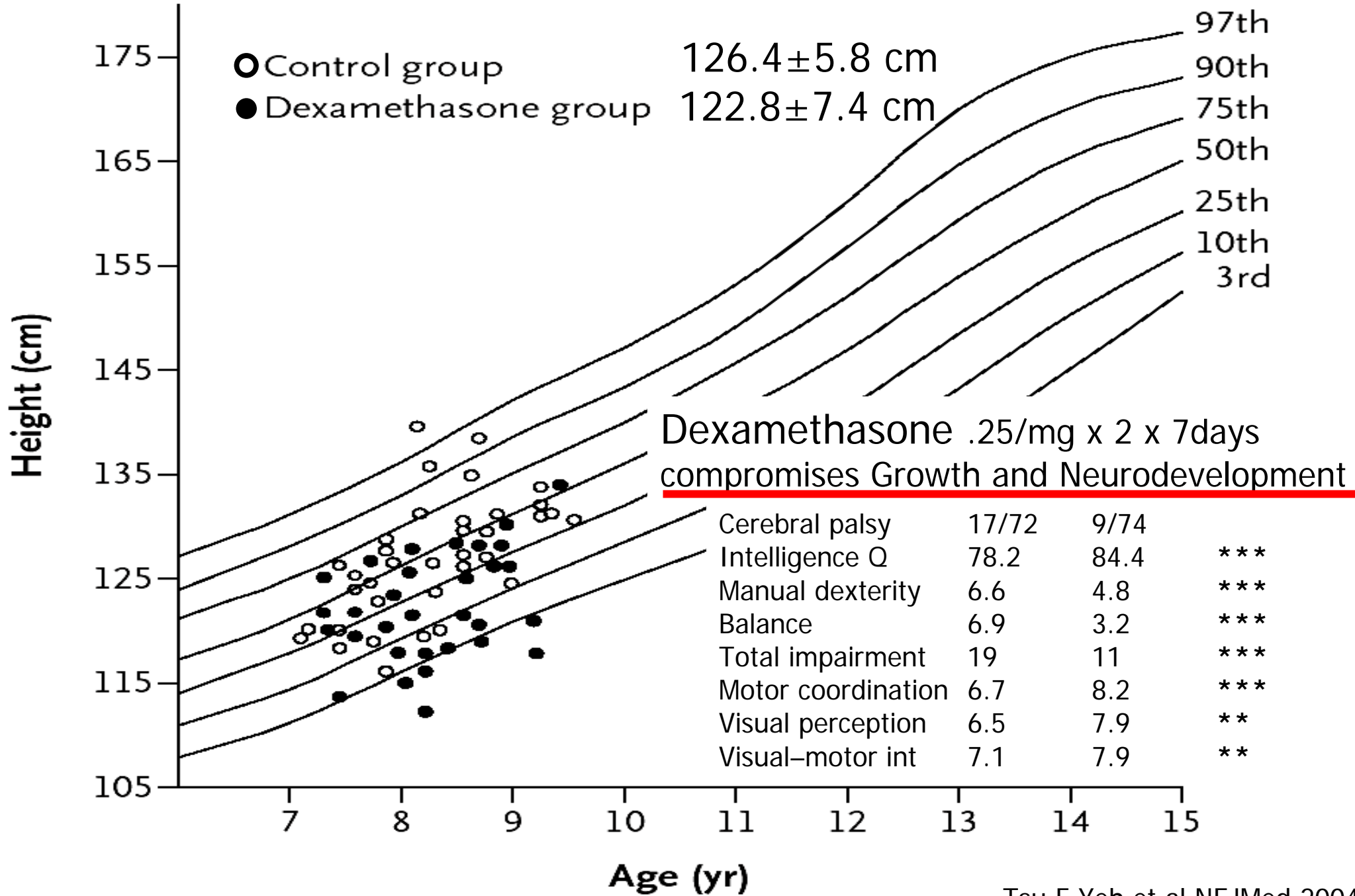


TOTAL Chi-square 4.1 (n=379)

Evidencia basada en la Práctica



- ⌘ Debemos aprender de nuestros errores y de nuestros éxitos
- ⌘ Examinar las causas de la variación entre centros, definir mejores practicas.
- ⌘ Realizar estudios basados en mejores prácticas
- ⌘ Investigar es necesario para seguir avanzando



Impact of Postnatal Systemic Corticosteroids on Mortality and Cerebral Palsy in Preterm Infants: Effect Modification by Risk for Chronic Lung Disease

2005;115;655-661 *Pediatrics*

Lex W. Doyle, MD*‡; Henry L. Halliday, MD§; Richard A. Ehrenkranz, MD||; Peter G. Davis, MD*‡; and John C. Sinclair, MD#¶

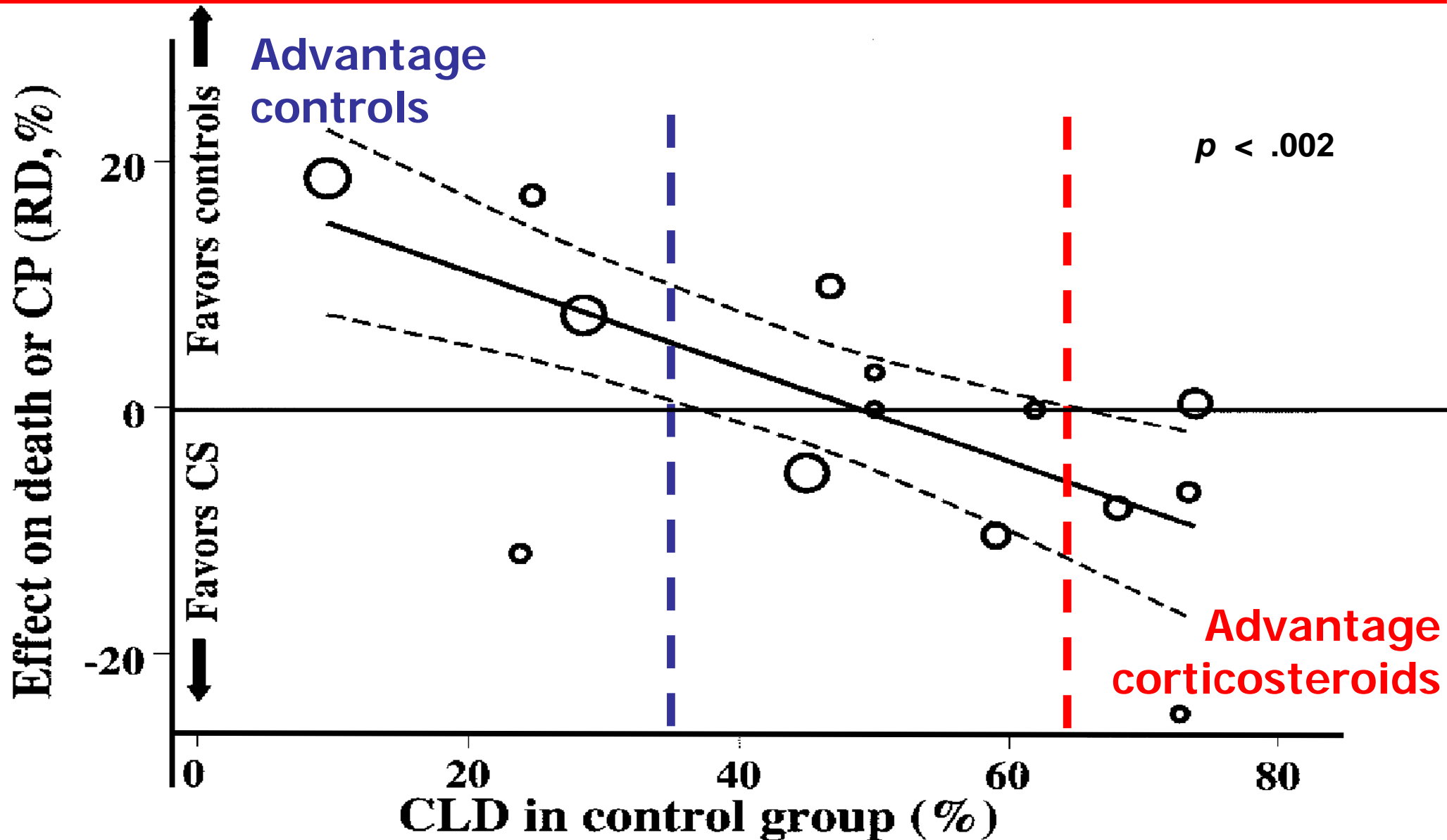
Objective.

In preterm infants, chronic lung disease (CLD) is associated with an increased risk for cerebral palsy (CP).

However, systemic postnatal steroid therapy to prevent or treat CLD, although effective in improving lung function, may cause CP.

Test if the effect of postnatal corticosteroid treatment on death and CP and to assess any modification of effect arising from risk for CLD.

Risk Difference (%) for death or CP among all participants vs rate of CLD (%) in Control group.



Results

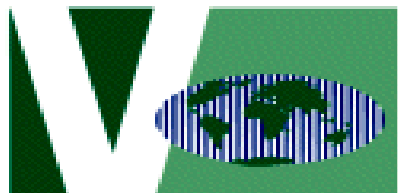
2005;115;655-661 *Pediatrics*

Significantly higher rate of CP after corticosteroid treatment (typical risk difference [RD]: 0.05; 95% [CI]: 0.02, 0.08)

Partly offset by a nonsignificant reduction in mortality (typical RD: 0.02; 95% CI: 0.06 to 0.02).

Corticosteroid treatment on the combined rate of mortality or CP (typical RD: 0.03; 95% CI: 0.01 to 0.08).

With risks for CLD below 35%, corticosteroid treatment significantly increased the chance of death or CP, whereas with risks for CLD exceeding 65%, it reduced this chance.



Vermont Oxford Network

improving care for low-birthweight babies

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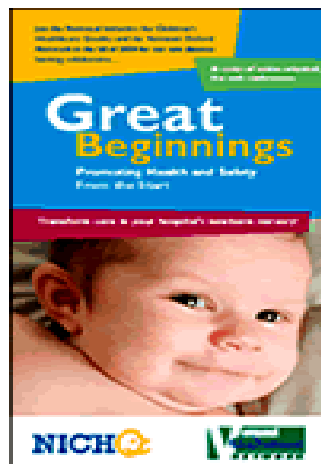
Search

Quality & Safety Course

Learn the fundamentals of improving the quality and safety of your Neonatal Intensive Care Unit. [Learn more . . .](#)

Great Beginnings

NICHQ (The National Initiative for Children's Healthcare Quality) and the Vermont Oxford Network are pleased to offer an Internet based quality improvement collaborative addressing the care of all newborn babies. [Learn more . . .](#)

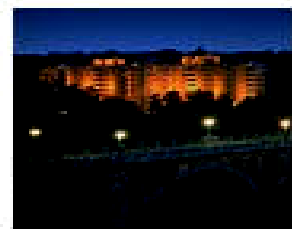


The Delivery Room Management Trial

is perhaps our most ambitious effort ever. The DRM Trial will evaluate three distinct approaches to stabilization and support of

Annual Meeting & Quality Congress

Join us in Washington, DC for our Annual Meeting for members and Quality Congress for all interested health professionals December 11-12, 2004 at the Omni Shoreham Hotel.



Mission:

The mission of the Vermont Oxford Network is to improve the quality and safety of medical care for newborn infants and their families through a coordinated program of research, education and quality

Voluntary Anonymous Reporting of Medical Errors

for Neonatal Intensive Care

Professionals ($n = 739$) from 54 hospitals

Of 1230 reports—the most frequent event categories

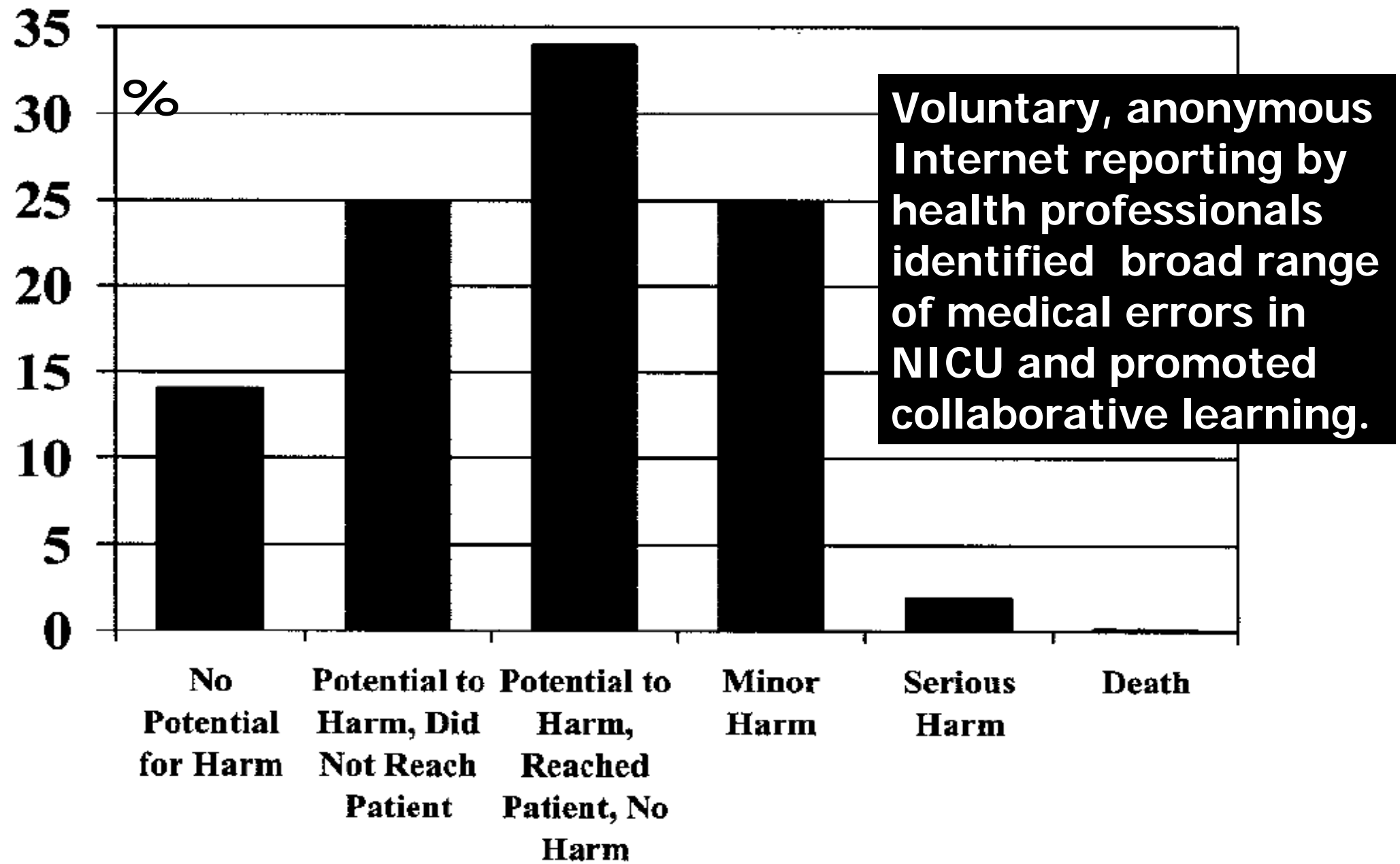
- 47% wrong medication, dose, schedule, or infusion rate
- 14% error in administration or method of using a treatment
- 11% patient misidentification
- 9% other system failure
- 7% error or delay in diagnosis
- 4% error in the performance of procedure or test



The most frequent contributory factors were

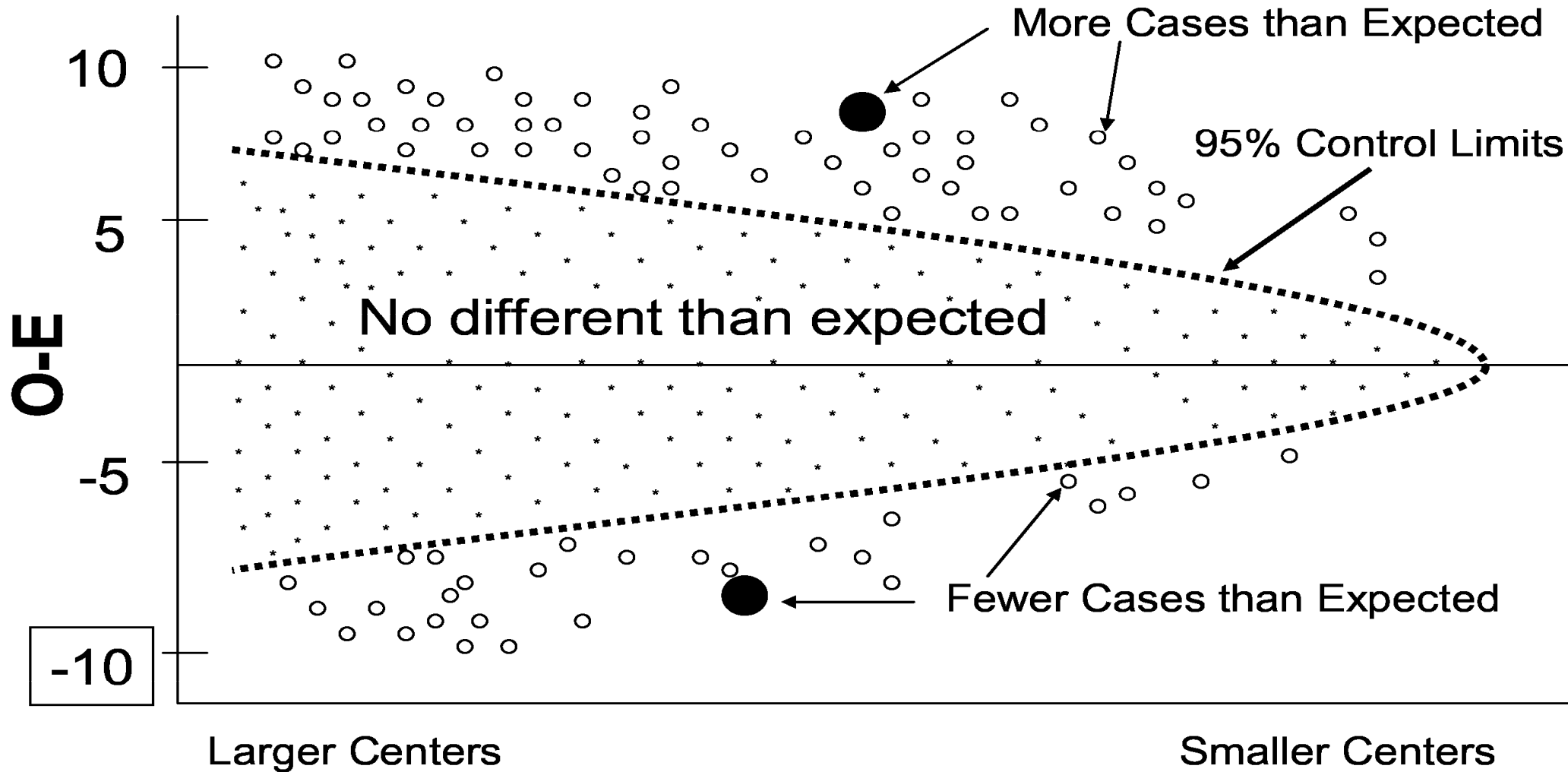
- 47% failure to follow policy or protocol
- 27% inattention - 22% communications problem
- 13% error in charting or documentation
- 12% distraction - 10% inexperience
- 10% labelling error - 9% poor teamwork

In 24 reports, family members assisted in discovery, contributed to the cause, or themselves were victims of the error

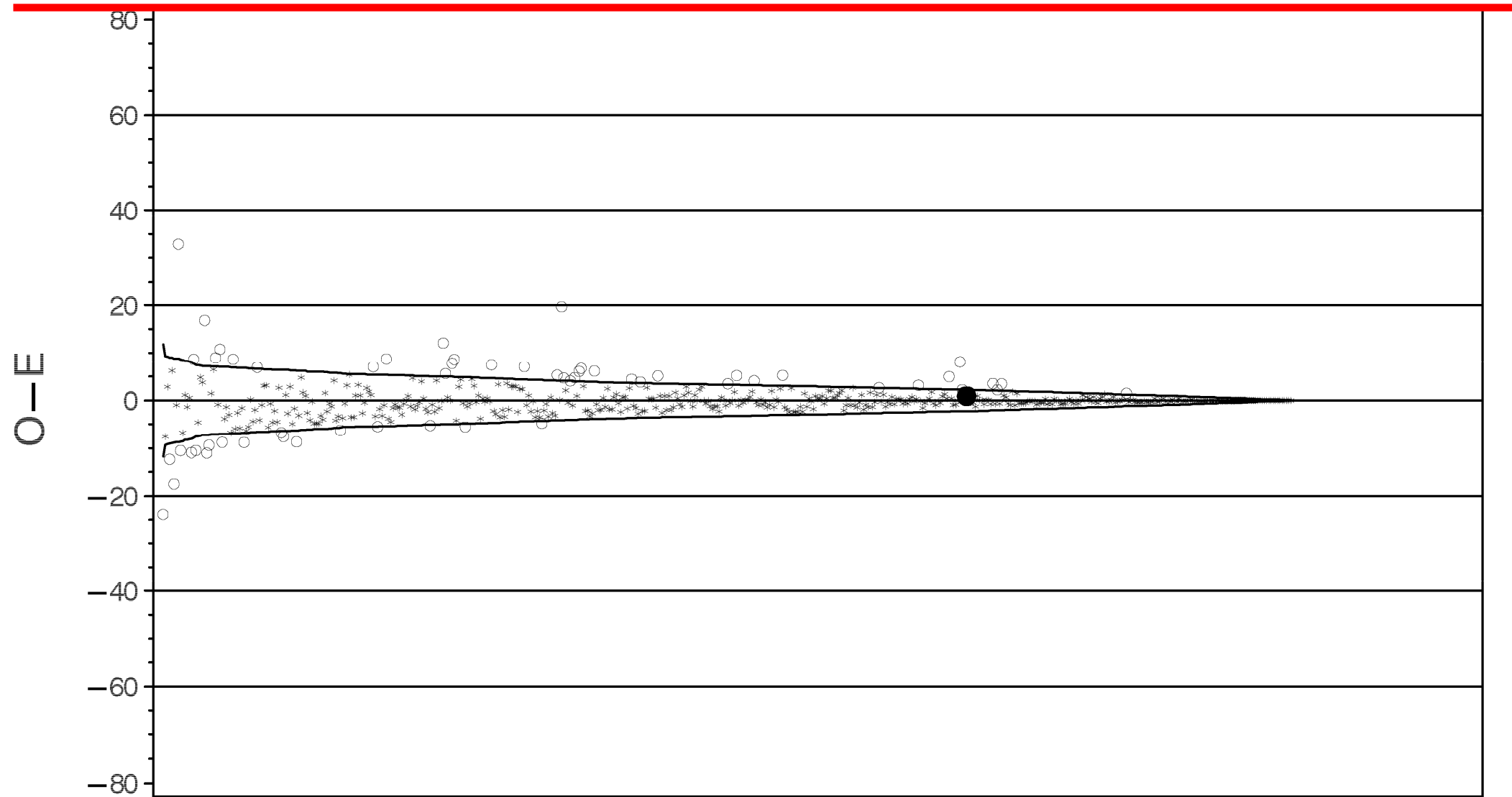


REPORTE DE INCIDENTES

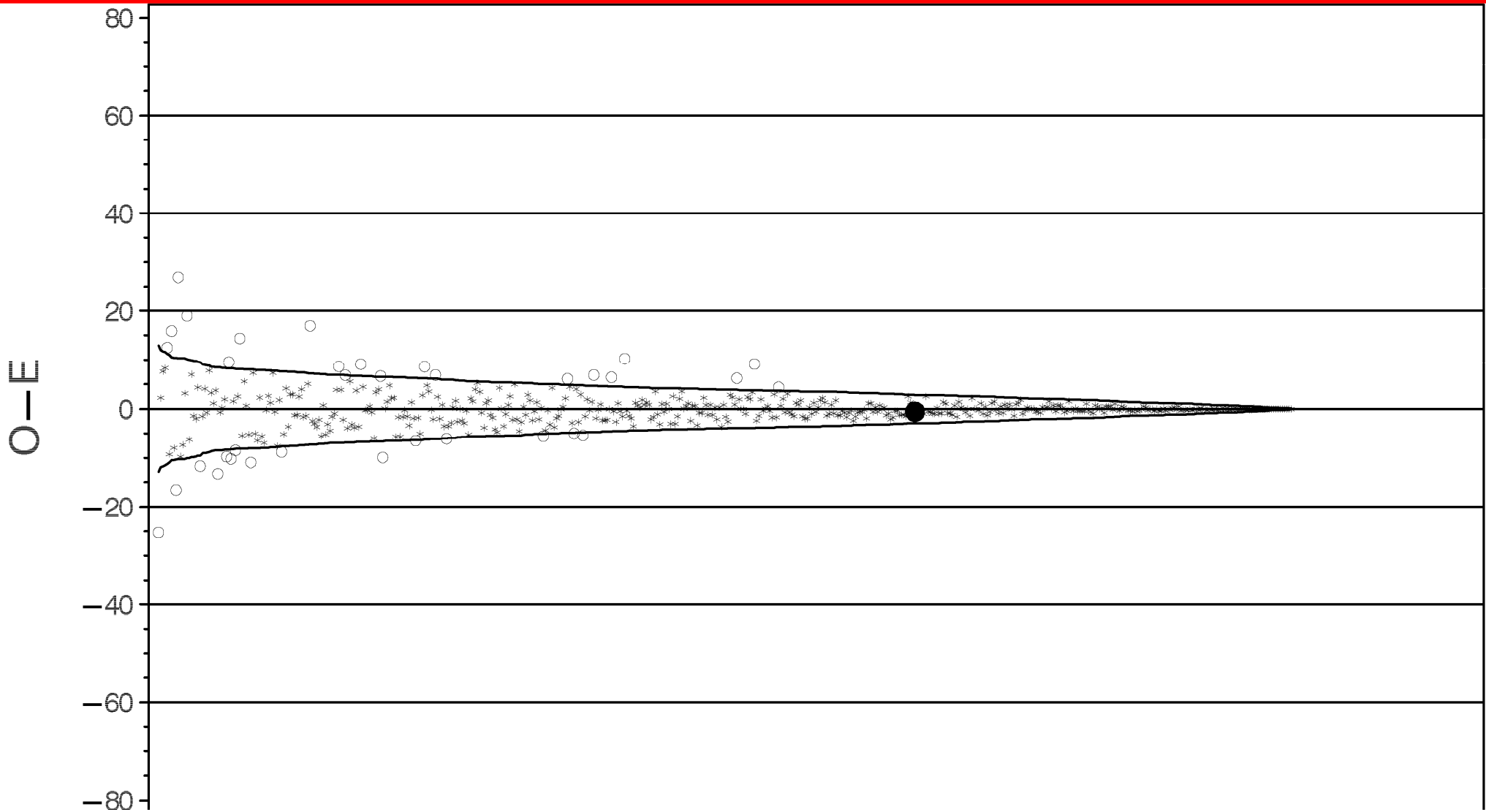
Observado – Esperado



PVL Observado – Esperado



Pneumothorax Observado – Esperado



CLD Observado – Esperado

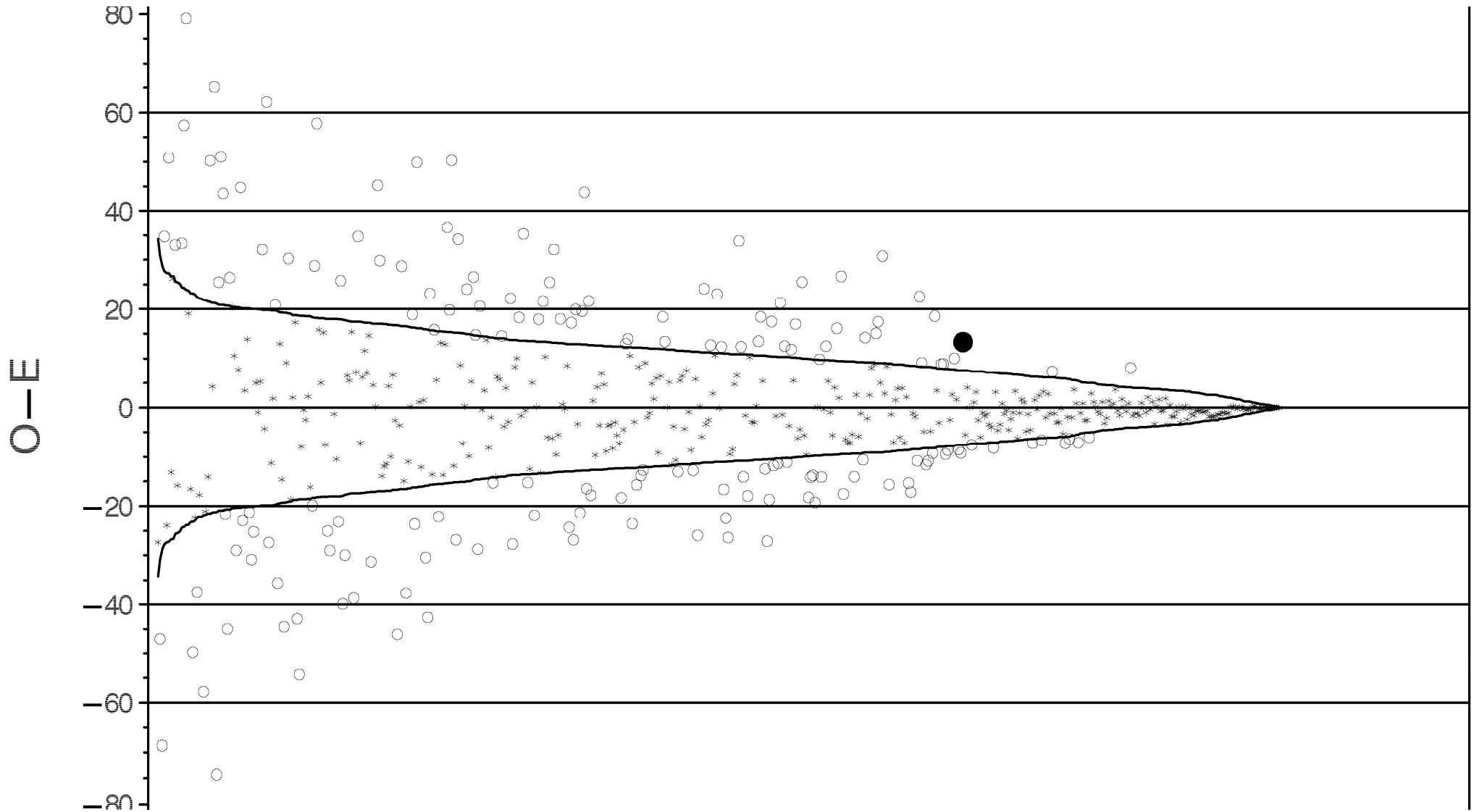
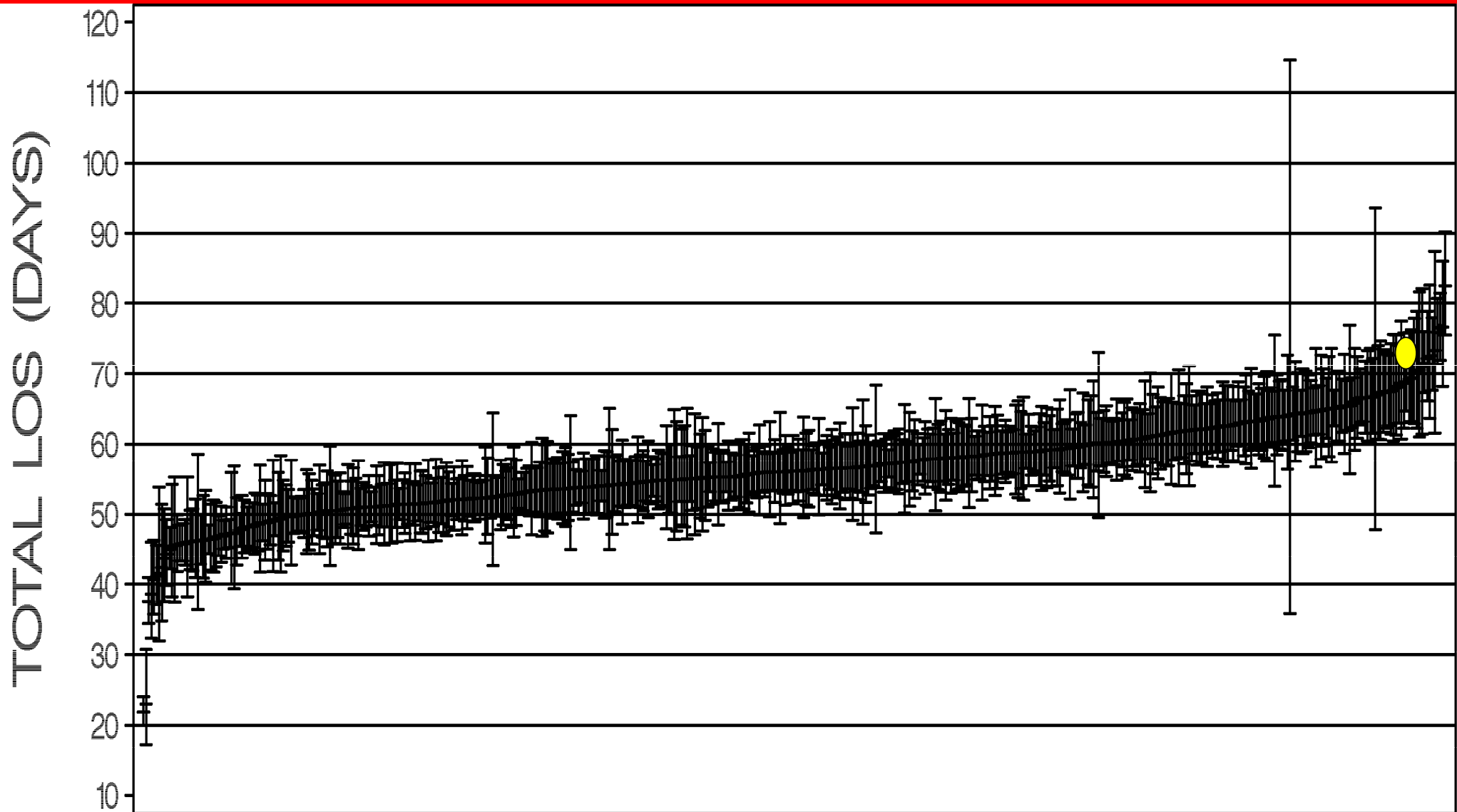


TABLE 3.12: MEDIAN AGE AT FIRST DOSE OF SURFACTANT
 FOR INFANTS WHO RECEIVED SURFACTANT
 INFANTS 501-1500 GRAMS, CENTER 585 AND TOTAL NETWORK 2004

CENTER 585 N & MEDIAN, NETWORK N & MEDIAN (NETWORK QUARTILES)

BIRTH WEIGHT (grams)	CENTER 585		NETWORK		
	N	MEDIAN (MINUTES)	N	MEDIAN (MINUTES)	
501-750	11	60	6,192	15	(9, 39)
751-1000	17	75	7,213	20	(10, 45)
1001-1250	21	150	6,184	30	(15, 77)
1251-1500	13	120	5,122	60	(33, 145)
501-1500	62	90	24,711	25	(12, 59)

Duracion estadia Observado – Esperado



Por que NO investigamos mas ?



- ⌘ Falta de tiempo; desinterés generalizado
- ⌘ Falta de compromiso real con la actividad de investigación, trabajo asistencial satura el tiempo
- ⌘ Faltan recursos y existe mala utilización recursos existentes
- ⌘ Faltan recursos humanos calificados en investigación clínica y en metodología estadística
- ⌘ Conformismo generalizado con situación actual



SCOPPIA DA NITRATI IN UN

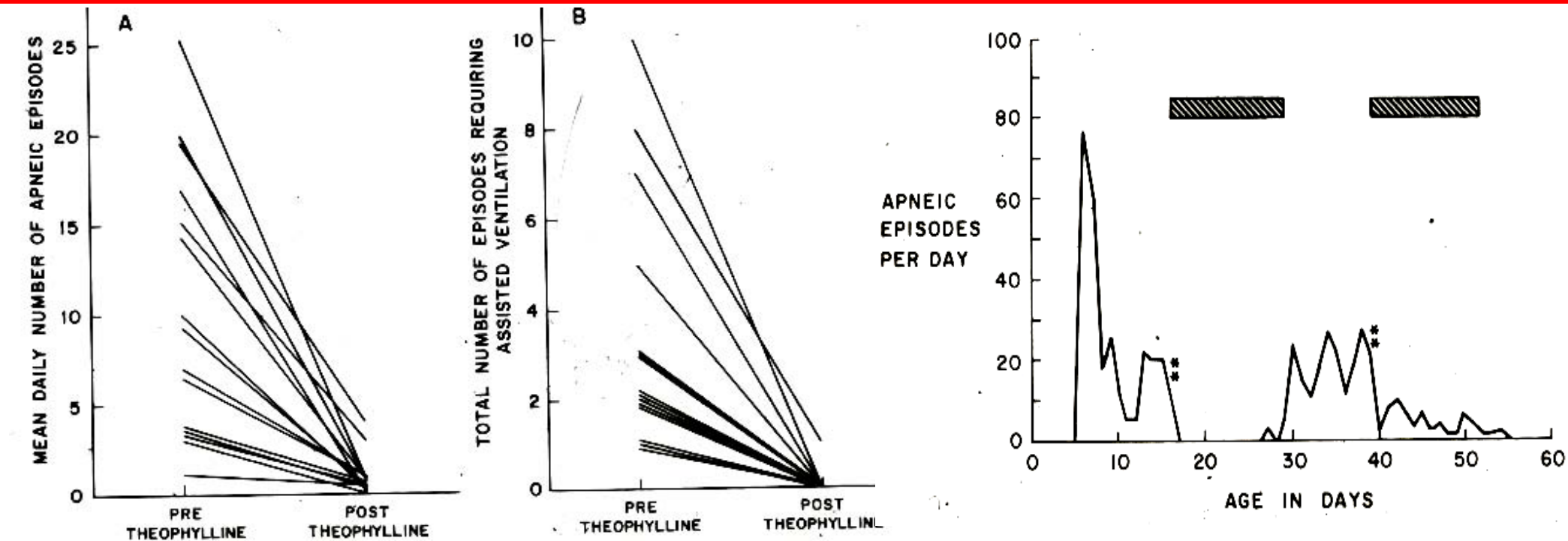
LE

Treatment of severe apnea in prematures with orally administered theophylline

R Uauy, DL Shapiro, B Smith and JB Warshaw

- Twelve premature infants with primary apnea were treated with theophylline as an alternative to mechanical ventilation.
- There was a significant (P smaller than 0.005) reduction in the mean daily number and the severity of apneic episodes after treatment. The only significant side effect was a rise in heart rate.

Volume 55, Issue 5, pp. 595-598, 05/01/1975 The American Academy of Pediatrics





A comparison of early-onset group B streptococcal neonatal infection and the respiratory-distress syndrome of the newborn

RC Ablow, SG Driscoll, EL Effmann, I Gross, CJ Jolles, R Uauy, and JB Warshaw

ORIGINAL ARTICLE

Abstract

Volume 294:65-70

January 8, 1976

Number 2

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In attempting to differentiate early-onset Group B streptococcal infection from hyaline-membrane disease we found features of severe Group B infection to be :

- 1. ROM for more than 12 hours before delivery (four of eight vs one of nine),*
- 2. Gram-positive cocci in the gastric aspirate (four of four vs none of one),*
- 3. Apnea and shock in the first 24 hours of life (seven of eight vs none of nine),*
- 4. The generation of lower peak inspiratory pressures on a volume-cycled respirator (mean of 36.5 +/- 2.8 vs 63.9 +/- 6.2 cm of water; P = 0.005).*

In eight fatal cases of Group B infection, four patients had radiographic features indistinguishable from HMD whereas the other cases were consistent with pneumonia.

Seven of the eight infected infants had no histologic evidence of coexisting HMD disease.

Microscopical features of Group B infection included cocci in unevenly distributed hyaline membranes and minimal atelectasis.

