Making Science and Research Guide Changes in Neonatal Resuscitation

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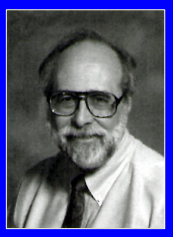
Dr. Moya has nothing to disclose

Neonatal Resuscitation Program

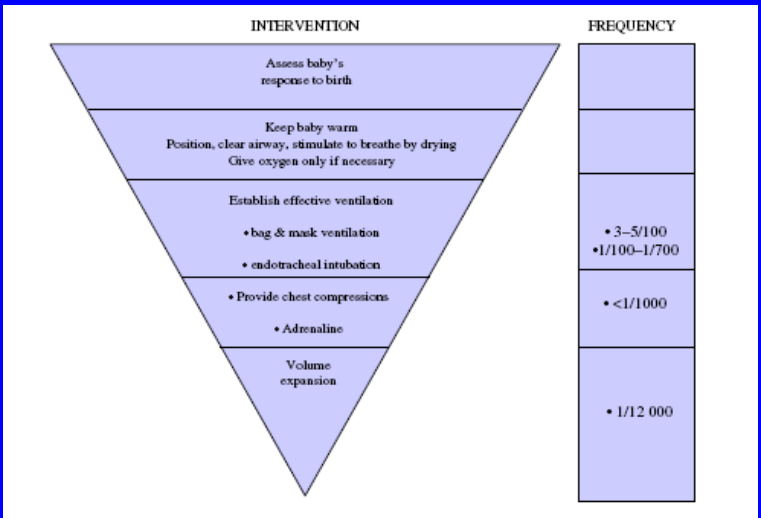
- Interest began in late 1970s and early 1980s
- 1985: joint AAP/AHA committee to develop a training program in neonatal resuscitation
- First NRP textbook (1987): based on consensus opinions of leaders in neonatology based on "accepted" practice
- First 2-day NRP course occurred Nov 1987
- Now recommendations increasingly based on higher level of evidence



Ron Bloom

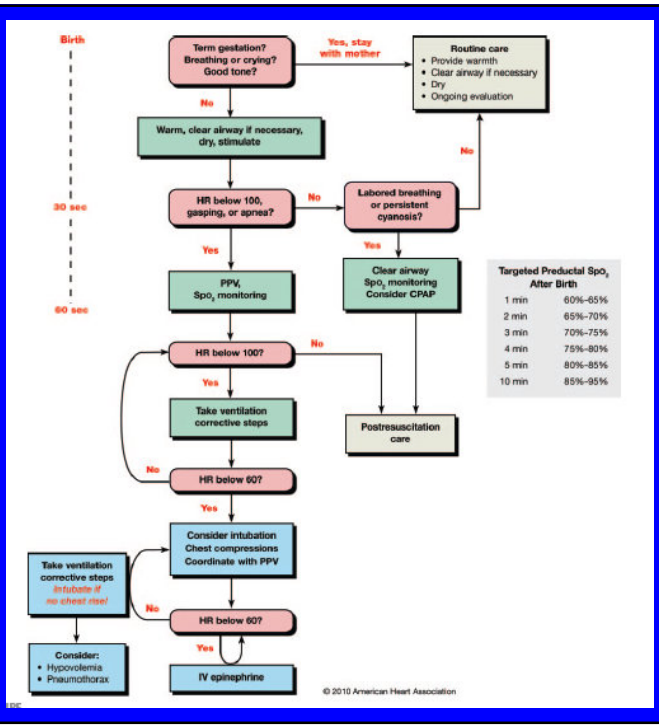
Cathy Cropley

How often is Neonatal Resuscitation used?



Vento M and Saugstad O, Sem Fetal Neonatal Med, 2010

Latest NRP Guideline



Avoiding Heat Loss

- Premature, especially VLBW infants continue to be at risk for hypothermia
- Association between hypothermia and increased mortality in premature newborns
- Hypothermia also adds to the morbidity of the preterm neonate
  - hypoglycemia, respiratory distress, hypoxia, metabolic acidosis, and coagulation defects

Avoiding Heat Loss

Recommendations:

- Increase temperature of delivery room (74-76ºF)
- Preheat radiant warmer
- Transport in a pre-warmed incubator
- Consider placing infant in a re-closable polyethylene bag (if < 30 weeks EGA)
- Use exothermic mattress

Avoid hyperthermia

Avoiding Heat Loss

Use of plastic bags or plastic wrapping

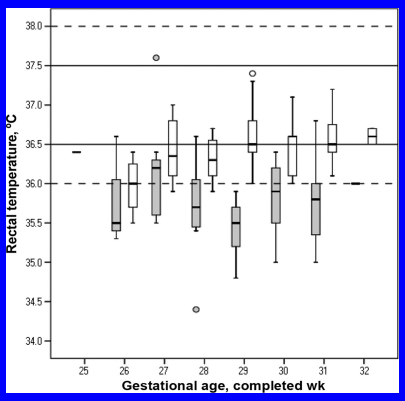
- 2 RCT's and 3 Observational studies with retrospective controls confirm efficacy of this technique, in addition to customary radiant heat, to improve admission temperature of premature infants compared with standard care
- Full resuscitation and conventional care can continue unhindered once the neonate is in the bag

- Small risk of hyperthermia

Humidified/Heated Gases During Stabilization at Birth- Observational Study

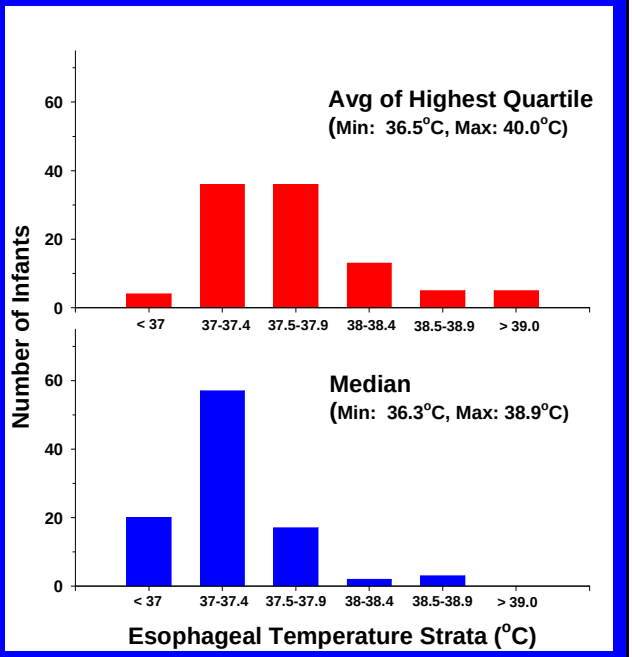
- Two subsequent study periods, N= 112
- Used Heater/Humidifer along with Neopuff
- Plastic wrap before drying for < 30 weeks GA

Characteristic	Cold Cohort	Heated Cohort
Mean BW (g)	1190 ± 337	1206 ± 332
Mean GA (wk)	28.8 ± 1.9	28.4 ± 1.6
Time birth to NICU (min)	19 ± 5	20 ± 5
5 min Apgar (IQR)	8 (7-9)	8 (7-9)
Cesarean delivery	47%	56%
DR Intubation	12%	11%



Te Pas A. et al, J Pediatrics 125:e1427, 2010

Distribution Of Control Infants Among Strata of Esophageal Temperature



NEJM 2005;353:1574-84
Pediatrics 2008;122:497-7

Association Between Esophageal Temperature and Outcome for Control Infants*

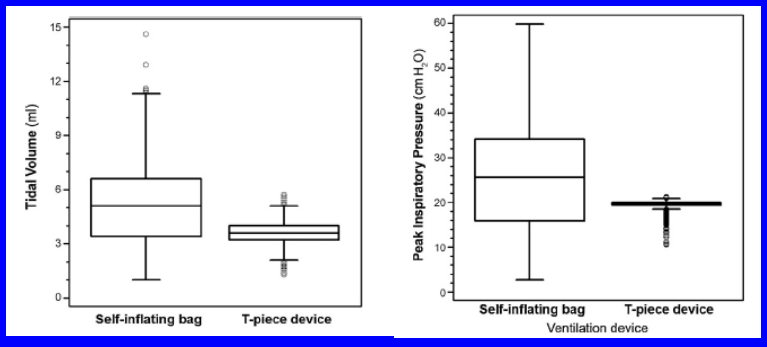
Esophageal Temperature (°C)	Death or Disability N = 99	Death N = 99	Disability N = 65
Highest quartile	4.0 (1.5 – 11.2)	6.2 (2.1 – 17.9)	1.8 (0.4 – 8.2)
Median	3.3 (0.9 – 11.2)	5.9 (1.5 – 22.7)	1.0 (0.2 – 5.1)

*Adjusted for race, gender, level of encephalopathy, gestational age
Odds ratio per °C increase (95% confidence interval)

Positive Pressure Ventilation

Which device to use for PPV?

Randomized study of 120 health professionals using low compliance Mannequin aiming for 20/5 pressures



Roehr C et al, Resuscitation 2010

Which device to use for PPV?

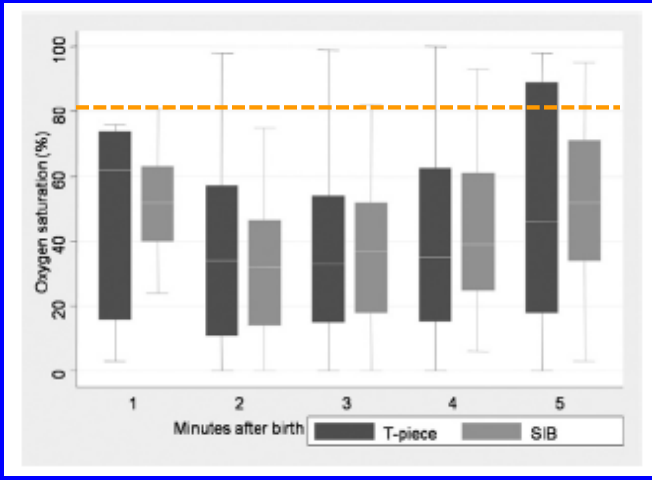
Randomized study of 120 health professionals using low compliance Mannequin aiming for 20/5 pressures

Comparison of systems according to individual experience in NR.

Experience: NR per year	n	SI-bags			T-piece device		
		Median	$IQR_{25-75\%}$	p-Value	Median	$IQR_{25-75\%}$	p-Value
PIP (cmH_2O)							
0	60	28.6	20.6	0.275	19.8	0.5	0.187
1–2	26	22.9	16		19.7	0.5	
>2	34	19.3	19.3		19.7	0.8	
Vt (ml)							
0	60	5.3	3.9	0.239	3.7	0.8	0.859
1–2	26	4.8	3.1		3.6	0.8	
>2	34	4.1	3.4		3.6	0.6	

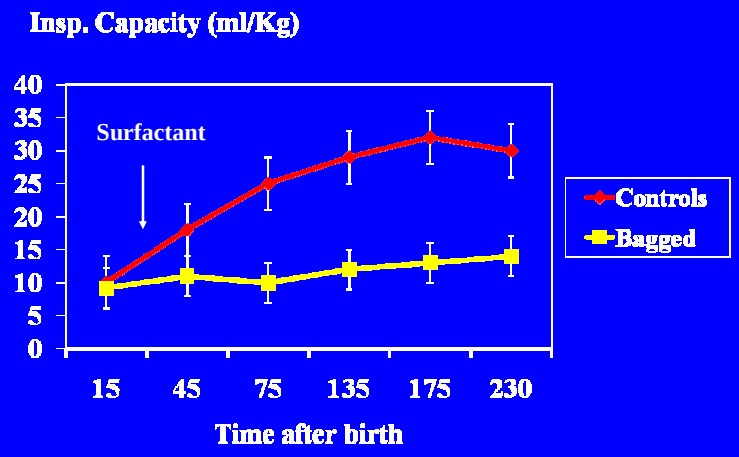
Roehr C et al, Resuscitation 2010

Randomized Trial of T-Piece vs Self Inflating Bag for Ventilation of Extremely Preterm Infants



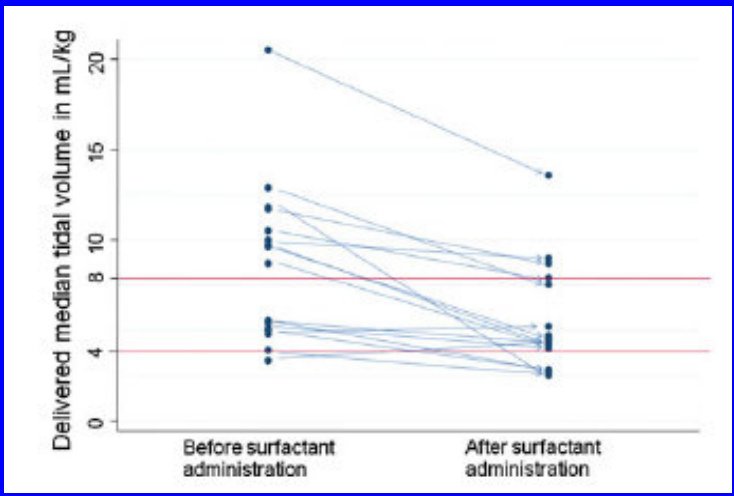
Dawson J et al, J Pediatrics 2011

NEONATAL RESUSCITATION AND LUNG INJURY IN PRETERM LAMBS



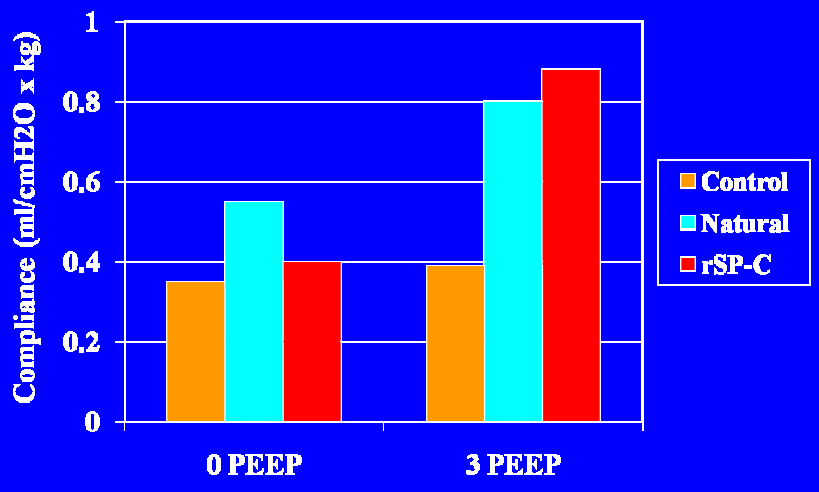
Bjorklund L. et al. Pediatr Res 42: 348, 1997

Tidal Volume During Surfactant Administration in the Delivery Room



Schmolzer G et al, Intensive Care Med 2011

The effect of surfactant depends on PEEP



Davis et al. Am J Resp Crit Care Med 1998; 157: 553.

In the era of CPAP:

What infants need surfactant In the DR?

Recent trials of CPAP and Surfactant

	COIN	SUPPORT	CURPAP
N	610	1316	208
GA (weeks)	25-28+6	24-27+6	25 to 28+6
Any AS	94%	96-97%	96-98%
Exclusion	Not breathing at 5 min Intubation No resp.support or O2	No consent Malformations	Apgar <3 @ 5min Intubation Poor Resp. Drive
Intervention	Nasal CPAP of 8cm or intubation + MV	Nasal CPAP of 5cm or Intubation + surfactant	Prophylactic surfactant or CPAP 6-7cm
Surfactant	Only after intubation and based on local protocols		Prophylactic or if FiO2 > 40%
MV intubation	FiO2 > 60% Apnea PCO2> 60 and pH <7.25	FiO2 > 50% PCO2>65 Low BP with treatment	FiO2 > 40% Apnea PCO2> 65 and pH <7.2
MV extubation	Not mandated and based on local protocols	FiO2<50%/35% MAP <10/8 PCO2 <65/50	FiO2 < 40% MAP < 7-8 PCO2< 65 and pH >7.2

CPAP or Intubation for Very Preterm Infants – The COIN Trial

	CPAP N= 307	INTUBATION N= 303	OR (95% CI) or P
Intubation rate in CPAP group	55% / 40%	100%	
Death before 36 wks	6.5%	5.9%	1.10 (0.57-2.12)
Death or O2 at 36 wks	33.9%	38.9%	0.80 (0.58-1.12)
Surfactant treatment	38% 57%	77%	<0.001
Pneumothorax	9.1%	3.0%	0.001
Median days intubated and ventilated	3 (0-11)	4 (1-14)	<0.001

Morley C. et al, New Engl J Med 358: 700, 2008

CPAP or Intubation + Surfactant for Very Preterm Infants – SUPPORT Trial

	CPAP N= 663	SURFACTANT N= 653	OR (95% CI) or P
Gest. Age	26.2 ± 1.1	26.2 ± 1.1	
Death by 36 wks	14.2%	17.5%	0.81 (0.63-1.03)
Death or BPD at 36 wks	48.7%	54.1%	0.91 (0.83-1.01)
Surfactant treatment	67%	99%	<0.001
Any air leak to 14 days	6.8%	7.4%	0.89 (0.60-1.32)
Median days intubated and ventilated	10 (2-32)	13 (2-36)	<0.05

83%

Finer N. et al, New Engl J Med 362: 1970, 2010

Prophylactic or Early Selective Surfactant with CPAP –CURPAP Trial

	PROPHYLACTIC SURFACTANT N= 105	CPAP and SURFACTANT N= 103	OR (95% CI) or P
Gest. Age	27.0 ± 1.0	27.0 ± 1.0	
Death by 36 wks	6.5%	5.9%	1.10 (0.57-2.12)
Survival in RA at 36 wks	78.1%	78.6%	0.99 (0.86-1.14)
Surfactant treatment	100%	48.5%	<0.001
Pneumothorax	6.7%	1.0%	6.82 (0.86-53.7)
Need for mechanical ventilation first 5 d	31.4%	33.0%	0.95 (0.64-1.41)

75%

Sandri F. et al, Pediatrics 125: e1402, 2010

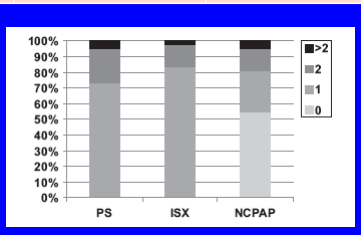
Randomized trial of Initial Respiratory Management of Preterm Infants

	Proph. Surfactant	Intubate+ Surf+ Extubate	NCPAP
N	209	216	223
GA	26-28+6 weeks		
Any AS	98.6 %	98.6 %	98.7 %
Exclusion	Life Threatening Condition or Malformations		
Intervention	Intubation + surfactant	Intubation + surfactant Extubate 15-30 min if O2 < 60%	NCPAP 5-7cm
Surfactant	After intubation and Within 5-15 min	After intubation and Within 5-15 min	Only after intubation
Intubation	In delivery room	In delivery room	FiO2 > 40% Apnea PCO2> 65
MV extubation	FiO2< 30%, MAP < 7 After stable for 6 hours		

Dunn M et al, Pediatrics 2011

Randomized trial of Initial Respiratory Management of Preterm Infants

	Prophylactic Surfactant N= 209	Intubation Surf + Extubate N= 216	NCPAP N= 223
Surfactant	98.6 %	98.2 %	45.1 %
Mech. Ventilation	100 %	59.3 %	52.3 %
Pneumothorax	4.8 %	3.2 %	5.4 %

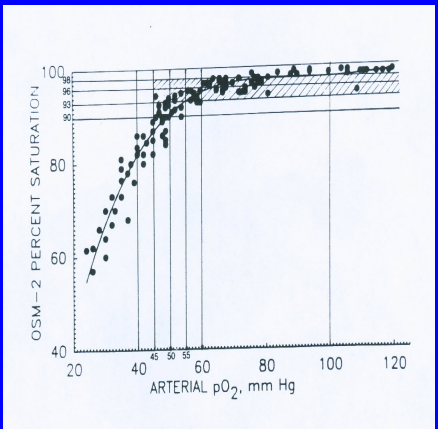


Dunn M et al, Pediatrics 2011

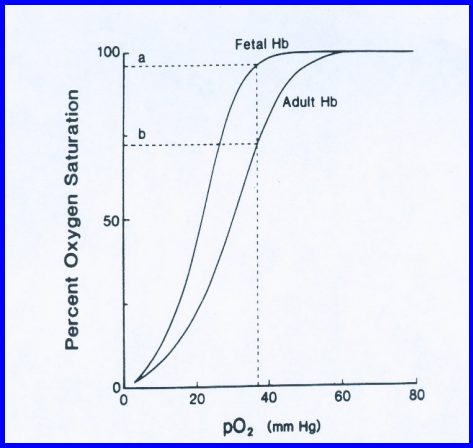
How much oxygen needs to be used for resuscitation?

Hb saturation and PO_2

Co-oximeter sat and PO2



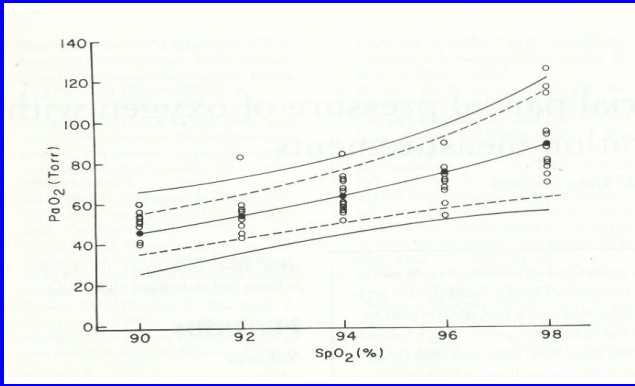
Adult vs Fetal Hb



Pulse Oximetry

Prediction of PO_2 with Pulse Oximetry

- 22 infants 28-40 wks, most on IMV
- PO_2 needed to obtain sats 90-92-94-96-98%
- Range to keep PO_2 50-80 mmHg would be 94-97%



Brockway and Hay, J Ped 133:63, 1998

Pulse Oximetry

Prevention of hyperoxia

SpO_2 *	Number	% PO_2 >100	Range
99	15	80	80-230
98	27	22	65-140
97	76	11	50-200
96	87	8	50-140
95	91	9	50-130
94	73	3	55-105
93	53	0	50-90

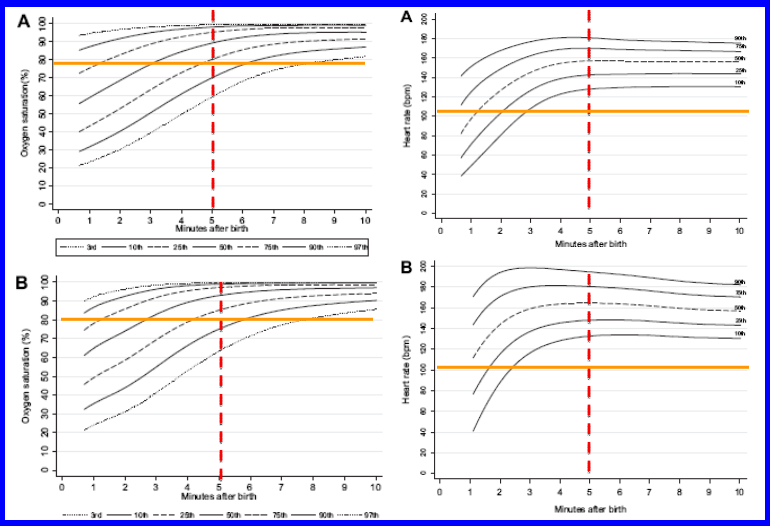
* Fractional saturation

Cochran and Shaw, Eur J Ped 154: 222, 1995

Oxygen Saturation and Heart Rate in Early Neonatal Period

32-36 wk

> 37 wk



Dawson J and Morley C, Sem Fetal Neonatal Med, 2010

Oxygen for Neonatal Resuscitation

Moderately asphyxiated term infants

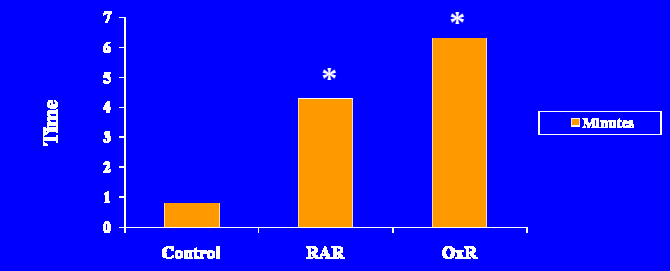
	Controls N= 26	RAR N= 19	OxR N= 21
GA	39.4 ± 2.1	38.6 ± 1.7	40.2 ± 0.8
BW (Kg)	3.25 ± 0.24	3.38 ± 0.31	3.19 ± 0.24
FHR <80	2/26	10/19*	12/21*
Intubation	0/26	0/19	0/26
Apgar 1 min	8 (7-9)	4 (2-6)*	4 (1-6)*
Apgar 5 min	9 (8-9)	8 (7-9)	7 (5-8)*

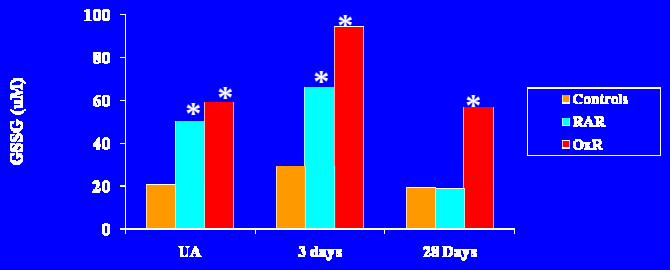
* P< 0.01

Vento M. et al, Pediatrics 107: 642, 2001

Oxygen for Neonatal Resuscitation

Moderately asphyxiated term infants





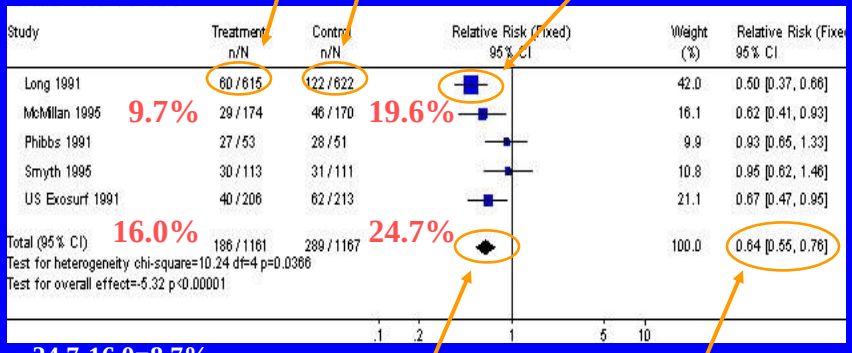
Vento M. et al, Pediatrics 107: 642, 2001

How to interpret results

Effect of Surfactant on Incidence of Pneumothorax

How often did outcome occur in each group

Indication of size of study



24.7-16.0=8.7%

100% / 8.7%=11.5

NNT=11-12

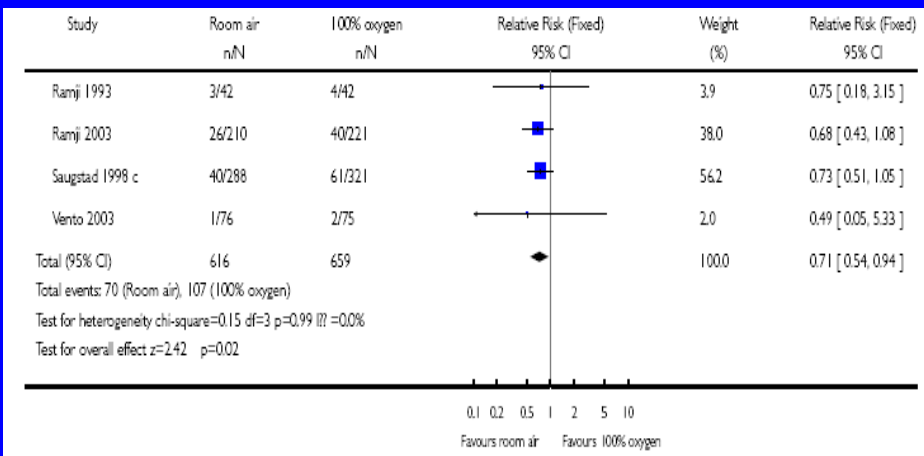
Bottom line

Magnitude of change

Or 1 less pneumothorax for every 11-12 babies treated with surfactant

Systematic review of resuscitation with air or oxygen

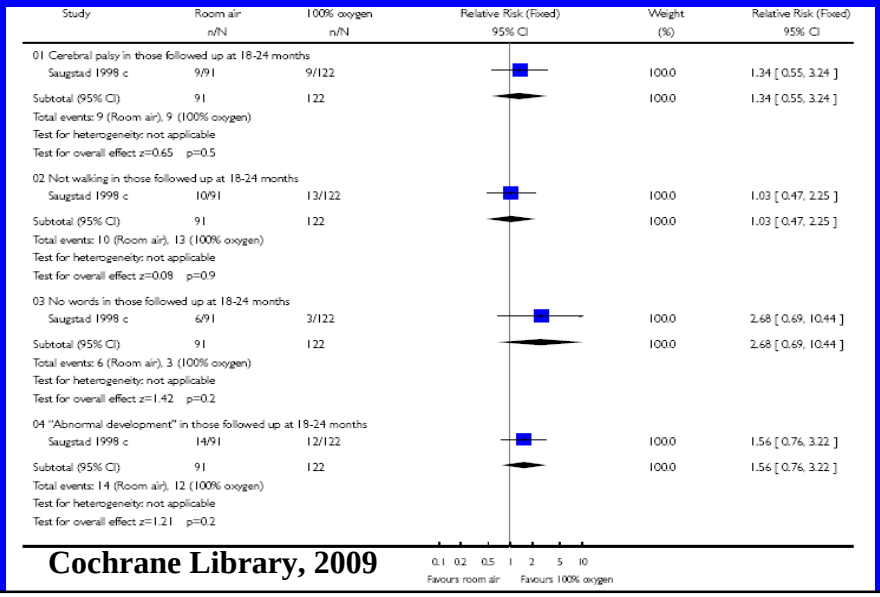
Death at latest follow up



Cochrane Library, 2009

Resuscitation with air or oxygen

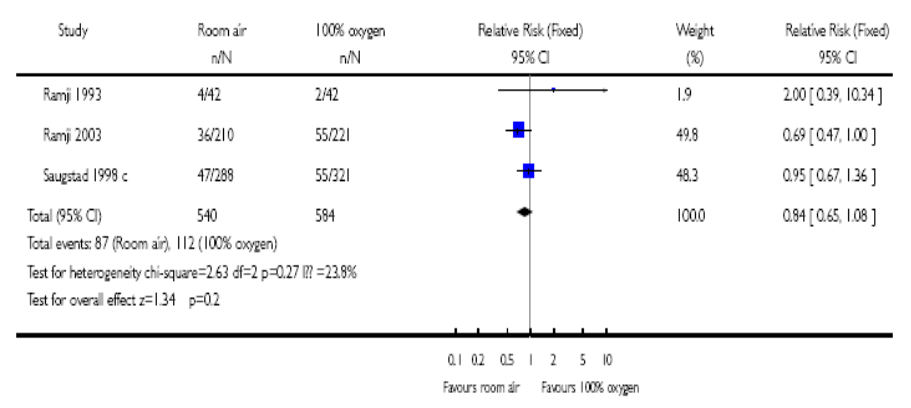
Long term neurodevelopmental outcome



Cochrane Library, 2009

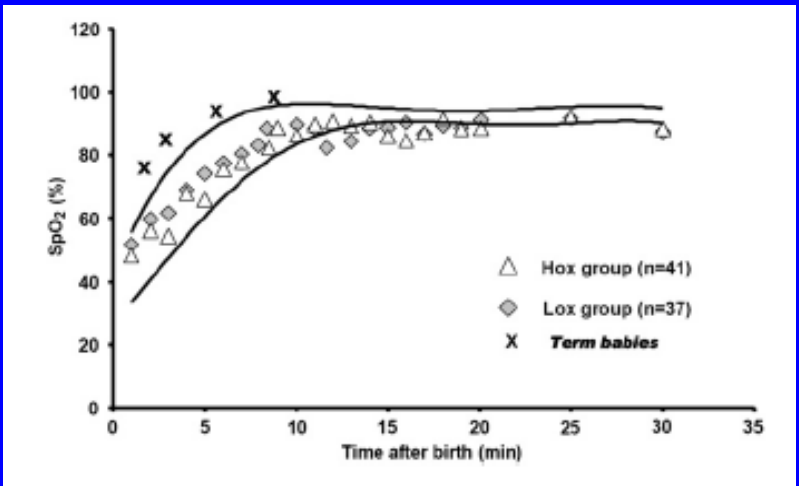
Resuscitation with air or oxygen

HIE stage 2-3



Cochrane Library, 2009

Resuscitation of Preterm Infants with Different Concentrations of Oxygen



Vento M et al, Pediatrics 2009

What Concentration of Oxygen to Use In DR Resuscitation of Preterm Infants?

- Not enough data available yet
- Several randomized studies have shown That it is feasible to start with oxygen < 100%
- It is imperative to be able to blend oxygen and to monitor saturations
- Currently we start at 30% for infants ≤ 30 wk
- Increases based on saturation targets and monitoring

Major Changes in NRP

- Initial assessment includes breathing/crying and tone, NOT color
- Bulb suctioning for obstructed airway or PPV
- Every delivery room should be able to:
  - Have the ability to blend oxygen
  - Provide pulse oximetry
- Begin resuscitation of term infants with air
- The oxygen concentration to be used for preterm infants is not known but often needs to be above 30% initially
- Time for intubation up to 30 seconds
- Intubate before giving chest compressions
- Preferred route for epinephrine is UVC

Outcome of ELBW infants who received CPR in DR

Table II. Short-term and long-term outcomes of infants who received DR-CPR compared with infants who did not receive DR-CPR

	DR-CPR		No DR-CPR			
	n*	%	n*	%	Unadjusted *P* value	Adjusted OR† (95% CI)
Short-term outcomes						
Death <12 hours	1333	16%	7352	4%	<.0001	3.69 (2.98-4.57)
Early-onset sepsis	1118	4%	7025	2%	<.0001	2.10 (1.48-2.99)
Pneumothorax	1119	12%	7027	9%	.0002	1.28 (1.04-1.58)
Pulm hemorrhage	1119	13%	7027	9%	.0009	1.21 (0.98-1.48)
PDA	1116	46%	7028	43%	.15	0.98 (0.85-1.12)
Grade 3 or 4 IVH	986	25%	6139	16%	<.0001	1.47 (1.23-1.74)
PVL by 36 weeks	971	6%	6434	5%	.06	1.13 (0.84-1.51)
Late-onset sepsis	1116	38%	7020	35%	.06	0.95 (0.83-1.09)
NEC stage 2 or 3	1117	10%	7028	10%	.56	0.82 (0.66-1.02)
Postnatal steroids	1119	44%	7023	35%	<.0001	1.20 (1.05-1.38)
BPD (O_2 at 36 weeks)	796	58%	5858	46%	<.0001	1.34 (1.13-1.59)
Hospital death ≤120 days	1333	42%	7352	21%	<.0001	2.22 (1.93-2.57)
Long-term outcomes						
Death by follow-up	1332	44%	7338	24%	<.0001	2.06 (1.79-2.37)
NDI	579	44%	4389	35%	.0001	1.23 (1.02-1.49)
NDI or death‡	1167	72%	6127	54%	<.0001	1.70 (1.46-1.99)
MDI <70	587	36%	4420	29%	.0003	1.20 (0.98-1.45)
PDI <70	574	29%	4375	19%	<.0001	1.59 (1.29-1.96)
Moderate or severe CP	628	10%	4716	6%	.0002	1.64 (1.22-2.20)
Blind in both eyes	624	0.3%	4717	0.8%	.22	§
Hearing aid in both ears	627	3%	4694	1%	.009	1.92 (1.12-3.27)

Wyckoff M et al, J Pediatrics 2012

When Should Resuscitation Efforts Be Stopped?

- The outcome of term babies with very low Apgar scores beyond 10 minutes in spite of resuscitation efforts is very poor
- Most of the benefit of therapeutic hypothermia has been seen in infants with moderate degrees of HIE