CPAP: Evidencia Actual

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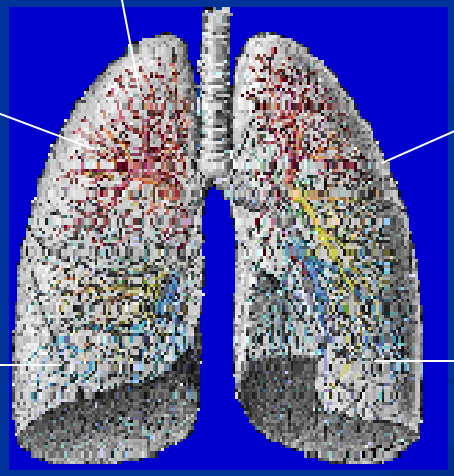
DAÑO PULMONAR

Volutrauma/
Barotrauma

Hipoxemia



Infección

Inflamación

Desnutrición

SUSCEPTIBILIDAD DEL PULMÓN DEL R. NACIDO A LA INJURIA

- Poca distensibilidad alveolar y mucha de las vías aéreas.
- Sistemas de defensa antioxidantes inmaduros.
- Macrófagos y leucocitos inmaduros.
- Mecanismos de barrido de la vía aérea alterados.
- Sistemas antiproteolíticos y antielastolíticos pobremente desarrollados.
- Aumento de la permeabilidad de la membrana alvéolo-capilar.

DAÑO PULMONAR ASOCIADO AL VENTILADOR.

Posibles mecanismos

- Volúmenes más que presiones.
- Presión transalveolar y reapertura de los alvéolos.
- Colapso y reapertura repetida de los alvéolos.
- Muy baja presión positiva al final de la espiración.
- Daño oxidativo.

CPAP Definición:

- CPAP, Presión Positiva Continua de la Vía Aérea, es un mecanismo que mantiene una presión positiva en la vía aérea del recién nacido durante todo el ciclo respiratorio mientras el niño está con respiración espontánea.

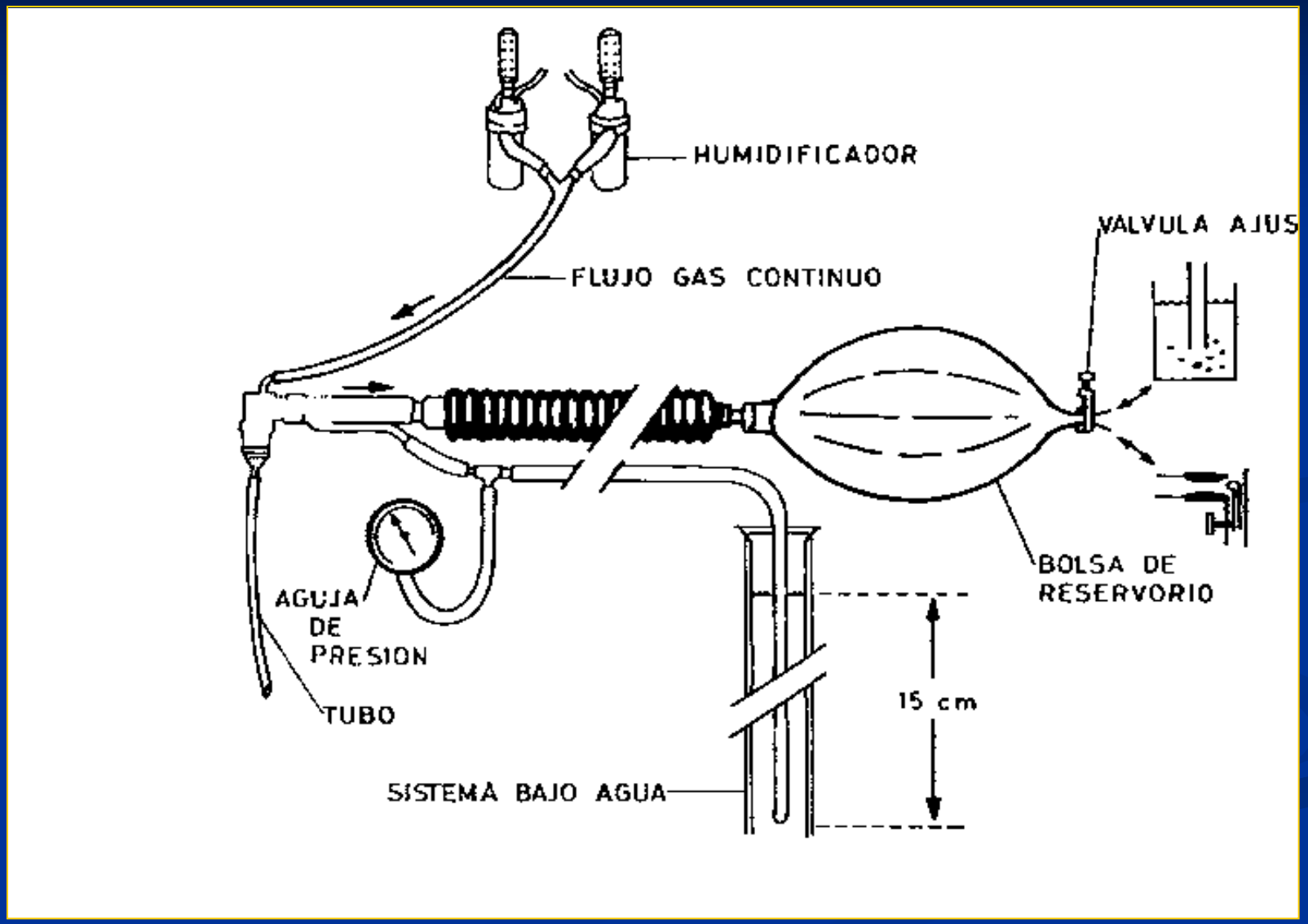
Beneficios del CPAP

1. Estabiliza la vía aérea y pared torácica.
2. Mejora CRF.
3. Mejora relación V/Q.
4. Previene el colapso alveolar.
5. Reduce intubación.

CPAP de Gregory

- Gregory et al, 1971: CPAP demostró mejorar intercambio gaseoso y resultados en prematuros con Enfermedad de Membrana Hialina.

CPAP de Gregory



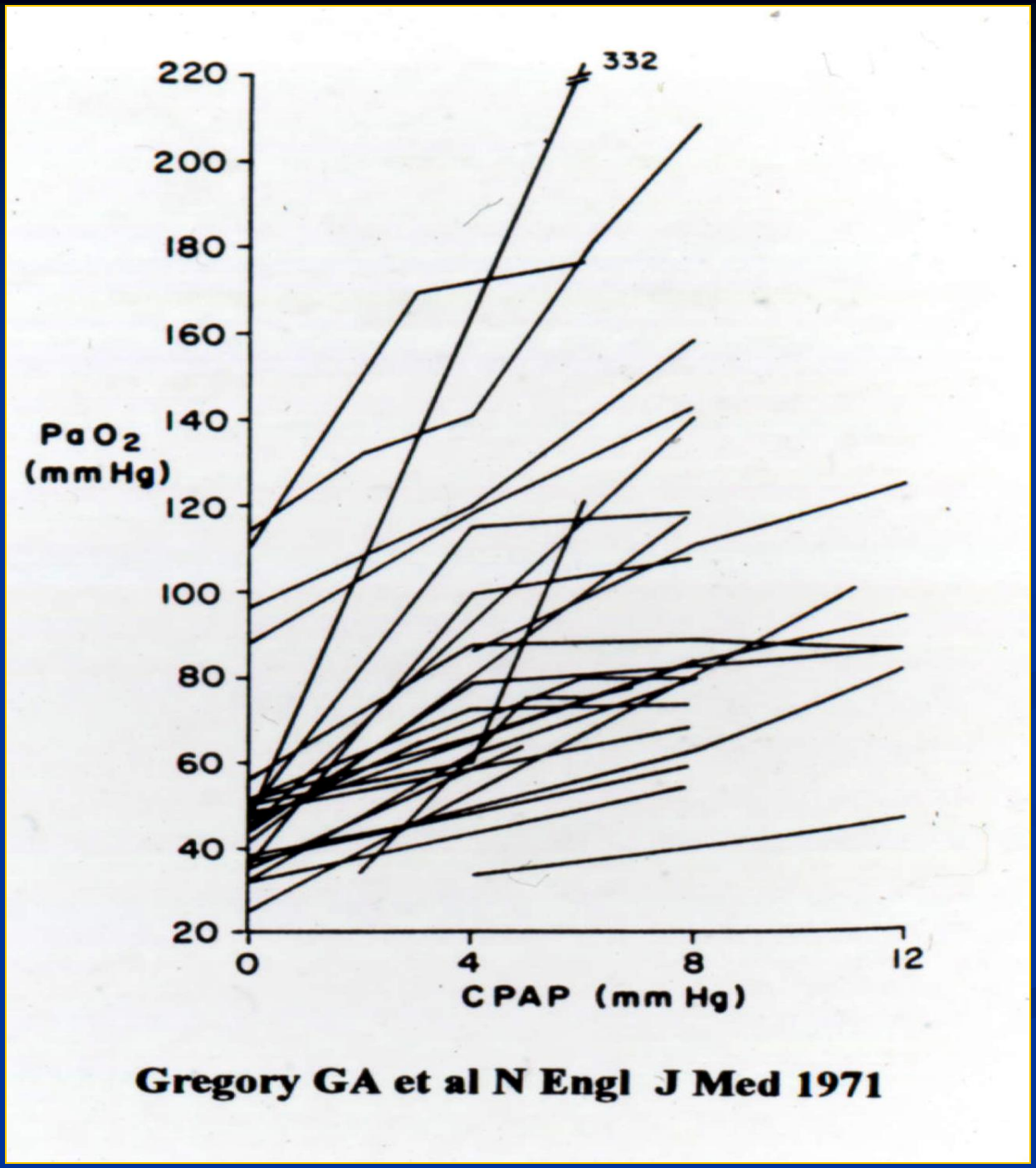
The New England
Journal of Medicine

Volume 284 JUNE 17, 1971 Number 24

TREATMENT OF THE IDIOPATHIC RESPIRATORY-DISTRESS SYNDROME WITH CONTINUOUS POSITIVE AIRWAY PRESSURE*

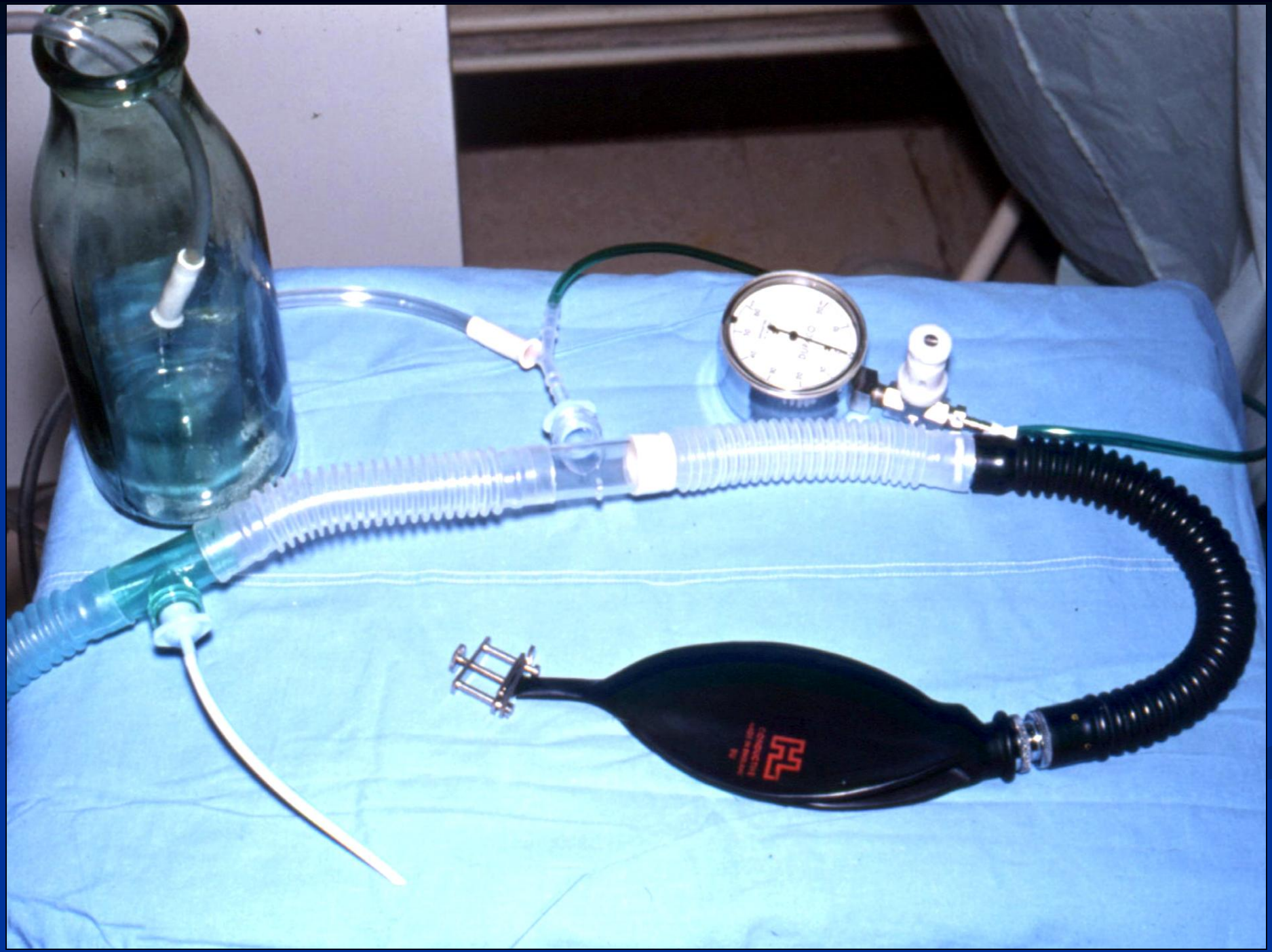
GEORGE A. GREGORY, M.D., JOSEPH A. KITTERMAN, M.D., RODERIC H. PHIBBS, M.D., WILLIAM H. TOOLEY, M.D., AND WILLIAM K. HAMILTON, M.D.

Abstract We applied a continuous positive airway pressure to 20 infants (birth weight 930 to 3800 g) severely ill with the idiopathic respiratory-distress syndrome. They breathed spontaneously. Pressure, up to 12 mm of mercury, was delivered through an endotracheal tube to 18 infants and via a pressure chamber around the infant's head to two. Arterial oxygen tension rose in all, permitting us to lower the inspired oxygen an average of 37.5 per cent within 12 hours. Minute ventilation decreased with increased continuous positive airway pressure, but this had little effect on arterial carbon dioxide tension, pH, arterial blood pressure and lung compliance. Sixteen infants survived, including seven of 10 weighing less than 1500 g at birth.



Gregory GA et al N Engl J Med 1971

1 mmHg = 1,36 cmH_2O



Experiencia inicial UC

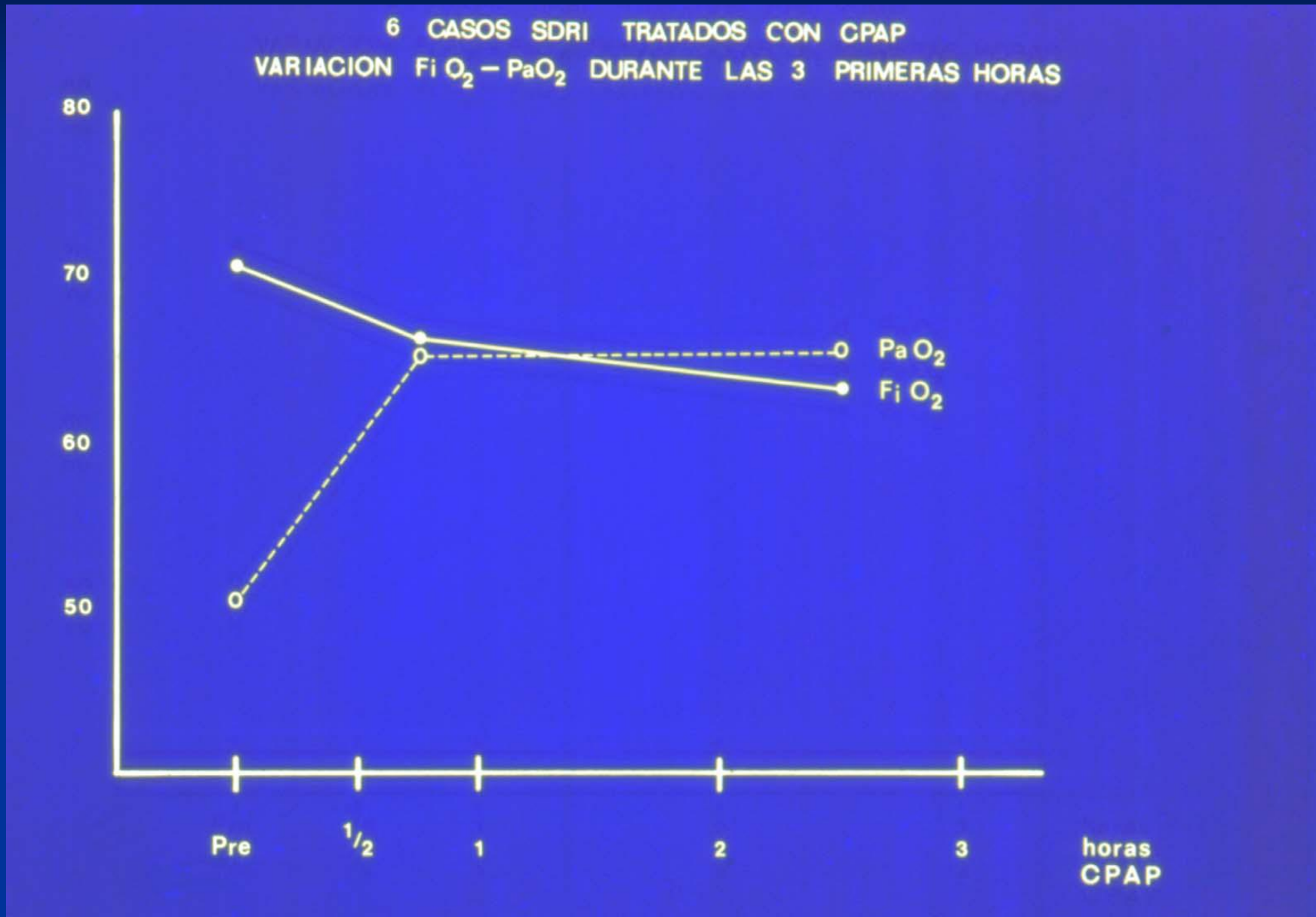


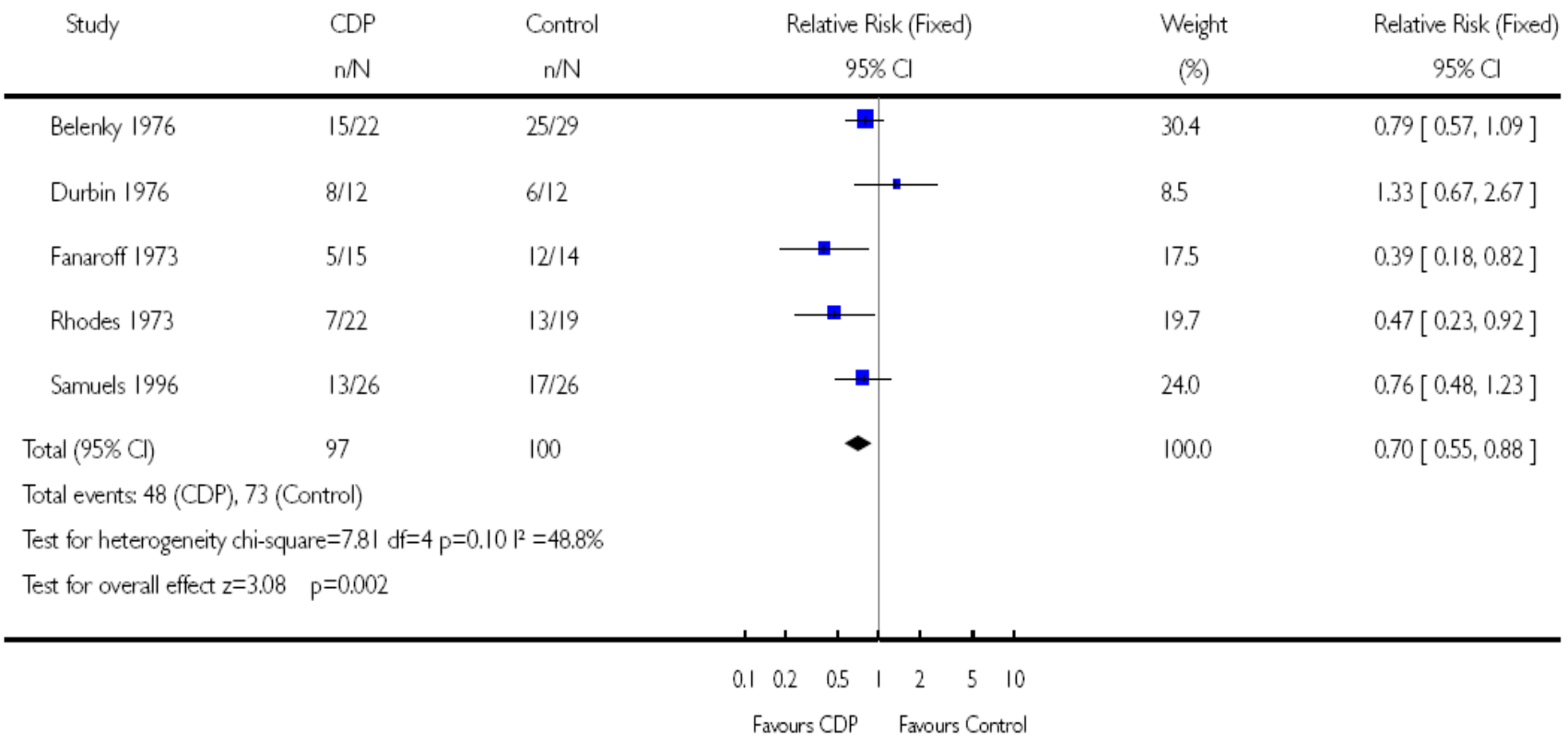
Fig. 1. Comparison 01. CDP vs standard care

01.01 Failure (death or use of additional ventilatory assistance)

Review: Continuous distending pressure for respiratory distress syndrome in preterm infants

Comparison: 01 CDP vs standard care

Outcome: 01 Failure (death or use of additional ventilatory assistance)



Ho JJ, Subramaniam P, Henderson-Smart DJ, Davis PG. Continuous distending pressure for respiratory distress syndrome in preterm infants. *The Cochrane Database of Systematic Reviews* 2002, Issue 2. Art. No.: CD002271. DOI: 10.1002/14651858.CD002271.

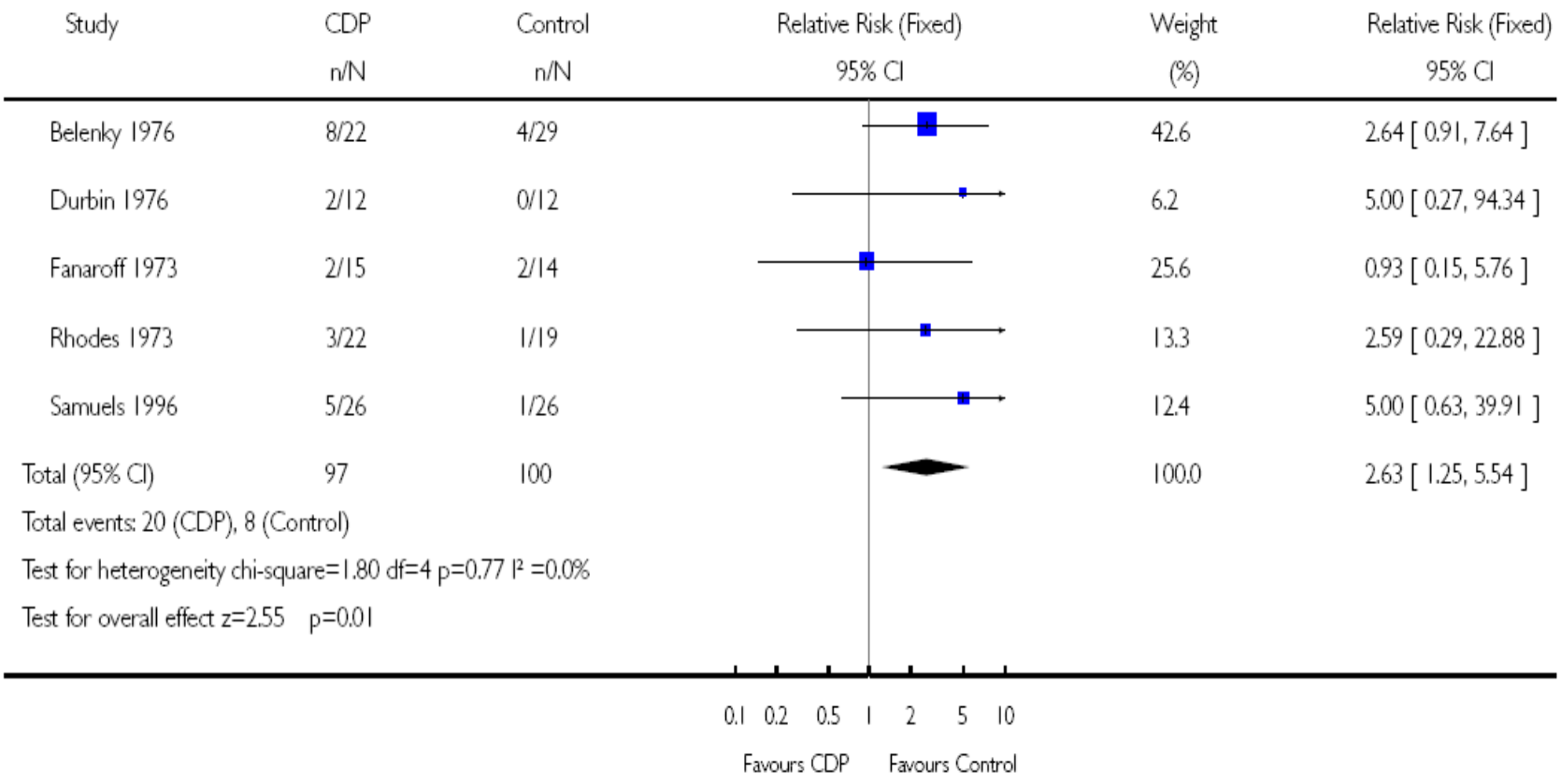
Fig. 7. Comparison 01. CDP vs standard care

01.07 Any pneumothorax

Review: Continuous distending pressure for respiratory distress syndrome in preterm infants

Comparison: 01 CDP vs standard care

Outcome: 07 Any pneumothorax



Ho JJ, Subramaniam P, Henderson-Smart DJ, Davis PG. Continuous distending pressure for respiratory distress syndrome in preterm infants. *The Cochrane Database of Systematic Reviews* 2002, Issue 2. Art. No.: CD002271. DOI: 10.1002/14651858.CD002271.

Fig. 1. Comparison 01. Early vs late CDP

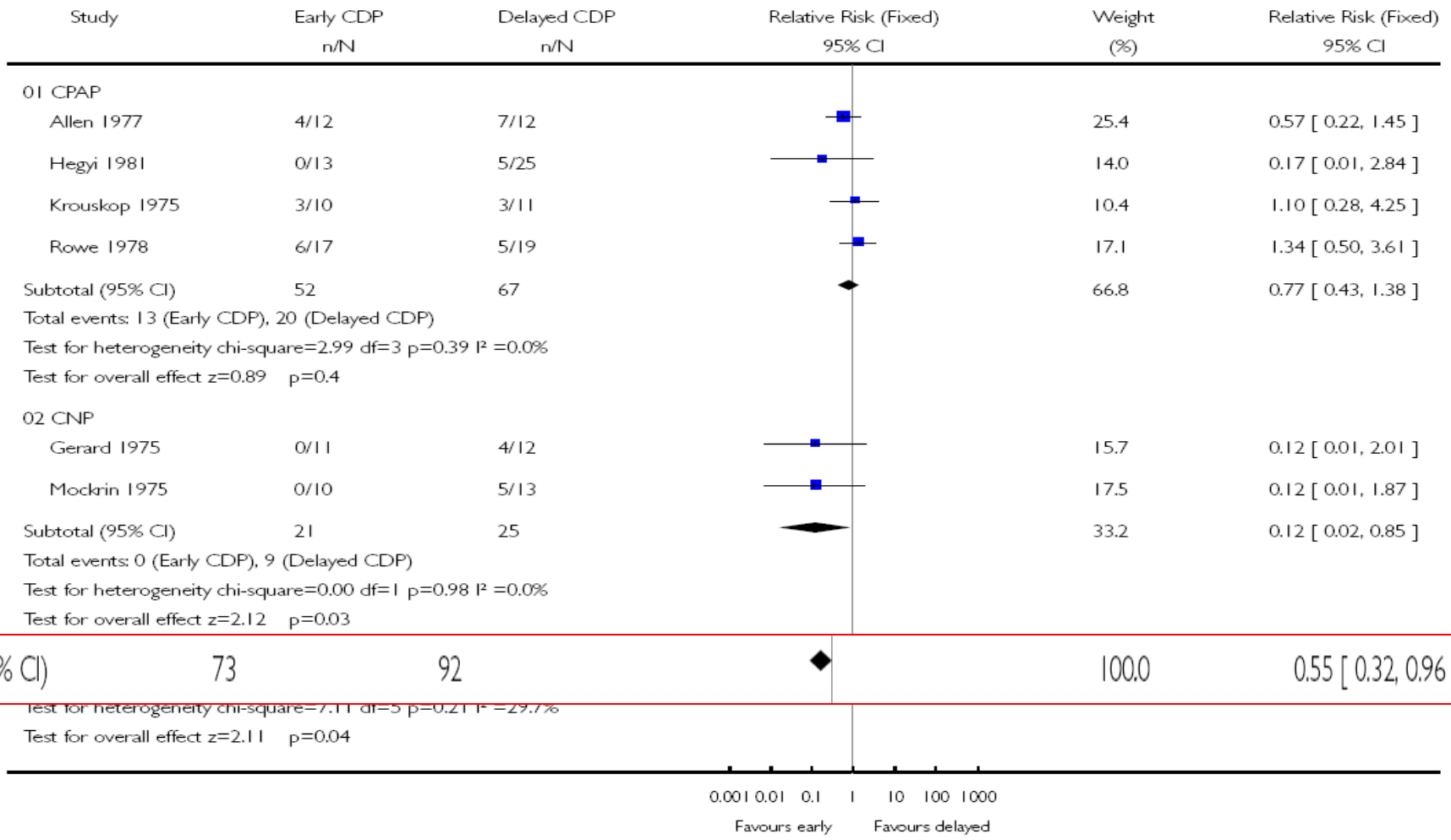
01.01 Use of IPPV

Review: Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants

Comparison: 01 Early vs late CDP

Outcome: 01 Use of IPPV

Uso de VM



Ho JJ, Henderson-Smart DJ, Davis PG. Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants. *The Cochrane Database of Systematic Reviews* 2002, Issue 2. Art. No.: CD002975. DOI: 10.1002/14651858.CD002975.

Analysis 1.5. Comparison 1 Early vs late CDP, Outcome 5 Duration of oxygen in survivors (days).

Review: Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants

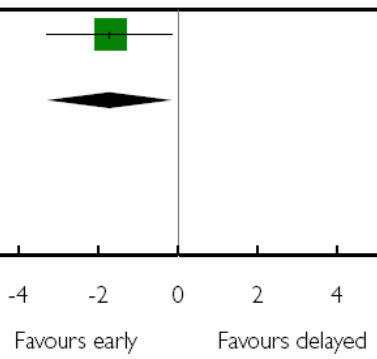
Comparison: 1 Early vs late CDP

Outcome: 5 Duration of oxygen in survivors (days)

Study or subgroup	Early CDP N	Mean(SD)	Late CDP N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Allen 1977	12	9.4 (1.3)	8	11.1 (2)		100.0 %	-1.70 [-3.27, -0.13]
Total (95% CI)	**12**		**8**			**100.0 %**	**-1.70 [-3.27, -0.13]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.12 (P = 0.034)



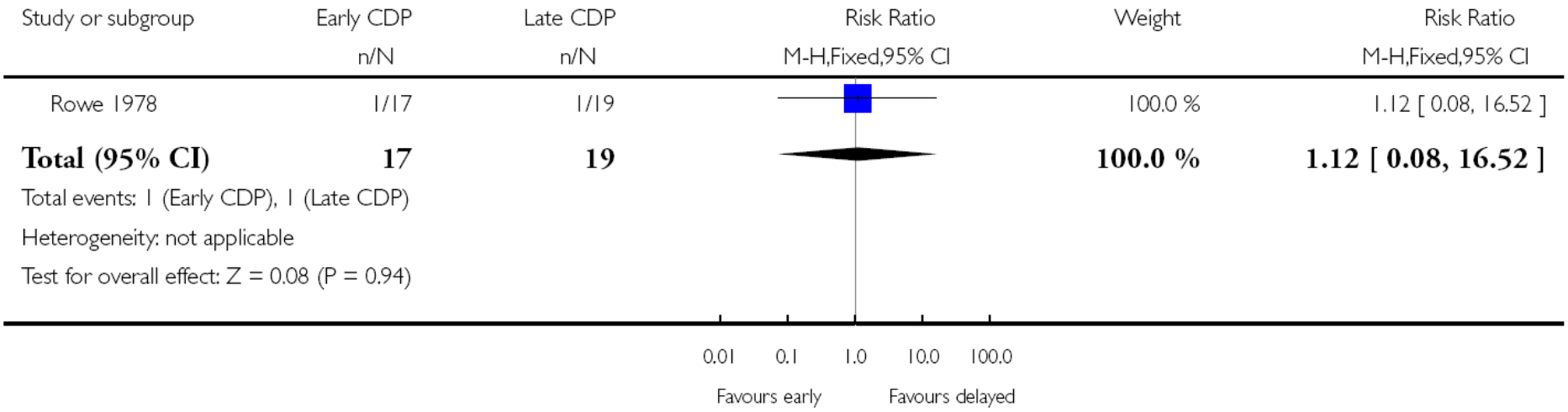
Ho JJ, Henderson-Smart DJ, Davis PG. Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants. *The Cochrane Database of Systematic Reviews* 2002, Issue 2. Art. No.: CD002975. DOI: 10.1002/14651858.CD002975.

Analysis 1.10. Comparison 1 Early vs late CDP, Outcome 10 Bronchopulmonary dysplasia.

Review: Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants

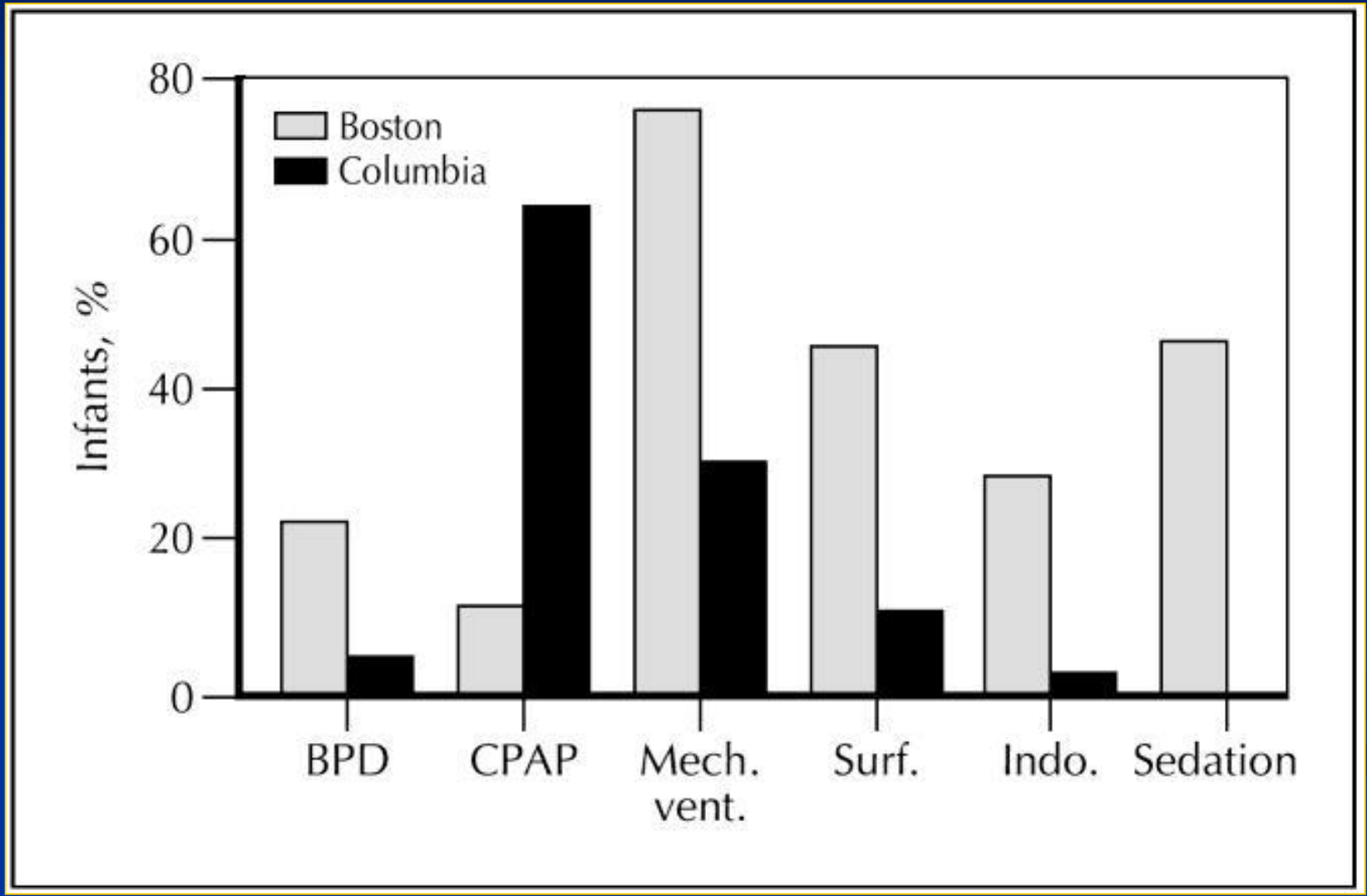
Comparison: 1 Early vs late CDP

Outcome: 10 Bronchopulmonary dysplasia



Ho JJ, Henderson-Smart DJ, Davis PG. Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants. *The Cochrane Database of Systematic Reviews* 2002, Issue 2. Art. No.: CD002975. DOI: 10.1002/14651858.CD002975.

Resultados Clinicos de RN 500-1500 g 1991-1993 Boston Hospitals vs Columbia Hospital



Jobe A. Curr Opin Pediatr 2001; 13: 124-129

Ventilación mecánica vs. no intubación en RN muy bajo peso

	1992 n=665	1993 n=664	1994 n=672	*p*
Intubados (%)	78	78	66	<0.05
O_2 a los 28d (%)	21	20	17	<0.05
Muerte ó O_2 a los 28d (%)	32	29	27	NS
Muerte ó O_2 en < 1.0 kg (%)	62	54	52	<0.05
Muerte ó O_2 en 1-1.5 kg (%)	14	12	9	<0.05
CPAP (%)	4	5	6	NS

Poets and Sens. Pediatrics 98:24, 1996

CPAP precoz en RN extremo bajo peso

	CPAP N=67	Intubación Rutinaria N=56	*p*
Intub. Sala partos (%)	40	84	<0.01
Intubados (%)	65	93	<0.01
Mortalidad (%)	22	27	NS
O_2 a las 36 sem. (%)	12	32	<0.05
HIV > 2 (%)	16	38	<0.01

Lindner et al. Pediatrics 103:961, 1999

CPAP en RN 1-1.5 Kg.

	CPAP n=59	Control n=57	p value
Intubados (%)	14	65	<0.001
Surfactante (%)	12	40	<0.001
Ventilación (d)	2	6	<0.05
Oxígeno suplem. (d)	2	4	<0.01
O_2 a los 28 d (%)	0	11	<0.05
O_2 a los 28 d ó muerte (%)	3	16	<0.05
O_2 a las 36 s ó muerte (%)	3	11	0.25

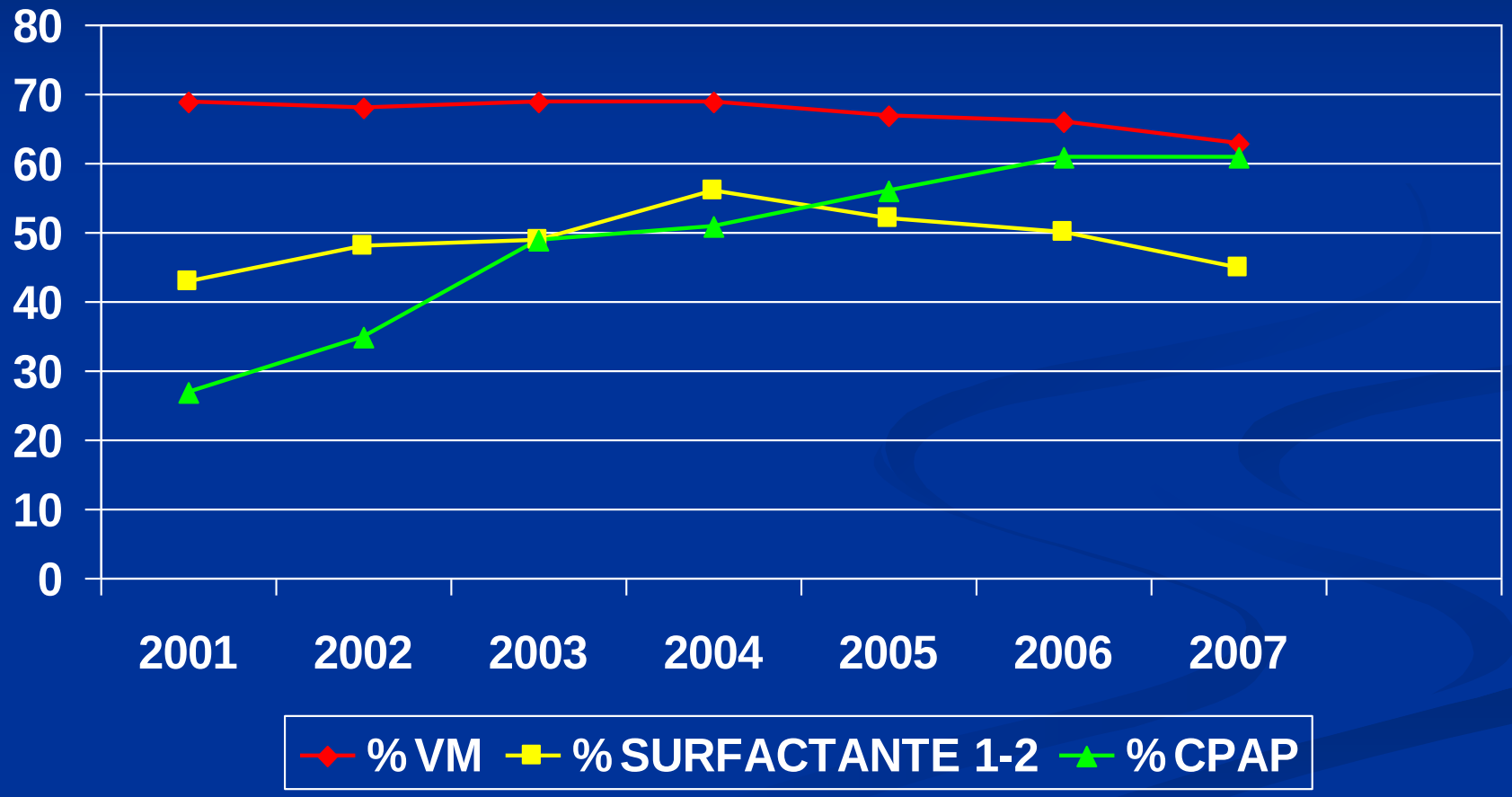
de Klerk and de Klerk. J Paedr Child Health 37:161:2001

Evolución respiratoria postnatal

Antecedente	2001 n= 956	2002 n = 908	2003 n= 1009	2004 n= 1091	2005 n = 1143	2006 n = 1186	2007 n=956	Global 7.240
SDR	74%	69,2%	71,4%	75,1%	75%	78,2%	73,9	74%
Ventilación Mecánica	69%	68%	69%	69%	67%	66%	63%	67%
CPAP	27%	35%	49%	50%	56%	61%	61%	49%
V. Alta Frecuencia	3%	6%	6%	8%	7%	9%	7%	7%

Informe BD 2008

Uso comparativo de Surfactante - VM - CPAP



Informe BD 2008

Evolución respiratoria postnatal

Antecedente	2001 n= 956	2002 n = 908	2003 n= 1009	2004 n= 1091	2005 n = 1143	2006 n = 1186	2007 n=956	Global 7.240
DBP	25,7%	23,3%	27,2%	26,4%	28,4%	30,8%	27,7%	27,2%
O2 36 sem EC	22,8%	20,2%	19,7%	18,9%	18,5%	19,7%	15,8%	19,3%
Esteroides postnatal	9,5%	7,9%	6,6%	5,6%	6,5%	5,7%	3,8%	6,4%
O_2 domiciliario	8%	6%	6%	6,7%	5,4%	7,2%	7,1%	6,6%

Informe BD 2008

Estrategias de uso de CPAP en RNMBP

- NCPAP después de la extubación en niños recuperándose de SDR.
- Uso temprano como alternativa a la ventilación mecánica, intubación y uso de surfactante.
- Uso precoz con surfactante profiláctico.

NCPAP después de la extubación en niños recuperándose de SDR.

N-CPAP vs Hood después de extubación en prematuros

Analysis 1.1. Comparison 1 Nasal CPAP vs Headbox, Outcome 1 Failure.

Review: Nasal continuous positive airway pressure immediately after extubation for preventing morbidity in preterm infants

Comparison: 1 Nasal CPAP vs Headbox

Outcome: 1 Failure apneas, acidosis respiratoria, ↑ req. O_2

Study or subgroup	NCPAP n/N	Headbox n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Annibale 1994	15/40	17/42		10.4 %	0.93 [0.54, 1.59]
Chan 1993	19/60	22/60		13.8 %	0.86 [0.52, 1.42]
Davis 1998	16/47	27/45		17.3 %	0.57 [0.36, 0.90]
Dimitriou 2000	15/75	25/75		15.6 %	0.60 [0.34, 1.04]
Engelke 1982	0/9	6/9		4.1 %	0.08 [0.00, 1.19]
Higgins 1991	7/29	23/29		14.4 %	0.30 [0.16, 0.60]
Peake 2005	16/49	24/48		15.2 %	0.65 [0.40, 1.07]
So 1995	4/25	13/25		8.1 %	0.31 [0.12, 0.81]
Tapia 1995	7/29	2/30		1.2 %	3.62 [0.82, 16.01]
Total (95% CI)	**363**	**363**		**100.0 %**	**0.62 [0.51, 0.76]**

Heterogeneity: $Chi^2 = 17.93$, $df = 8$ ($P = 0.02$); $I^2 = 55\%$

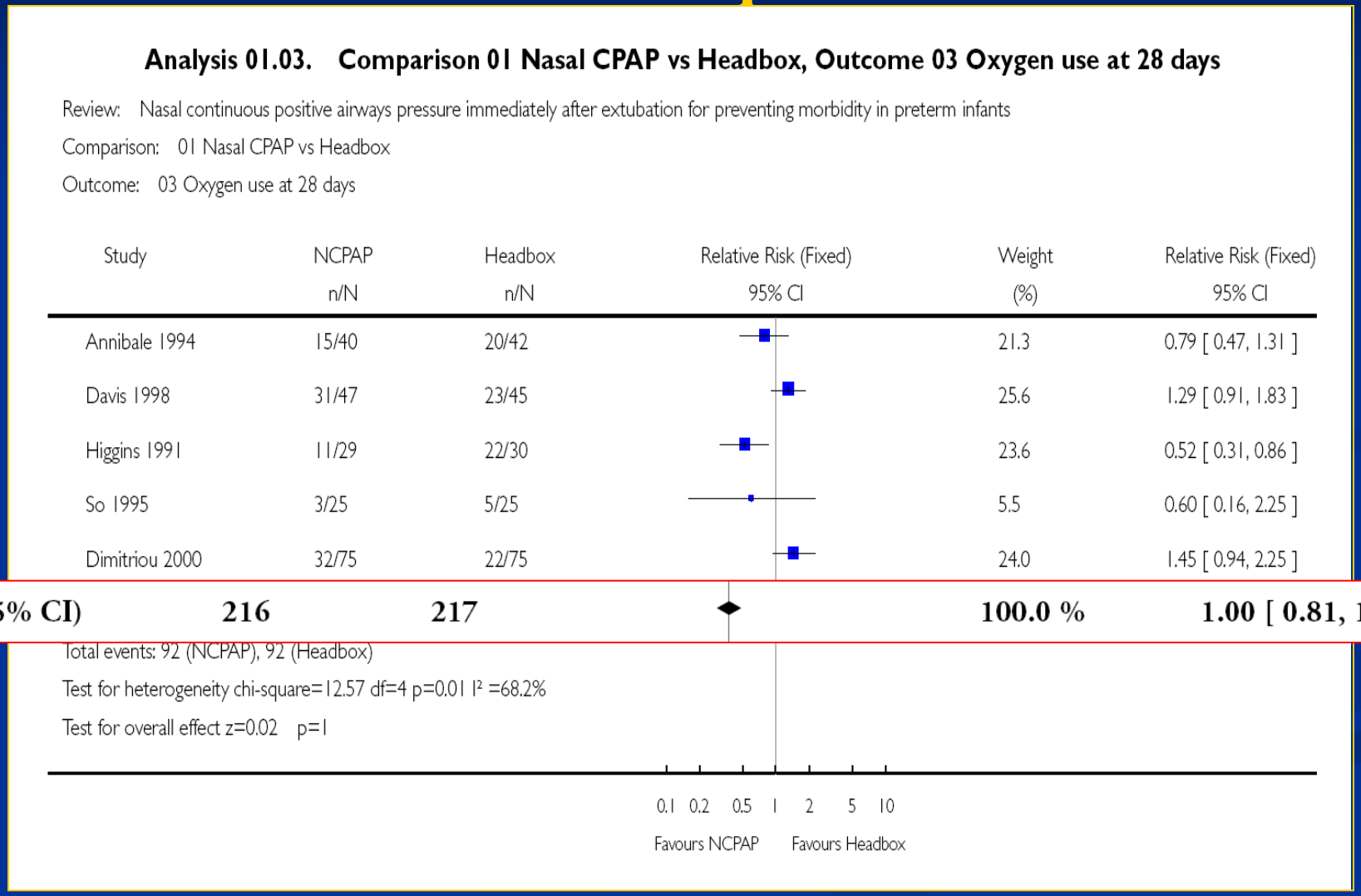
Test for overall effect: $Z = 4.58$ ($P < 0.00001$)

0.2 0.5 1 2 5

Favours NCPAP Favours Headbox

The Cochrane Library, *Davis PG, Henderson-Smart DJ 2003*

N-CPAP vs Hood después de extubación en prematuros



The Cochrane Library, *Davis PG, Henderson-Smart DJ 2003*

Uso de nCPAP temprano como alternativa a la ventilación mecánica, intubación y uso de surfactante.

CPAP temprano para prevenir ventilación

- Estudios observacionales han sugerido que en RN muy bajo peso el uso de nCPAP desde la sala de partos es posible y podría reducir la necesidad de intubación y la incidencia de DBP sin aumentar la morbilidad.
- Metanálisis de primeros estudios no mostró beneficios.

Fig. 1. Comparison 01. Prophylactic CPAP vs control

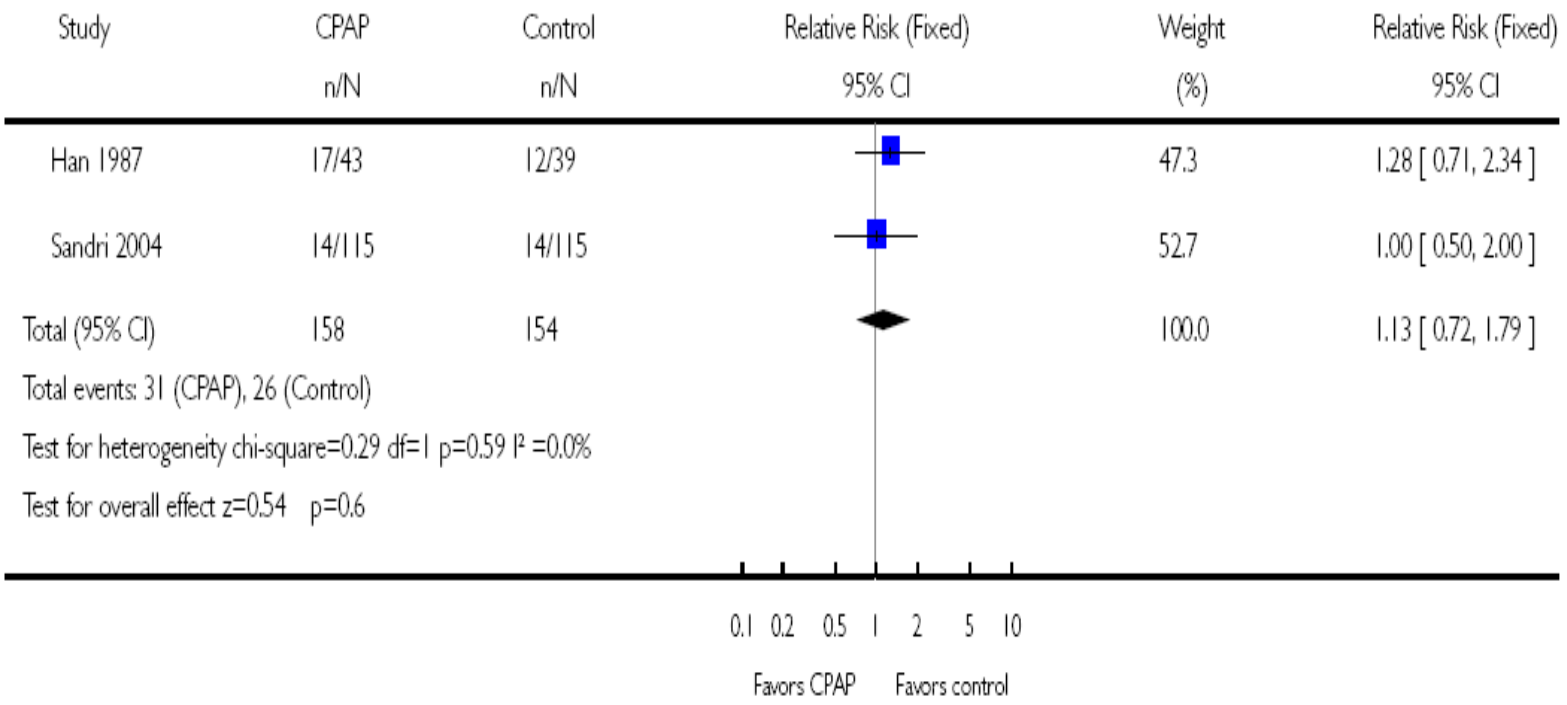
01.01 Use of IPPV

Review: Prophylactic nasal continuous positive airways pressure for preventing morbidity and mortality in very preterm infants

Comparison: 01 Prophylactic CPAP vs control

Outcome: 01 Use of IPPV

Uso VM



Subramaniam P, Henderson-Smart DJ, Davis PG. Prophylactic nasal continuous positive airways pressure for preventing morbidity and mortality in very preterm infants. *The Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD001243.pub2. DOI: 10.1002/14651858.CD001243.pub2.

Fig. 3. Comparison 01. Prophylactic CPAP vs control

01.03 Chronic lung disease at 36 weeks

Review: Prophylactic nasal continuous positive airways pressure for preventing morbidity and mortality in very preterm infants

Comparison: 01 Prophylactic CPAP vs control

Outcome: 03 Chronic lung disease at 36 weeks

DBP a las 36 sem

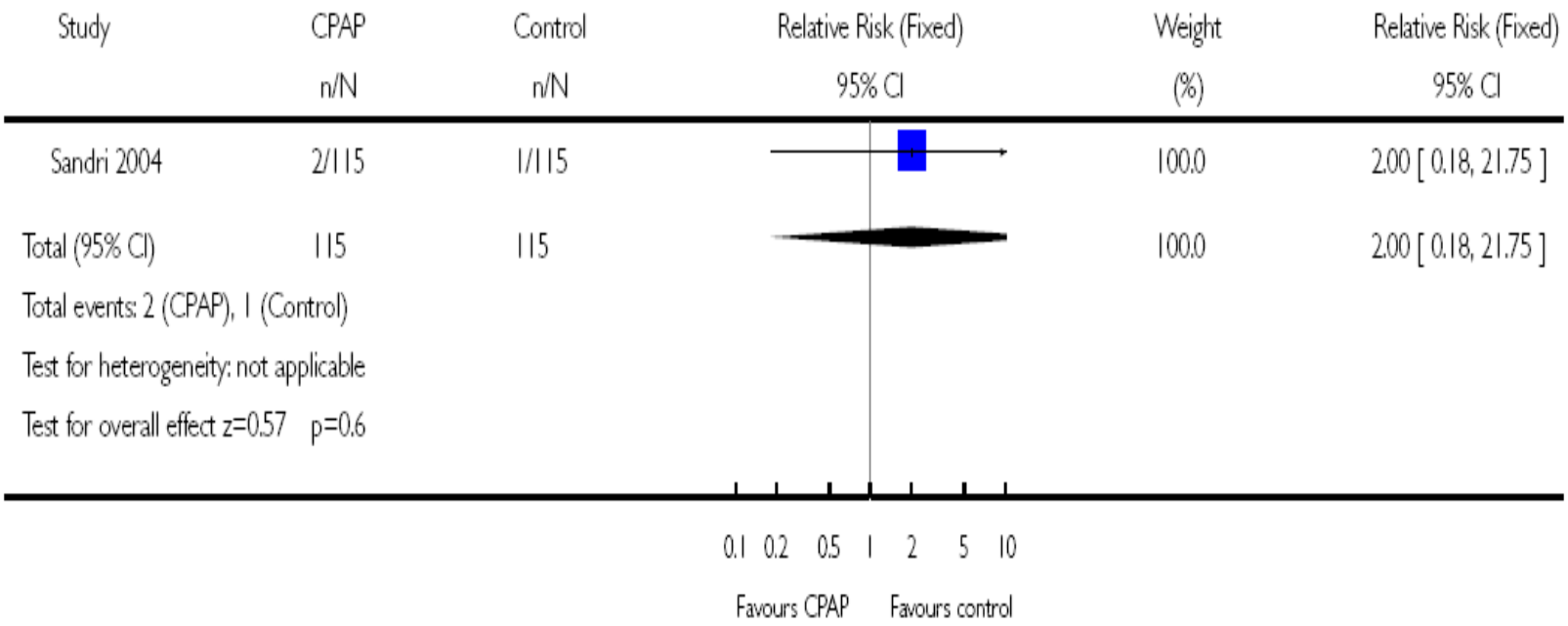


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Fig. 5. Comparison 01. Prophylactic CPAP vs control

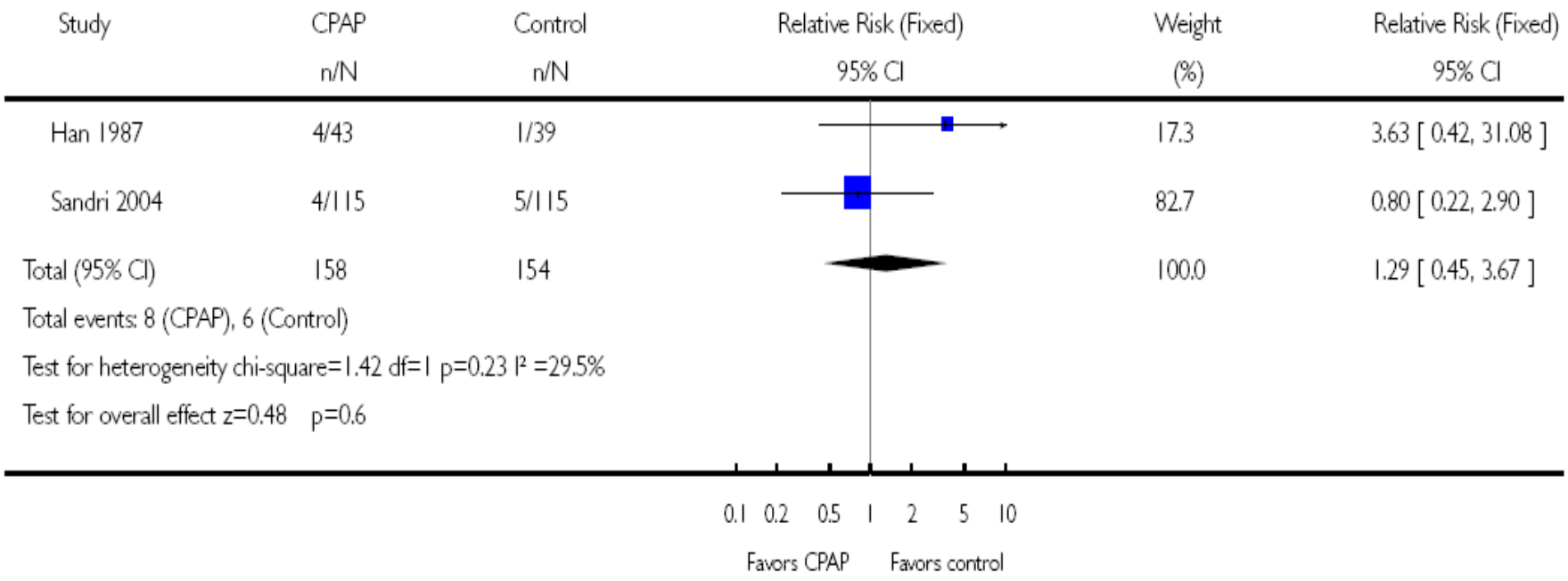
01.05 Neonatal death

Review: Prophylactic nasal continuous positive airways pressure for preventing morbidity and mortality in very preterm infants

Comparison: 01 Prophylactic CPAP vs control

Outcome: 05 Neonatal death

Muerte Neonatal



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Estudio COIN

(COntinuous PositiveAirway Pressure or INtubation at Birth)

- Estudio randomizado para responder pregunta de si en RNMBP el uso de CPAP nasal pronto después de nacer reduce la incidence de muerte o DBP comparado con intubación y ventilación.
- Estudio multicéntrico internacional: Australia, Nueva Zelandia, EEUU, Canada, y Europa.
- 610 RNMBP entre 25 a 28 semanas, respirando espontáneamente a los 5 minutos de haber nacido, pero con necesidad de apoyo respiratorio debido a un mayor esfuerzo respiratorio, quejido o cianosis.

Estudio COIN

(COntinuous PositiveAirway Pressure or INtubation at Birth)

- 5 minutos después del nacimiento pacientes randomizados a CPAP (iniciado con 8 cm H_2O) o intubación y ventilation.
- Outcome primario: muerte o DBP (definido como requerimiento de O_2 a las 36 semanas).

Table 1. Baseline Demographic and Clinical Characteristics of the Patients.*

Characteristic	CPAP (N=307)	Intubation (N=303)	P Value†
Gestational age (wk)	26.91±1.0	26.87±1.0	0.63
Gestational age of 25 or 26 wk (%)	33	35	0.59
Birth weight (g)	964±212	952±217	0.48
Use of antenatal corticosteroids (%)	94	94	0.76
Cesarean section (%)	66	69	0.51
Mother in labor (%)	65	66	0.82
Rupture of membranes (days before birth)			
Median	0	0	0.65
Interquartile range	0–2	0–1	
Male sex (%)	49	56	0.05
Multiple births (%)	35	32	0.57
Resuscitation device used (%)‡			0.13
None	19.5	13.9	
Self-inflating bag	14.7	16.5	
Self-inflating bag plus CPAP	13.0	14.2	
Flow-inflating bag	5.2	6.6	
Neopuff or bubble CPAP	47.2	46.5	
Apgar score at 5 minutes			
Median	9	8	0.001
Interquartile range	8–9	8–9	

* Plus–minus values are means ±SD. CPAP denotes continuous positive airway pressure.

† P values were calculated by the t-test, the chi-square test, or the Mann–Whitney test.

‡ In this category, eight infants (1.3%) were excluded because the resuscitation method was classified as "other."

Morley CJ et al. N Engl J Med 2008;358:700-8.

Table 2. Death or Need for Oxygen Treatment or Respiratory Support at 36 Weeks' Gestational Age, According to Gestational Age at Birth.*

Outcome	All Infants (25 to 28 Weeks' Gestation)			25 or 26 Weeks' Gestation			27 or 28 Weeks' Gestation		
	CPAP (N=307)	Intubation (N=303)	Odds Ratio (95% CI)	CPAP (N=100)	Intubation (N=105)	Odds Ratio (95% CI)	CPAP (N=207)	Intubation (N=198)	Odds Ratio (95% CI)
	%			%			%		
Death or oxygen treatment	33.9	38.9	0.80 (0.58–1.12)	53.0	53.3	0.99 (0.57–1.71)	24.6	31.3	0.72 (0.46–1.11)
Death, oxygen treatment, or respiratory support	35.2	40.3	0.81 (0.58–1.12)	55.3	55.3	0.99 (0.57–1.72)	25.6	32.3	0.72 (0.47–1.11)
Death before 36 weeks' gestation	6.5	5.9	1.10 (0.57–2.12)	13.0	7.6	1.81 (0.72–4.58)	3.4	5.1	0.66 (0.25–1.76)
Survivors treated with oxygen	29.3	35.1	0.76 (0.54–1.09)	46.0	49.5	0.87 (0.49–1.55)	22.0	27.7	0.74 (0.46–1.17)

* Odds ratios are for the comparison between infants receiving nasal continuous positive airway pressure (CPAP) and those receiving intubation and ventilation.

Morley CJ et al. N Engl J Med 2008;358:700-8.

Table 3. Death or Need for Oxygen Treatment or Respiratory Support at 28 Days of Age, According to Gestational Age at Birth.*

Outcome	All Infants (25 to 28 Weeks' Gestation)			25 or 26 Weeks' Gestation			27 or 28 Weeks' Gestation		
	CPAP (N=307)	Intubation (N=303)	Odds Ratio (95% CI)	CPAP (N=100)	Intubation (N=105)	Odds Ratio (95% CI)	CPAP (N=207)	Intubation (N=198)	Odds Ratio (95% CI)
	%			%			%		
Death or oxygen treatment	53.7	64.7	0.63 (0.46–0.88)	75.0	84.8	0.54 (0.27–1.08)	43.2	54.0	0.65 (0.44–0.96)
Death, oxygen treatment, or respiratory support	64.4	75.6	0.58 (0.41–0.83)	89.0	94.3	0.49 (0.17–1.39)	52.4	65.7	0.58 (0.39–0.86)
Death before 28 days	5.2	5.0	1.06 (0.51–2.18)	11	5.7	2.04 (0.72–5.74)	2.4	4.5	0.52 (0.17–1.58)
Survivors treated with oxygen	51.0	62.8	0.62 (0.44–0.86)	71.9	83.8	0.49 (0.24–1.00)	41.8	51.9	0.67 (0.45–0.99)

* Odds ratios are for the comparison between infants receiving nasal continuous positive airway pressure (CPAP) and those receiving intubation and ventilation.

Morley CJ et al. N Engl J Med 2008;358:700-8.

Table 4. Comparison of Secondary Outcomes.*

Outcome	CPAP (N=307)	Intubation (N=303)	P Value†
Surfactant treatment (%)	38	77	<0.001
Methylxanthine treatment (%)	84	71	<0.001
Days receiving any ventilatory support (no.)			
Median	21	26	0.24
Interquartile range	7–40	7–45	
Days receiving intubation and ventilation (no.)			
Median	3	4	<0.001
Interquartile range	0–11	1–14	
Days receiving CPAP (no.)			
Median	13	16	0.81
Interquartile range	4–30	3–32	
Days receiving oxygen treatment (no.)			
Median	42	49	0.07
Interquartile range	17–71	27–75	
Days until full enteral feeding (no.)			
Median	18	17	0.54
Interquartile range	12–28	11–29	
Days until regaining of birth weight (no.)			
Median	13	13	0.96
Interquartile range	10–16	10–16	
Days in any hospital (no.)			
Median	74	79	0.09
Interquartile range	61–94	65–97	
Complications (%)			
Pneumothorax	9.1	3.0	0.001
Pulmonary interstitial emphysema	5.5	3.6	0.33
Intraventricular hemorrhage grade 3 or 4	8.9	9.3	0.89
Cystic periventricular leukomalacia	2.9	4.0	0.51
Necrotizing enterocolitis grade 2 or 3	3.9	5.0	0.67
Any retinopathy of prematurity	53.1	59.4	0.12
Patent ductus arteriosus	32.4	37.0	0.24
Patent ductus arteriosus ligated	15.2	17.9	0.71
Discharged home treated with oxygen (%)	7.6	9.5	0.46
Late corticosteroid treatment (%)	12.7	13.2	0.81

* CPAP denotes continuous positive airway pressure.
† P values were calculated with the use of Fisher's exact test or the Wilcoxon rank-sum test.

Morley CJ et al. N Engl J Med 2008;358:700-8.

CPAP de Burbuja Temprano en RNMBP.

Grupo Colaborativo NEOCOSUR

- **Objetivo:** Determinar si estrategia de BCPAP profiláctico puede disminuir necesidad de VM en primera semana sin afectar morbi-mortalidad.
- **Diseño:** RCT, 256 RNMBP 800 a 1500 gr. Respirando espontáneamente a los 5 minutos.
  - Grupo BCPAP: 5 cmH_2O. Si SDR y FiO_2 > 35% → INSURE.
  - Grupo Standard: Si SDR y FiO_2 > 35% → Surfactante y VM.

Tapia et al. PAS Meeting 2010.

CPAP de Burbuja Temprano en RNMBP

Parameter	BCPAP group (n=131)	Standard Therapy group (n=125)	p
GA (wks)	29,86 (29,5-30,3)	29,54 (29,2-29,9)	0,242
Birth Weight (g)	1196 (1162-1229)	1197 (1163-1230)	0,993
Gender (male) (%)	51,1	51,2	0,993
Prenatal Steroids (%)	90,8	88	0,460
RDS (%)	50	56	0,337
Mechanical Ventilation (%)	29,8	52	0,001
Surfactant (%)	27,5	46,4	0,002
IVH III-IV (%)	4,6	6,5	0,502
Pneumotorax (%)	3,1	5,6	0,315
Oxygen at 36 weeks %	6,9	9,6	0,426
Death (%)	8,4	9,6	0,737
Nasal damage(minor) %	8,4	0	0,001

Tapia et al. PAS Meeting 2010.

Estudio Support:
CPAP precoz vs. Surfactante en RNEBP

- 1316 RNEBP 24+0 a 27+6 semanas.
- Diseño 2x2 factorial.
- Randomizados a intubación y surfactante (dentro de la primera hora) o a CPAP en la sala de partos con un protocolo de ventilación limitada.
- El resultado primario fue muerte o DBP a las 36 semanas.

Estudio SUPPORT

Table 1. Demographic and Clinical Characteristics of the Study Participants.*

Variable	CPAP (N=663)	Surfactant (N=653)
Gestational age — no. (%)		
24 wk 0 days–25 wk 6 days	285 (43.0)	280 (42.9)
26 wk 0 days–27 wk 6 days	378 (57.0)	373 (57.1)
Assignment to low target oxygen-saturation range in 2-by-2 factorial design — no./total no. (%)		
Gestational age of 24–25 wk	142/285 (49.8)	134/280 (47.9)
Gestational age of 26–27 wk	194/378 (51.3)	184/373 (49.3)
Male sex — no. (%)	342 (51.6)	370 (56.7)
Race or ethnic group — no. (%)†		
Non-Hispanic black	254 (38.3)	235 (36.0)
Non-Hispanic white	250 (37.7)	271 (41.5)
Hispanic	138 (20.8)	121 (18.5)
Other or unknown	21 (3.2)	26 (4.0)
Birth weight — g	834.6±188.2	825.5±198.1
Gestational age at birth — wk	26.2±1.1	26.2±1.1
Maternal use of antenatal corticosteroids — no./total no. (%)		
Any	642/663 (96.8)	623/652 (95.6)
Full course	486/660 (73.6)	453/649 (69.8)
Death of infant in the delivery room — no. (%)	1 (0.2)	5 (0.8)

* Plus–minus values are means ±SD. None of the differences between groups were significant. CPAP denotes continuous positive airway pressure.
† Race or ethnic group was reported by the mother or guardian of each child.

SUPPORT Study Group. NEJM 2010

Estudio SUPPORT

Table 2. Apgar Scores of Newborns and Interventions in the Delivery Room and NICU.*

Variable	CPAP (N=663)	Surfactant (N=653)	Relative Risk with CPAP (95% CI)	Adjusted P Value
	no./total no. (%)			
Apgar score <3				
At 1 min	154/661 (23.3)	167/653 (25.6)	0.92 (0.76–1.11)	0.38
At 5 min	26/663 (3.9)	32/653 (4.9)	0.82 (0.5–1.34)	0.43
PPV in the delivery room	435/662 (65.7)	606/652 (92.9)	0.71 (0.67–0.75)	<0.001
CPAP in the delivery room	538/663 (81.1)	146/653 (22.4)	3.66 (3.16–4.25)	<0.001
Intubation in the delivery room				
For any reason	227/660 (34.4)	609/652 (93.4)	0.37 (0.34–0.42)	<0.001
For resuscitation	215/660 (32.6)	176/652 (27.0)	1.21 (1.02–1.43)	0.02
Surfactant treatment				
In the delivery room	93/660 (14.1)	335/652 (51.4)	0.28 (0.23–0.34)	<0.001
In the delivery room or NICU	443/660 (67.1)	646/653 (98.9)	0.67 (0.64–0.71)	<0.001
Chest compressions in the delivery room	36/660 (5.5)	40/653 (6.1)	0.86 (0.57–1.31)	0.48
Epinephrine in the delivery room	13/660 (2.0)	27/653 (4.1)	0.48 (0.25–0.91)	0.02

* CI denotes confidence interval, CPAP continuous positive airway pressure, NICU neonatal intensive care unit, and PPV positive-pressure ventilation.

SUPPORT Study Group. NEJM 2010

Estudio SUPPORT

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

SUPPORT Study Group. NEJM 2010

Estudio SUPPORT

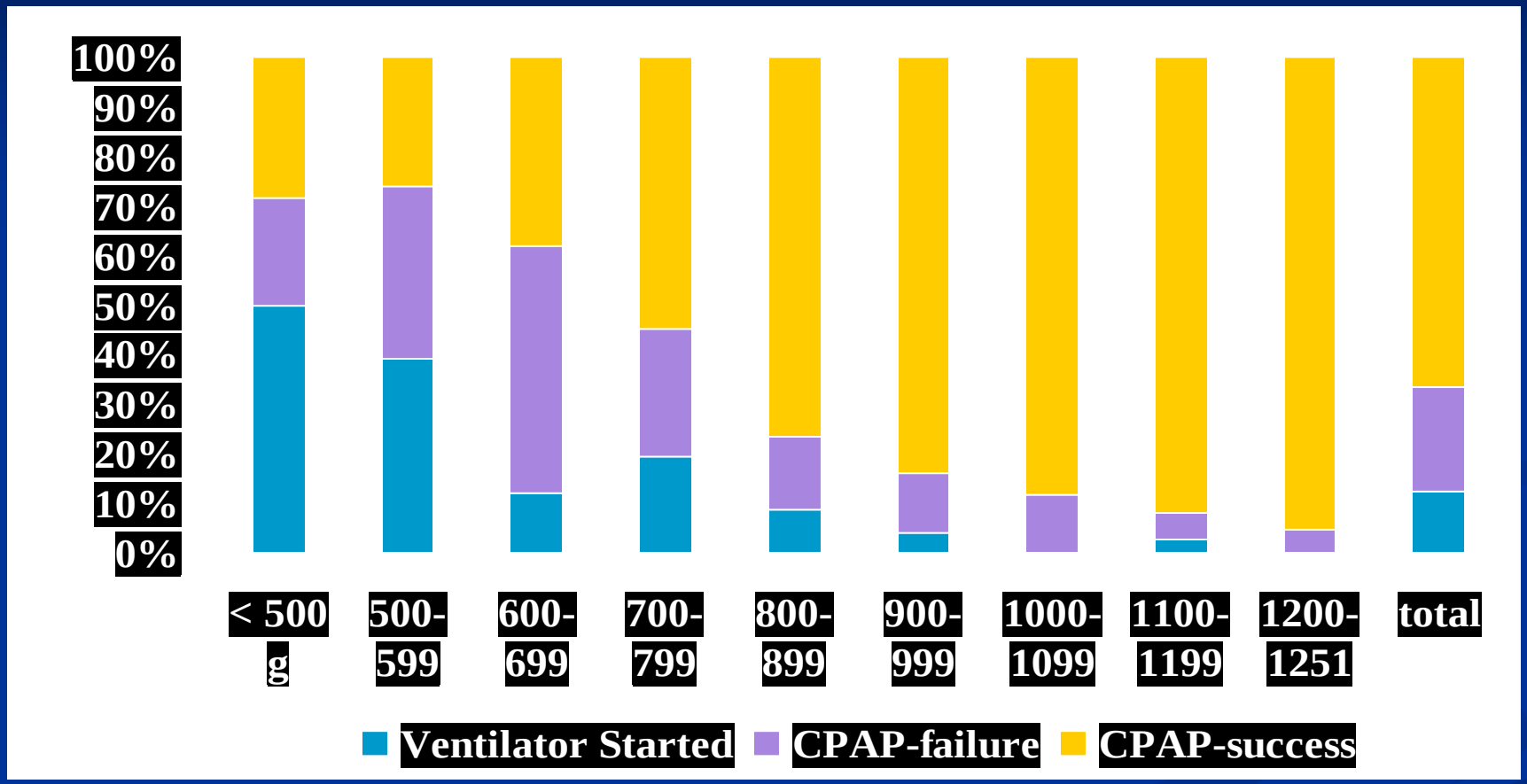
	CPAP	Surfactante			
Need for supplemental oxygen — no. of days‡					0.12
Adjusted mean	62.2±1.6	65.3±1.6		−3.1 (−7.1 to 0.8)	
Unadjusted median	52	56			
Interquartile range	20 to 86	27 to 91			
Need for mechanical ventilation — no. of days‡§					0.03
Adjusted mean	24.8±1.0	27.7±1.1		−3.0 (−5.6 to −0.3)	
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

SUPPORT Study Group. NEJM 2010

Uso precoz de CPAP con surfactante profiláctico o precoz.

Falla precoz de NCPAP en RNMBP (≤ 1250 gr.):

Children's Hospital of New York, Columbia University 1999-2002



Variables asociadas con falla NCPAP: VPP al nacer (OR 2.4 [1.02-5.5]); A-a DO_2 > 180 (OR 2.9 [1.3-6.5]) y EMH severo RDS en radiografía (OR 6.4 [2.7-15])

Ammari A et al. J Pediatr 2005; 147: 341

¿Administración de Surfactante en Combinación con CPAP Nasal?

- **Retrasar la intubación y Ventilación Mecánica puede ser importante para evitar daño pulmonar.**
  - Estudios animales sugieren que uso CPAP desde nacimiento se asocia con menor daño pulmonar.
  - El CPAP temprano puede estimular la producción de surfactante.
  - Intubación y Surfactante son "eventos traumaticos"
  - Los resultados de los estudios de surfactante pueden no aplicarse a niños estables en CPAP.
- **Demora en uso surfactante puede asociarse con una respuesta más pobre y deterioro de pacientes con EMH.**
- **Administración de surfactante precoz y extubación a CPAP pueden ser beneficiosas aumentando la posibilidad de manejo exitoso con CPAP precoz.**

Surfactante y N-CPAP para RN con EMH

Niños 25 - 35 semanas con EMH moderada a severa

randomizados a CPAP nasal + surfactante ó CPAP solo

	Surf + CPAP(35)	CPAP (33)
Edad Gestacional	30	29
Edad de entrada (hrs)	13	10
Ventilación Mecánica	43%	85%*
Días O_2	6	6
Muerte a los 28 días	6%	15%
Oxígeno a los 28 días	9%	9%

Verder et al NEJM 1994

NCPAP y Surfactante precoz en < 30 semanas

60 niños randomizados a recibir surfactante precoz o tardío. Todos estaban en NCPAP para tratar EMH. Estudio se detuvo por mejor resultado en grupo estudio

TABLE 2. Data on Study End Points

End point	Early Treatment	Late Treatment	*P* Value	Statistics
Mechanical ventilation and/or death <7 days, number (%)	7 (21)	17 (63)	.0013	Logistic regression
Mechanical ventilation and/or death before discharge, number (%)	9 (27)	19 (70)	.004	χ^2
Mechanical ventilation before discharge, number (%)	8 (25)	17 (68)	.005	χ^2
a/APo_2 after 6 hours, mean ± SD	0.48 ± 0.18	0.36 ± 0.18	.02	Multiple regression

Verder et al. Pediatrics 1999;103(2). URL:http://www.pediatrics.org/cgi/content/full/103/2/e24

CPAP y surfactante precoz en RN < 30 semanas

	Experimental n=33	Control n=27	p value
VMI (%)	25	68	<0.01
Muerte (%)	9	26	0.16
O_2 a las 36 sem (%)*	3	4	0.66
O_2 a las 36 sem o muerte (%)	12	30	<0.05

* En sobrevivientes

Verder et al. Pediatrics 103:E24, 1999

CPAP precoz/ Surfactante Profiláctico

- 42 RN, 25-28 sem, intubados al nacer y 1 dosis surfactante.
- Randomizados dentro de 1 hr de recibir surfactante a Vent Conv ó extubación a nCPAP.
- 38% nCPAP no requirieron ventilación. ($p<0.01$)
- 47% vs. 81% intubados a las 72 hrs. ($p<0.05$)

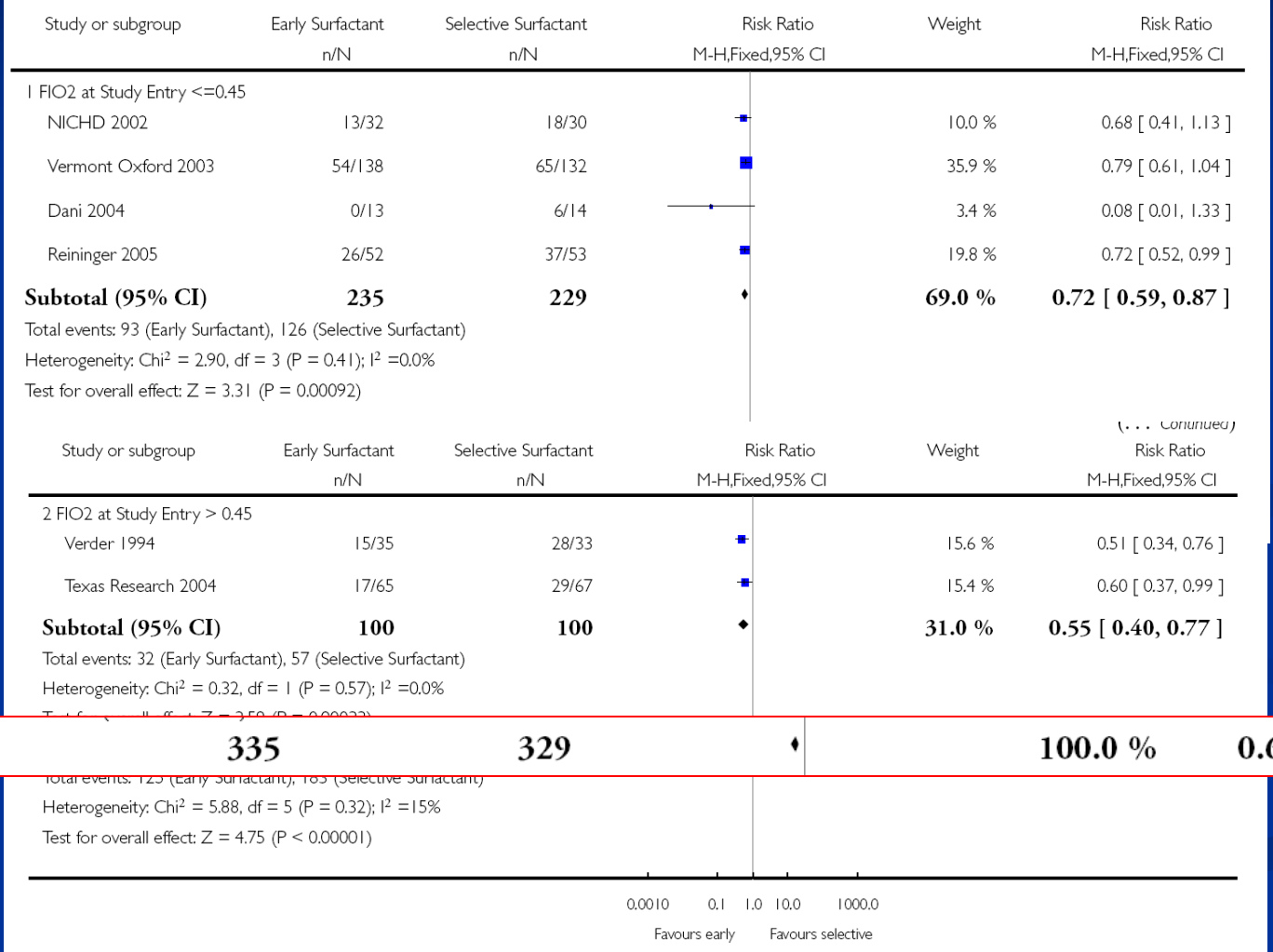
Tooley and Dyke. Acta Paediatrica. 2003; 92(10):1170-1174

Analysis 1.1. Comparison 1 Early surfactant, rapid extubation to NCPAP vs. selective surfactant, ventilation in babies with RDS., Outcome 1 Need for mechanical ventilation..

Review: Early surfactant administration with brief ventilation vs. selective surfactant and continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome

Comparison: 1 Early surfactant, rapid extubation to NCPAP vs. selective surfactant, ventilation in babies with RDS.

Outcome: 1 Need for mechanical ventilation.



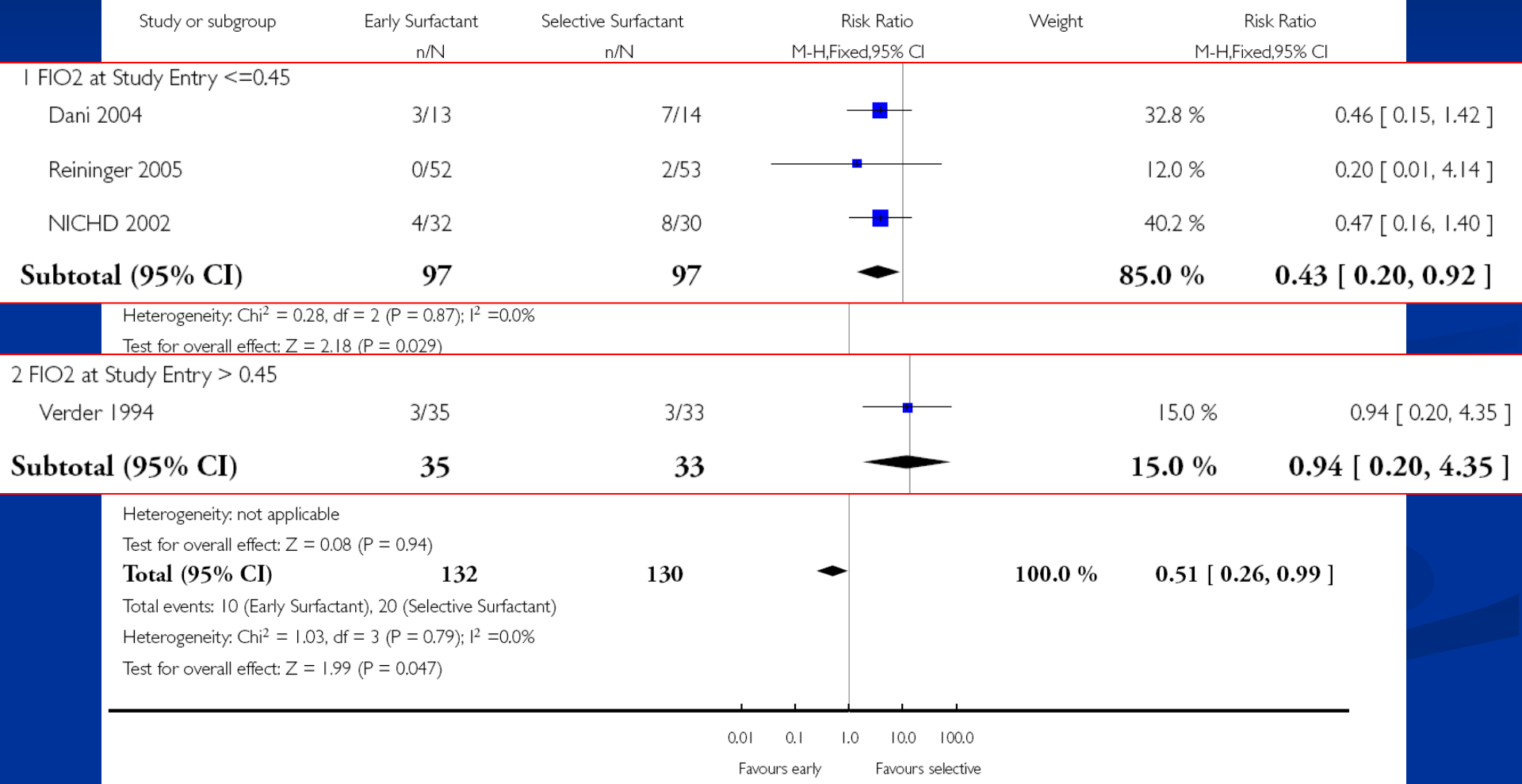
Stevens TP, Blennow M, Myers EH, Soll R. Early surfactant administration with brief ventilation vs.selective surfactant and continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome. *CochraneDatabase of Systematic Reviews* 2007, Issue 4. Art. No.: CD003063. DOI: 10.1002/14651858.CD003063.pub3.

Analysis 1.2. Comparison 1 Early surfactant, rapid extubation to NCPAP vs. selective surfactant, ventilation in babies with RDS., Outcome 2 Bronchopulmonary dysplasia: need for oxygen at 28 days chronologic age..

Review: Early surfactant administration with brief ventilation vs. selective surfactant and continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome

Comparison: 1 Early surfactant, rapid extubation to NCPAP vs. selective surfactant, ventilation in babies with RDS.

Outcome: 2 Bronchopulmonary dysplasia: need for oxygen at 28 days chronologic age.



Stevens TP, Blennow M, Myers EH, Soll R. Early surfactant administration with brief ventilation vs.selective surfactant and continued mechanical ventilation for preterm infants with or at risk for respiratory distress syndrome.*CochraneDatabase of Systematic Reviews* 2007, Issue 4. Art. No.: CD003063. DOI: 10.1002/14651858.CD003063.pub3.

Estudio Colombiano

Surfactante Muy Precoz Sin Ventilación Mandatoria en RN Prematuros Tratados con CPAP Precoz: Un Estudio Randomizado, Controlado.

Rojas MA et al. *Pediatrics* 2009;123;137-142.

Estudio Colombiano

- Objetivo:
  - Determinar si el agregar el uso de surfactante precoz (dentro de la primera hora de vida) al uso precoz de nCPAP, en RN prematuros con SDR y que respiran espontáneamente, es superior a sólo nCPAP en su capacidad de reducir la necesidad de Ventilación Mecánica.
- 279 RN 27 a 31 semanas.
- Grupo estudio: INSURE

TABLE 1 Baseline Characteristics in the Study Groups

Characteristic	Control Group ($N = 137$)	Treatment Group ($N = 141$)
Birth weight, mean ± SD, g	1293 ± 324	1299 ± 325
Gestational age, mean ± SD, wk	29.3 ± 1.4	29.3 ± 1.4
Male, *n* (%)	67 (49)	78 (55)
5-min Apgar score, median (range)	9 (3–10)	8 (4–10)
C-section, *n* (%)	116 (84)	116 (82)
Prenatal steroids, *n* (%)	119 (88)	121 (88)
Chorioamnionitis, *n* (%)	7 (5)	10 (7)

Control group: early NCPAP only; treatment group: early NCPAP plus very early surfactant therapy.

Rojas MA et al. *Pediatrics* 2009;123;137-142.

TABLE 2 Primary and Other Major Outcomes

Outcome	Control Group ($N = 137$), n (%)	Treatment Group ($N = 141$), n (%)	RR (95% CI)
MV	53 (39)	37 (26)	0.69 (0.49–0.97)[a]
Mortality			
All deaths	13 (9)	13 (9)	1.00 (0.48–2.05)
<7 d	5 (4)	8 (6)	1.61 (0.54–4.75)
<28 d	12 (8)	11 (7)	0.91 (0.42–1.98)
≥28 d	1 (1)	2 (1)	2.06 (0.19–22.20)
Pneumothorax/PIE	12 (9)	3 (2)	0.25 (0.07–0.85)[a]
CLD[b]	73/124 (59)	63/128 (49)	0.84 (0.66–1.05)
IVH, grade III or IV	3 (2)	2 (1)	0.71 (0.12–4.16)
PVL	1 (1)	0	0.35 (0.01–8.64)

Control group: early NCPAP only; treatment group: early NCPAP plus very early surfactant therapy.

[a] $P \leq .05$.

[b] Oxygen treatment at 36 weeks' postmenstrual age; denominator = survivors to 36 weeks' postmenstrual age.

Rojas MA et al. *Pediatrics* 2009;123;137-142.

Estudio CURPAP:

Surfactante Profiláctico o Temprano-Selectivo en RNEBP

- 208 RNEBP, 25 a 28 semanas EG.
- Randomizados a surfactante profiláctico seguido de nCPAP vs nCPAP precoz y surfactante selectivo.
- Resultado de medición primario: necesidad de Ventilación Mecánica en los primeros 5 días.

Estudio CURPAP:

Surfactante Profiláctico o Temprano-Selectivo en RNEBP

TABLE 1 Baseline Demographic and Clinical Characteristics of the Patients

Characteristic	Prophylactic Surfactant ($N = 105$)	nCPAP ($N = 103$)
GA, mean ± SD, wk	27.0 ± 1.0	27.00 ± 1.0
GA 25–26 wk, *n* (%)	32.0 (30.5)	31.0 (30.0)
Antenatal corticosteroids, *n* (%)		
Complete course	82 (78.1)	81 (78.6)
Incomplete course	19 (18.1)	20 (19.4)
Cesarean delivery, *n* (%)	75 (71.0)	74 (72.0)
Birth weight, mean ± SD, g	967 ± 221	913 ± 200
Male gender, *n* (%)	57 (54.3)	54 (52.4)
Multiple births, *n* (%)	33 (31.4)	30 (29.1)
Apgar score at 5 min, median (range)	8 (5–10)	8 (4–10)
CRIB score, median (range)	1 (0–9)	2 (0–15)

All data were not statistically different in the 2 study groups. CRIB indicates clinical risk index for babies.

Sandri F et al. *Pediatrics* 2010;125;e1402-e1409

Estudio CURPAP:

Surfactante Profiláctico o Temprano-Selectivo en RNEBP

TABLE 2 Primary Outcome: Need for MV Within 5 Days

GA, *n* (%)	Prophylactic Surfactant (*N* = 105)	nCPAP (*N* = 103)	RR (95% CI)
25–28 wk 6 d	33 (31.4)	34 (33.0)	0.95 (0.64–1.41)
25–26 wk 6 d	15 (46.9)	12 (38.7)	1.21 (0.68–2.16)
27–28 wk 6 d	18 (24.7)	22 (30.6)	0.81 (0.47–1.37)

Sandri F et al. *Pediatrics* 2010;125;e1402-e1409

Estudio CURPAP:

Surfactante Profiláctico o Temprano-Selectivo en RNEBP

TABLE 3 Death and Type of Survival

Outcome	28 d of Age			36 wk Postmenstrual Age		
	Prophylactic Surfactant, *n* (%)	nCPAP, *n* (%)	RR (95% CI)	Prophylactic Surfactant, *n* (%)	nCPAP, *n* (%)	RR (95% CI)
Survivors in room air	43 (41.0)	32 (31.1)	1.32 (0.91–1.90)	82 (78.1)	81 (78.6)	0.99 (0.86–1.14)
Survivors with oxygen only	11 (10.5)	15 (14.6)	0.72 (0.35–1.49)	5 (4.8)	5 (4.9)	0.98 (0.29–3.29)
Survivors on respiratory support (MV or nCPAP)	44 (41.9)	47 (45.6)	0.92 (0.67–1.25)	9 (8.6)	6 (5.8)	1.47 (0.54–3.99)
Death						
25–28 wk 6 d	7 (6.7)	9 (8.7)	0.76 (0.30–1.97)	9 (8.6)	11 (10.7)	0.80 (0.35–1.86)
25–26 wk 6 d	2 (6.3)	3 (9.7)	0.65 (0.13–3.10)	4 (12.5)	3 (9.7)	1.29 (0.34–4.96)
27–28 wk 6 d	5 (6.8)	6 (8.3)	0.82 (0.27–2.45)	5 (6.8)	8 (11.1)	0.71 (0.20–2.61)

Sandri F et al. *Pediatrics* 2010;125;e1402-e1409

Estudio CURPAP:

Surfactante Profiláctico o Temprano-Selectivo en RNEBP

TABLE 4 Secondary Outcomes

Outcomes	Prophylactic Surfactant ($N = 105$), n (%)	nCPAP ($N = 103$), n (%)	RR (95% CI)
Pneumothorax	7 (6.7)	1 (1.0)	6.82 (0.86–53.75)
Pulmonary interstitial emphysema	3 (2.9)	4 (3.9)	0.74 (0.17–3.21)
Pulmonary hemorrhage	3 (2.9)	2 (1.9)	1.47 (0.25–8.76)
Intraventricular hemorrhage grades 3–4	6 (5.7)	8 (7.8)	0.73 (0.27–2.03)
25–26 wk 6 d	3 (9.4)	4 (12.9)	0.73 (0.19–2.75)
27–28 wk 6 d	3 (4.1)	4 (5.6)	0.74 (0.19–2.89)
Patent ductus arteriosus	43 (41.0)	51 (49.5)	0.83 (0.62–1.10)
Medically treated	28 (26.7)	35 (34.0)	
Surgically ligated	6 (5.7)	3 (2.9)	
Retinopathy of prematurity			
Any	30 (28.6)	30 (29.1)	0.98 (0.65–1.48)
Stage ≥2	7 (6.7)	7 (6.8)	0.98 (0.36–2.70)
Necrotizing enterocolitis	7 (6.7)	9 (8.7)	0.76 (0.30–1.90)
Cystic periventricular leukomalacia	3 (2.9)	2 (1.9)	1.47 (0.25–8.76)
Sepsis	45 (42.9)	43 (41.7)	1.02 (0.75–1.40)
Moderate and severe BPD in survivors			
25–28 wk 6 d	14/98 (14.3)	11/94 (11.7)	1.22 (0.58–2.50)
25–26 wk 6 d	7/30 (23.3)	7/28 (25.0)	0.93 (0.38–2.30)
27–28 wk 6 d	7/68 (10.3)	4/66 (6.1)	1.70 (0.55–5.30)
Use of systemic postnatal corticosteroids	14 (13.3)	11 (10.7)	1.25 (0.59–2.62)

Sandri F et al. *Pediatrics* 2010;125;e1402-e1409

¿SE PUEDE EVITAR VENTILACIÓN MECÁNICA USANDO NCPAP?

- Muchos prematuros de extremo bajo peso > 750 g pueden no necesitar ventilación mecánica y el CPAP puede ser una buena alternativa para el manejo de la EMH.

- Muchos prematuros de extremo bajo peso < 750 g necesitarán ser intubados, pero el intento de manejo con nCPAP desde la sala de partos es posible y puede prevenir la intubación hasta en un tercio de ellos.

- No es claro que la administración profiláctica de surfactante y extubación a N-CPAP sea más efectiva que el uso de nCPAP muy precoz/profiláctico y uso de surfactante temprano/selectivo.

¿PUEDE EL USO DE NCPAP DISMINUIR LA INCIDENCIA DE DBP?

- Ninguna de estas estrategias ha probado tener un impacto definitivo en la incidencia de DBP o resultados a largo plazo.

- En este momento aún se realizan Estudios Randomizados Controlados para resolver estas preguntas y esperamos metanálisis.


AVANCES EN PEDIATRIA NEONATAL
Pontificia Universidad Católica de Chile
Santiago 1,2,3 Agosto 1988